European Association of Urology

Pocket Guidelines

2018 edition

Introduction

We are pleased to present the 2018 edition of the European Association of Urology (EAU) Guidelines. The EAU Guidelines are the most comprehensive, continuously updated, guidelines available for urologists and related specialties. Produced by a dedicated Guidelines Office, involving approximately 300 international experts drawn from across Europe and beyond, the EAU Guidelines are internationally recognised as an excellent, high-quality, resource for assisting clinicians in their everyday practice.

Clinical guidelines are a highly influential tool for improving clinical care, unifying healthcare provision and managing healthcare-associated resources across Europe and beyond. Consequently, they must be transparent, free of bias, give a balanced account of risks and benefits and take into consideration patient preferences. To this end, the 2018 guidelines sees the implementation of a new system for grading guidelines recommendations based upon a modified GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach. Consequently, each and every recommendation contained within the guidelines, along with the evidence underpinning it, has been reassessed and a Strength Rating Form produced (posted online at: www.uroweb.org/guidelines). Recommendations now take into account the available evidence, the strength and overall quality of that evidence, the balance between desirable and undesirable consequences of any given recommendation compared with alternative interventions, whilst also taking into account patients' values and preferences. A further change can also be found in the way in which the strength of

each recommendation is represented. Recommendations are no longer denoted by alphabetic characters, but rather by the words 'strong' or 'weak', with each panel providing both 'strong' and 'weak' recommendations 'for' or 'against' a specific intervention. We hope that you find the new format useful and that they provide helpful, clear and unambiguous guidance.

Going forward, a key aim of the EAU Guidelines office is to increase patient involvement in Guidelines development. The ultimate aim of this project being the establishment of an effective framework that can ensure that the voices of patients are captured in the development of future guidelines recommendations. The EAU Guidelines Office believes that structured patient engagement will result in recommendations that lead to better treatment compliance and improved health outcomes. This promises to be a challenging but a worthwhile long-term endeavour.

The annual publication of the EAU Guidelines would not be possible without the steadfast support of every user of the Guidelines globally, our EAU membership, our greatly respected Guidelines Panels, Guidelines Associates, the EAU Executive Committee and Management team and, last but not least, the National Societies. So, on behalf of the EAU Guidelines Office Board, thank you for your support and inspiration.

We hope you find the 2018 update of the EAU Guidelines a pleasure to use!

Prof. James N'Dow
Chairman EAU Guidelines Office

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Level of evidence and grading systems

The EAU Guidelines Office have transitioned to a modified GRADE methodology for the 2018 EAU Pocket Guidelines [1, 2]. Each recommendation within the 2018 Pocket Guidelines is accompanied by an online strength rating form which addresses a number of key elements, namely:

1. the overall quality of the evidence which exists for the recommendation, references used in this text are graded according to a classification system modified from the Oxford Centre for Evidence-Based Medicine Levels of Evidence (see Table 1) [3];
2. the magnitude of the effect (individual or combined effects);
3. the certainty of the results (precision, consistency, heterogeneity and other statistical or study related factors);
4. the balance between desirable and undesirable outcomes;

5. the impact of patient values and preferences on the intervention;
6. the certainty of those patient values and preferences.

These key elements are the basis which panels use to define the strength rating of each recommendation. The strength of each recommendation is represented by the words 'strong' or 'weak' [4]. The strength of each recommendation is determined by the balance between desirable and undesirable consequences of alternative management strategies, the quality of the evidence (including certainty of estimates), and nature and variability of patient values and preferences. The strength rating forms will be available online.

Table 1: Level of evidence*

Level	Type of evidence
1a	Evidence obtained from meta-analysis of randomised trials.
1b	Evidence obtained from at least one randomised trial.
2a	Evidence obtained from one well-designed controlled study without randomization.
2b	Evidence obtained from at least one other type of well-designed quasi-experimental study.
3	Evidence obtained from well-designed non-experimental studies, such as comparative studies, correlation studies and case reports.
4	Evidence obtained from expert committee reports or opinions or clinical experience of respected authorities.

** Modified from [3]*

References

1. Guyatt, G.H., *et al.* GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ, 2008. 336: 924.
2. Guyatt, G.H., *et al.* What is "quality of evidence" and why is it important to clinicians? BMJ, 2008. 336: 995.
3. Phillips, B., *et al.* Oxford Centre for Evidence-based Medicine Levels of Evidence. Updated by Jeremy Howick March 2009.
4. Guyatt, G.H., *et al.* Going from evidence to recommendations. BMJ, 2008. 336: 1049.

EAU GUIDELINES ON NON-MUSCLE-INVASIVE (TaT1, CIS) BLADDER CANCER

(Limited text update March 2018)

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Introduction

The EAU Working Group has published guidelines on Non-muscle-invasive bladder cancer (NMIBC), TaT1 tumours and carcinoma *in situ* (CIS).

Staging and classification systems

The 2017 TNM (Tumour, Node, Metastasis Classification) is used for staging (Table 1). For grading, both the 1973 and 2004 WHO Grading classifications are used (Table 2).

Table 1: TNM Classification 2017

T - Primary Tumour		
TX	Primary tumour cannot be assessed	
T0	No evidence of primary tumour	
Ta	Non-invasive papillary carcinoma	
Tis	Carcinoma *in situ*:'flat tumour'	
T1	Tumour invades subepithelial connective tissue	
T2	Tumour invades muscle	
	T2a	Tumour invades superficial muscle (inner half)
	T2b	Tumour invades deep muscle (outer half)
T3	Tumour invades perivesical tissue	
	T3a	Microscopically
	T3b	Macroscopically (extravesical mass)
T4	Tumour invades any of the following: prostate stroma, seminal vesicles, uterus, vagina, pelvic wall, abdominal wall	
	T4a	Tumour invades prostate stroma, seminal vesicles, uterus or vagina
	T4b	Tumour invades pelvic wall or abdominal wall
N – Regional Lymph Nodes		
NX	Regional lymph nodes cannot be assessed	
N0	No regional lymph node metastasis	
N1	Metastasis in a single lymph node in the true pelvis (hypogastric, obturator, external iliac, or presacral)	
N2	Metastasis in multiple regional lymph nodes in the true pelvis (hypogastric, obturator, external iliac, or presacral)	
N3	Metastasis in common iliac lymph node(s)	

M - Distant Metastasis	
M0	No distant metastasis
M1a	Non-regional lymph nodes
M1b	Other distant metastases

The prognostic value of both WHO 1973 and 2004 grading systems has been confirmed. The WHO 2004 system has not yet been fully incorporated into prognostic models.

Carcinoma *in situ*

Carcinoma *in situ* (CIS) is a flat, high-grade, non-invasive urothelial carcinoma, and classified into the following clinical types:

- Primary: isolated CIS with no previous or concurrent papillary tumours and no previous CIS;
- Secondary: CIS detected during follow-up of patients with a previous tumour that was not CIS;
- Concurrent: CIS in the presence of any other urothelial tumour in the bladder.

Table 2: WHO grading in 1973 and in 2004

1973 WHO grading
Grade 1: well differentiated
Grade 2: moderately differentiated
Grade 3: poorly differentiated
2004 WHO grading system *(Papillary lesions)*
Papillary urothelial neoplasm of low malignant potential (PUNLMP)
Low-grade (LG) papillary urothelial carcinoma
High-grade (HG) papillary urothelial carcinoma

Recommendations for bladder cancer classification (NMIBC)	Strength rating
Use the 2017 TNM system for classification of the depth of tumour invasion (staging).	Strong
Use both the 1973 and 2004/2016 WHO grading systems for histological classification.	Strong
Do not use the term "superficial bladder cancer".	Strong
Mention the tumour stage and grade whenever the terminology NMIBC is used in individual cases.	Strong

Diagnosis

A comprehensive patient history is mandatory. Haematuria is the most common finding. Physical examination does not reveal NMIBC.

Recommendations for the primary assessment of non-muscle-invasive bladder cancer (NMIBC)	Strength rating
Take a patient history, focusing on urinary tract symptoms and haematuria.	Strong
Renal and bladder ultrasound and/or computed tomography-intravenous urography may be used during the initial work-up in patients with haematuria.	Weak
Once a NMIBC has been detected, perform a computed tomography urography in selected cases (e.g., tumours located in the trigone, multiple- or high-risk tumours).	Strong

Perform cystoscopy in patients with symptoms suggestive of bladder cancer or during surveillance. It cannot be replaced by cytology or by any other non-invasive test.	Strong
In men, use a flexible cystoscope, if available.	Strong
Describe all macroscopic features of the tumour (site, size, number and appearance) and mucosal abnormalities during cystoscopy. Use a bladder diagram.	Strong
Use voided urine cytology as an adjunct to cystoscopy to detect high-grade tumour.	Strong
Perform cytology on fresh urine or urine with adequate fixation. Morning urine is not suitable because of the frequent presence of cytolysis.	Strong
Use the Paris system for cytology reporting.	Strong
Repeat urine cytology in patients with initial cytology results suspicious for high-grade urothelial carcinoma.	Weak

Papillary (TaT1) tumours

The diagnosis of papillary bladder cancer ultimately depends on cystoscopic examination of the bladder and histological evaluation of the tissue resected during transurethral resection (TURB). TURB is a crucial procedure in the diagnosis and treatment of TaT1 tumours and should be performed systematically in individual steps (see recommendations below). The strategy of resection depends on the size of the lesion. In selected cases, due to the risk of tumour persistence and understaging after initial TURB, a second resection (2nd TURB) is recommended.

Carcinoma *in situ*

Carcinoma *in situ* is diagnosed by a combination of cystoscopy, urine cytology, and histological evaluation of multiple bladder biopsies. Carcinoma *in situ* cannot be eradicated by TURB and further treatment is mandatory.

Recommendations for transurethral resection of the bladder (TURB), biopsies and pathology report	**Strength rating**
In patients suspected of having bladder cancer, perform a TURB followed by pathology investigation of the obtained specimen(s) as a diagnostic procedure and initial treatment step.	Strong
Perform TURB systematically in individual steps: • bimanual palpation under anaesthesia; • insertion of the resectoscope, under visual control with inspection of the whole urethra; • inspection of the whole urothelial lining of the bladder; • biopsy from the prostatic urethra (if indicated); • cold-cup bladder biopsies (if indicated); • resection of the tumour; • recording of findings in the surgery report/record; • precise description of the specimen for pathology evaluation.	Strong

Performance of individual steps	
Perform *en-bloc* resection or resection in fractions (exophytic part of the tumour, the underlying bladder wall and the edges of the resection area). The presence of detrusor muscle in the specimen is required in all cases except for TaG1/LG tumours.	Strong
Avoid cauterisation as much as possible during TURB to avoid tissue deterioration.	Strong
Take biopsies from abnormal-looking urothelium. Biopsies from normal-looking mucosa (trigone, bladder dome, and right, left, anterior and posterior bladder wall) are recommended when cytology is positive or when high-risk exophytic tumour is expected (non-papillary appearance). If equipment is available, perform fluorescence-guided (PDD) biopsies.	Strong
Take biopsy of the prostatic urethra in cases of bladder neck tumour, when bladder carcinoma *in situ* is present or suspected, when there is positive cytology without evidence of tumour in the bladder, or when abnormalities of the prostatic urethra are visible. If biopsy is not performed during the initial procedure, it should be completed at the time of the second resection.	Strong

Take the biopsy from abnormal areas in the prostatic urethra and from the precollicular area (between the 5 and 7 o' clock position) using a resection loop. In primary non-muscle-invasive tumours when stromal invasion is not suspected, cold-cup biopsy with forceps can be used.	Weak
Use methods to improve tumour visualisation (FC, NBI) during TURB, if available.	Weak
Refer the specimens from different biopsies and resection fractions to the pathologist in separately labelled containers.	Weak
The TURB protocol must describe tumour appearance, all steps of the procedure, as well as the extent and completeness of resection.	Strong
In patients with positive cytology, but negative cystoscopy, exclude an upper tract urothelial carcinoma, CIS in the bladder (random biopsies or PDD-guided biopsies) and tumour in the prostatic urethra (prostatic urethra biopsy).	Strong
Perform a second TURB in the following situations: • after incomplete initial TURB, or in case of doubt about completeness of a TURB); • if there is no muscle in the specimen after initial resection, with the exception of TaLG/G1 tumours and primary CIS; • in T1 tumours.	Strong

If indicated, perform a second TURB within two to six weeks after initial resection. This second TURB should include resection of the primary tumour site.	Weak
Register the pathology results of a second TURB as it reflects the quality of the initial resection.	Weak
Inform the pathologist of prior treatments (intravesical therapy, radiotherapy, etc.).	Strong
Pathological report	
The pathological report should specify tumour location, tumour grade, depth of tumour invasion, presence of CIS, and whether the detrusor muscle is present in the specimen.	Strong
The pathological report should specify the presence of lymphovascular invasion or unusual (variant) histology.	Strong

Predicting disease recurrence and progression

After TURB, patients should be stratified, according to prognostic factors, into risk groups which will facilitate treatment recommendations (see Table 3). For individual prediction of the risk of tumour recurrence and progression at different intervals after TURB, application of EORTC risk tables and calculator (http://www.eortc.be/tools/bladdercalculator/) is strongly recommended.

For bacillus Calmette-Guerin (BCG)-treated patients, scoring models have been created by the CUETO and the EORTC. The CUETO risk calculator is available at: http://www.aeu.es/Cueto.html.

Table 3: Treatment recommendations in TaT1 tumours and carcinoma *in situ* according to risk stratification

Risk category	Definition	Treatment recommendation
Low-risk tumours	Primary, solitary, TaG1 (PUNLMP, LG*), < 3 cm, no CIS.	One immediate instillation of intra-vesical chemotherapy after TURB.
Intermediate-risk tumours	All tumours not defined in the two adjacent categories (between the category of low and high-risk).	In patients with previous low recurrence rate (≤ one recurrence per year) and expected EORTC recurrence score < 5, one immediate instillation of intravesical chemotherapy after TURB. In all patients either one-year full-dose BCG treatment (induction plus three-weekly instillations at three, six and twelve months), or instillations of chemotherapy (the optimal schedule is not known) for a maximum of one year.

High-risk tumours	Any of the following: • T1 tumours; • G3 (HG**) tumour; • CIS; • Multiple, recurrent and large (> 3 cm) TaG1G2/LG tumours (all features must be present)*.	Intravesical full-dose BCG instillations for one to three years or radical cystectomy (in highest-risk tumours - *see below*).
	Subgroup of highest-risk tumours	
	T1G3/HG associated with concurrent bladder CIS, multiple and/or largeT1G3/HG and/or recurrent T1G3/HG, T1G3/HG with CIS in the prostatic urethra, some forms of variant histology of urothelial carcinoma, LVI.	Radical cystectomy (RC) should be considered. In those who refuse or are unfit for RC intravesical full-dose BCG instillations for one to three years.
	BCG-refractory tumours.	Radical cystectomy is recommended.

**Low grade is a mixture of G1 and G2.*
*** High grade is a mixture of some G2 and all G3.*

Recommendations for stratification of non-muscle-invasive bladder cancer	Strength rating
Stratify patients into three risk groups according to Table 3.	Strong
Apply the EORTC risk tables and calculator for the prediction of the risk of tumour recurrence and progression in different intervals after transurethral resection of the bladder, in individual patients.	Strong
Use the CUETO risk tables and the new EORTC risk groups for the prediction of the risk of tumour recurrence and progression in individual patients treated with bacillus Calmette-Guérin.	Strong

Disease management

Adjuvant treatment

Since there is considerable risk for recurrence and/or progression of tumours after TURB, adjuvant intravesical therapy is recommended for all stages (TaT1, and CIS).

- **Immediate single post-operative instillation of chemotherapy** within six hours after TURB can reduce recurrence rate in patients with low-risk and selected intermediate-risk tumours. The difference of efficacy between individual drugs (mitomycin C, epirubicin, or doxorubicin) has not been confirmed.
- **Further chemotherapy** instillations can improve recurrence-free survival in intermediate-risk tumours, but do not prevent progression. These instillations are associated with minor side-effects.
- **Intravesical immunotherapy with BCG** (induction and maintenance) is superior to intravesical chemotherapy in reducing recurrences and in preventing or delaying progression to muscle-invasive bladder cancer. However, intravesical BCG is more toxic.

The individual choice of further intravesical adjuvant therapy depends on the patient's risk (Table 3). In patients at highest risk of progression, radical cystectomy (RC) should be considered. Patients with BCG failure are unlikely to respond to further BCG therapy; RC is therefore the preferred option.

General recommendations for adjuvant therapy in TaT1 tumours and for therapy of CIS	**Strength rating**
Counsel smokers with confirmed non-muscle-invasive bladder cancer to stop smoking.	Strong
The type of further therapy after transurethral resection of the bladder should be based on the risk groups shown in Table 3.	Strong
In patients with tumours presumed to be at low risk and in those presumed to be at intermediate risk with previous low recurrence rate (≤ one recurrence per year) and expected EORTC recurrence score < 5, one immediate chemotherapy instillation is recommended.	Strong

In patients with intermediate-risk tumours (with or without immediate instillation), one-year full-dose bacillus Calmette-Guérin (BCG) treatment (induction plus three-weekly instillations at 3, 6 and 12 months), or instillations of chemotherapy (the optimal schedule is not known) for a maximum of one year is recommended. The final choice should reflect the individual patient's risk of recurrence and progression as well as the efficacy and side effects of each treatment modality.	Strong
In patients with high-risk tumours, full-dose intravesical BCG for one to three years (induction plus three-weekly instillations at 3, 6, 12, 18, 24, 30 and 36 months), is indicated. The additional beneficial effect of the second and third years of maintenance should be weighed against its added costs and inconveniences.	Strong
Offer transurethral resection of the prostate, followed by intravesical instillation of BCG to patients with CIS in the epithelial lining of the prostatic urethra.	Weak
Discuss immediate radical cystectomy (RC) with patients at highest risk of tumour progression.	Strong
Perform a RC in patients with BCG failure.	Strong
In patients with BCG-refractory tumours, who are not candidates for RC due to comorbidities, use preservation strategies (intravesical chemotherapy, chemotherapy and microwave-induced hyperthermia).	Weak

Recommendations – technical aspects for treatment	
Intravesical chemotherapy	
If given, administer a single immediate instillation of chemotherapy within 24 hours after TURB.	Weak
Omit a single immediate instillation of chemotherapy in any case of overt or suspected bladder perforation or bleeding requiring bladder irrigation.	Strong
Give clear instructions to the nursing staff to control the free flow of the bladder catheter at the end of the immediate instillation.	Strong
The optimal schedule and duration of further intravesical chemotherapy instillation is not defined; however, it should not exceed one year.	Weak
If intravesical chemotherapy is given, it is advised to use the drug at its optimal pH and to maintain the concentration of the drug by reducing fluid intake before and during instillation.	Strong
The length of individual instillation should be one to two hours.	Weak
BCG intravesical immunotherapy	
Absolute contraindications of BCG intravesical instillation are: • during the first two weeks after TURB; • in patients with visible haematuria; • after traumatic catheterisation; • in patients with symptomatic urinary tract infection.	Strong

Follow-up

As a result of the risk of recurrence and progression, patients with NMIBC need to be followed-up. However, the frequency and duration of cystoscopy and imaging should reflect the individual patient's degree of risk.

When planning the follow-up schedule and methods, the following aspects should be considered:

- The prompt detection of muscle-invasive and HG/G3 non-muscle-invasive recurrence is crucial because a delay in diagnosis and therapy can be life-threatening.
- Tumour recurrence in the low-risk group is nearly always low stage and LG/G1. Small, TaLG/G1 papillary recurrence does not present an immediate danger to the patient and early detection is not essential for successful therapy. Fulguration of small papillary recurrences on an outpatient basis could be a safe option that reduces the therapeutic burden. Multiple authors have even suggested temporary surveillance in selected cases.
- The first cystoscopy after TURB at three months is a very important prognostic indicator for recurrence and progression. Therefore, the first cystoscopy should always be performed three months after TURB in all patients with TaT1 tumours and CIS.
- In tumours at low risk, the risk of recurrence after five recurrence-free years is low.
- Discontinuation of cystoscopy or its replacement with less invasive methods can be considered.
- In tumours originally intermediate- or high risk, recurrences after ten years tumour-free are not unusual. Therefore, life-long follow-up is recommended.
- The follow-up strategy must reflect the risk of extravesical recurrence (prostatic urethra in men and upper urinary tract in both genders).

- The risk of upper urinary tract recurrence increases in patients with multiple- and high-risk tumours.
- Positive urine test results have a positive impact on the quality of performed follow-up cystoscopy, supporting the adjunctive role of urine tests during follow-up.
- In patients initially diagnosed with TaLG/G1-2 BC, US of the bladder may be a mode of surveillance in case cystoscopy is not possible or refused by the patient.

Recommendations for follow-up in patients after transurethral resection of the bladder	**Strength rating**
Base follow-up of TaT1 tumours and carcinoma *in situ* (CIS) on regular cystoscopy.	Strong
Patients with low-risk Ta tumours should undergo cystoscopy at three months. If negative, subsequent cystoscopy is advised nine months later, and then yearly for five years.	Weak
Patients with high-risk tumours should undergo cystoscopy and urinary cytology at three months. If negative, subsequent cystoscopy and cytology should be repeated every three months for a period of two years, and every six months thereafter until five years, and then yearly.	Weak
Patients with intermediate-risk Ta tumours should have an in-between (individualised) follow-up scheme using cystoscopy.	Weak
Regular (yearly) upper tract imaging (computed tomography-intravenous urography [CT-IVU] or IVU) is recommended for high-risk tumours.	Weak

Endoscopy under anaesthesia and bladder biopsies should be performed when office cystoscopy shows suspicious findings or if urinary cytology is positive.	Strong
Consider random (R)-biopsies or photodynamic diagnosis (PDD)-guided biopsies after intravesical treatment (at three or six months) in patients with CIS.	Weak
During follow-up in patients with positive cytology and no visible tumour in the bladder, R-biopsies or PDD-guided biopsies (if equipment is available) and investigation of extravesical locations (CT urography, prostatic urethra biopsy) are recommended.	Strong
In patients initially diagnosed with TaLG/G1-2 bladder cancer, use ultrasound of the bladder during surveillance in case cystoscopy is not possible or refused by the patient.	Weak

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN: 978-94-92671-01-1), available to all members of the European Association of Urology at their website: http://www.uroweb.org/guidelines/.

EAU GUIDELINES ON UROTHELIAL CARCINOMA OF THE UPPER URINARY TRACT (UTUCs)

(Limited text update March 2018)

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Epidemiology

UTUC are uncommon and account for only 5-10% of urothelial cell carcinomas (UCs). They have a similar morphology to bladder carcinomas and nearly all UTUCs are urothelial in origin.

Staging and grading systems

The UICC 2017 TNM (Tumour, Node, Metastasis Classification) for renal pelvis and ureter is used for staging (Table 1).

Tumour grade

There are currently two main classifications used for UTUC; the 1973 WHO classification, which classifies tumours into three grades, G1, G2 and G3, and the 2004 WHO classification, which classifies tumours into three groups:

- papillary urothelial neoplasia of low malignant potential;
- low-grade carcinomas;
- high-grade carcinomas.

Upper urinary tract tumours with low malignant potential are very rare.

Table 1: TNM Classification 2017

T - Primary tumour		
TX	Primary tumour cannot be assessed	
T0	No evidence of primary tumour	
	Ta	Non-invasive papillary carcinoma
	Tis	Carcinoma *in situ*
T1	Tumour invades subepithelial connective tissue	
T2	Tumour invades muscularis	
T3	(Renal pelvis) Tumour invades beyond muscularis into peripelvic fat or renal parenchyma (Ureter) Tumour invades beyond muscularis into periureteric fat	
T4	Tumour invades adjacent organs or through the kidney into perinephric fat	
N - Regional lymph nodes		
NX	Regional lymph nodes cannot be assessed	
N0	No regional lymph node metastasis	
N1	Metastasis in a single lymph node 2 cm or less in greatest dimension	
N2	Metastasis in a single lymph node more than 2 cm or multiple lymph nodes	
M - Distant metastasis		
M0	No distant metastasis	
M1	Distant metastasis	

Diagnosis

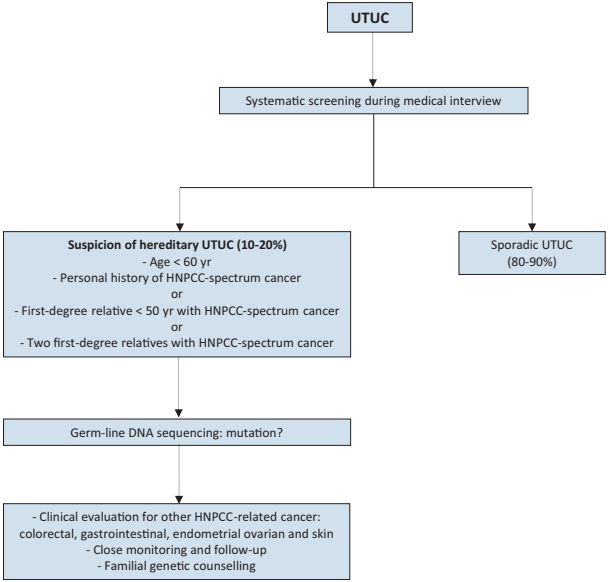
UTUCs are diagnosed using imaging, cystoscopy, urinary cytology and diagnostic ureteroscopy. The benefits of ureteroscopy for pre-operative assessment should also be discussed with the patient.

Recommendations	Strength rating
Perform a cystoscopy to rule out concomitant bladder tumour.	Strong
Perform a computed tomography urography for upper tract evaluation and for staging.	Strong
Use diagnostic ureteroscopy and biopsy only in cases where additional information will impact treatment decisions.	Strong

Prognosis

UTUC invading the muscle wall usually has a very poor prognosis. The main prognostic factors are listed in Figure 1.

Figure 1: UTUCs - Prognostic factors

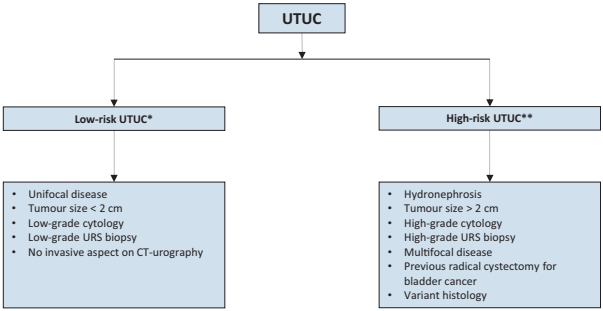


ASA = American Society of Anesthesiologists; BMI = body mass index; ECOG PS = Eastern Cooperative Oncology Group performance status performance score.

Risk stratification

It is necessary to 'risk-stratify' UTUC cases before treatment to identify those patients (and tumours) who are more suitable for kidney-sparing management rather than radical extirpative surgery (Figure 2).

Figure 2: Pre-intervention risk stratification of UTUCs



**All of these factors need to be present.*
*** Any of these factors need to be present.*
CTU = computed tomography urography;
URS = ureterorenoscopy.

Disease management (see also Figures 3 & 4)

Localised disease

Kidney-sparing surgery

Kidney-sparing surgery for low-risk UTUC consists of surgery preserving the upper urinary renal unit. It is used in imperative cases (renal insufficiency, solitary functional kidney). Kidney-sparing surgery can also be considered in select patients with serious renal insufficiency or solitary kidney.

Kidney-sparing surgery in low-risk UTUCs potentially allows avoiding the morbidity associated with open radical surgery without compromising oncological outcomes and kidney function.

Recommendations	Strength rating
Offer kidney-sparing management as primary treatment option to patients with low-risk tumours.	Strong
Offer a kidney-sparing management to patients with high-risk distal ureteral tumours.	Weak
Offer kidney-sparing management to patients with solitary kidney and/or impaired renal function, providing that it will not compromise survival. This decision will have to be made on a case-by-case basis with the patient.	Strong
Use a laser for endoscopic treatment of upper tract urothelial carcinoma.	Weak

The instillation of bacillus Calmette-Guérin or mitomycin C in the urinary tract by percutaneous nephrostomy or via a ureteric stent is technically feasible after kidney-sparing management or for treatment of carcinoma *in situ*. However, the benefits have not been confirmed.

Radical nephroureterectomy

Open RNU with bladder cuff excision is the standard treatment for high-risk UTUC, regardless of tumour location.

Recommendations	Strength rating
Perform radical nephroureterectomy in patients with high-risk tumours.	Strong
Technical steps of radical nephroureterectomy:	
Remove the bladder cuff.	Strong
Perform a lymphadenectomy in patients with high-risk tumours.	Weak
Offer a post-operative bladder instillation of chemotherapy to lower the intravesical recurrence rate.	Strong

Advanced disease

Radical nephroureterectomy (RNU) has no benefit in metastatic (M+) disease, but may be used in palliative care. As UTUC are urothelial tumours, platinum-based chemotherapy should give similar results to those in bladder cancer. Currently, insufficient data are available to provide any recommendations.

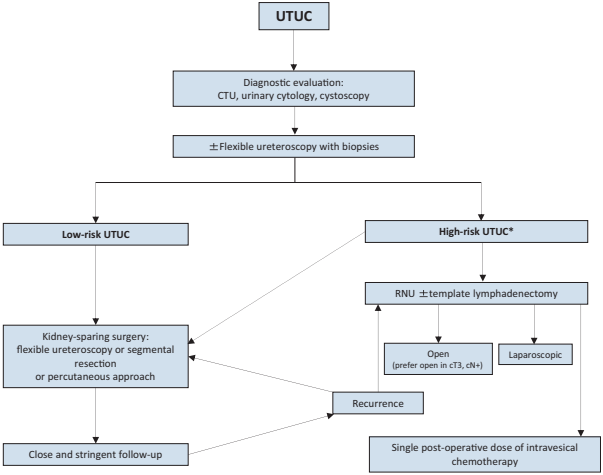
Radiotherapy is no longer relevant nowadays, not as a sole treatment option, nor as an adjunct to chemotherapy.

Follow-up after initial treatment

In all cases, there should be strict follow-up after radical management to detect metachronous bladder tumours, as well as invasive tumours, local recurrence and distant metastases. When kidney-sparing surgery is performed, the ipsilateral upper urinary tract requires careful follow-up due to the high risk of recurrence.

Recommendations	Strength rating
After radical nephroureterectomy:	
Low-risk tumours	
Perform cystoscopy at three months. If negative, perform subsequent cystoscopy nine months later and then yearly, for five years.	Weak
Perform computed tomography urography every year, for five years.	Weak
High-risk tumours	
Perform cystoscopy and urinary cytology at three months. If negative, repeat subsequent cystoscopy and cytology every three months for a period of two years, and every six months thereafter until five years, and then yearly.	Weak
Perform computed tomography urography every six months for two years, and then yearly.	Weak
After kidney-sparing management:	
Low-risk tumours	
Perform cystoscopy and computed tomography urography at three and six months, and then yearly for five years.	Weak
Perform ureteroscopy at three months.	Weak
High-risk tumours	
Perform cystoscopy, urinary cytology and computed tomography urography at three and six months, and then yearly.	Weak
Perform ureteroscopy and urinary cytology *in situ* at three and six months.	Weak

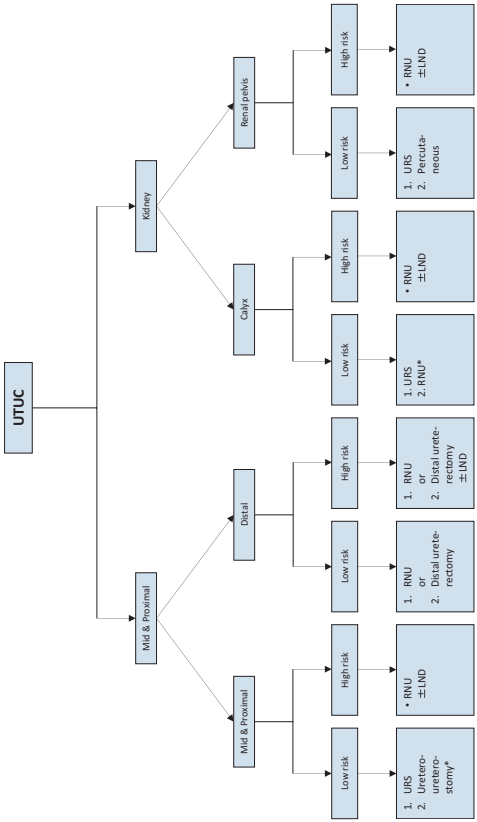
Figure 3: Proposed flowchart for the management of UTUC



**In patients with a solitary kidney, consider a more conservative approach.*
CTU = computed tomography urography;
RNU = nephroureterectomy.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN: 978-94-92671-01-1), available to all members of the European Association of Urology at their website: http://www.uroweb.org/guidelines/.

Figure 4: Surgical treatment according to location and risk status



1. First treatment option
2. Secondary treatment option

**In case not amendable to endoscopic management.*

EAU GUIDELINES ON MUSCLE-INVASIVE AND METASTATIC BLADDER CANCER

(Limited text update March 2018)

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Introduction

Optimal treatment strategies for Muscle-invasive Bladder Cancer (MIBC) require the involvement of a specialist multidisciplinary team and a model of integrated treatment strategies to avoid fragmentation of patient care.

Staging and grading systems

The 2017 TNM (Tumour, Node, Metastasis Classification) is used for staging (Table 1). For grading, the 1973 and 2016 WHO grading classifications are used (Table 2).

Table 1: TNM Classification 2017

T - Primary Tumour		
TX	Primary tumour cannot be assessed	
T0	No evidence of primary tumour	
Ta	Non-invasive papillary carcinoma	
Tis	Carcinoma *in situ*:'flat tumour'	
T1	Tumour invades subepithelial connective tissue	
T2	Tumour invades muscle	
	T2a	Tumour invades superficial muscle (inner half)
	T2b	Tumour invades deep muscle (outer half)
T3	Tumour invades perivesical tissue	
	T3a	Microscopically
	T3b	Macroscopically (extravesical mass)
T4	Tumour invades any of the following: prostate stroma, seminal vesicles, uterus, vagina, pelvic wall, abdominal wall	
	T4a	Tumour invades prostate stroma, seminal vesicles, uterus or vagina
	T4b	Tumour invades pelvic wall or abdominal wall
N – Regional Lymph Nodes		
NX	Regional lymph nodes cannot be assessed	
N0	No regional lymph node metastasis	
N1	Metastasis in a single lymph node in the true pelvis (hypogastric, obturator, external iliac, or presacral)	
N2	Metastasis in multiple regional lymph nodes in the true pelvis (hypogastric, obturator, external iliac, or presacral)	
N3	Metastasis in a common iliac lymph node(s)	

M - Distant Metastasis		
M0	No distant metastasis	
	M1a	Non-regional lymph nodes
	M1b	Other distant metastasis

Table 2: WHO grading in 1973 and 2016
1973 WHO grading Grade 1: well differentiated Grade 2: moderately differentiated Grade 3: poorly differentiated **2016 WHO grading system** *(Papillary lesions)* Papillary urothelial neoplasm of low malignant potential (PUNLMP) Low-grade (LG) papillary urothelial carcinoma (UC) High-grade (HG) papillary UC

Pathology of MIBC

Determination of morphological subtypes can be helpful in assessing the prognosis and treatment options of high-grade UCs (grade II or grade III) as discussed in these guidelines. The following differentiation is used:

1. urothelial carcinoma (more than 90% of all cases);
2. urothelial carcinomas with partial squamous and/or glandular differentiation;
3. micropapillary and microcystic UC;
4. nested variant (including large nested variety);
5. lymphoepithelioma;
6. plasmocytoid, giant cell, signet ring, diffuse, undifferentiated;
7. some UCs with trophoblastic differentiation;
8. small-cell carcinomas;
9. sarcomatoid carcinomas.

Recommendations for the assessment of tumour specimens	Strength rating
Record the depth of invasion (categories pT2a and pT2b, pT3a and pT3b or pT4).	Strong
Record margins with special attention paid to the radial margin, prostate, ureter, urethra and peritoneal fat and uterus and vaginal top.	
Record the number of lymph nodes (LNs), the number of positive LNs and extranodal spread.	
Record lymphatic or blood vessel invasion and extranodal extension.	
Record the presence of carcinoma *in situ*.	

Recommendations for the primary assessment of presumably invasive bladder tumours*	Strength rating
Describe all macroscopic features of the tumour (site, size, number and appearance) and mucosal abnormalities during cystoscopy. Use a bladder diagram.	Strong
Take a biopsy of the prostatic urethra in cases of bladder neck tumour, when bladder carcinoma *in situ* is present or suspected, when there is positive cytology without evidence of tumour in the bladder, or when abnormalities of the prostatic urethra are visible.	Strong
Take a biopsy at the time of the second resection, if no biopsy was taken during the initial procedure.	Strong

In women undergoing subsequent orthotopic neobladder construction, obtain procedural information (including histological evaluation) of the bladder neck and urethral margin, either prior to, or at the time of cystoscopy.	Strong
Specify the grade, depth of tumour invasion, and whether the lamina propria and muscle tissue are present in the specimen in the pathological report.	Strong

** For general information on the assessment of bladder tumours, see the EAU Guidelines on Non-muscle-invasive Bladder Cancer.*

Recommendations for staging of muscle-invasive bladder cancer (MIBC)	**Strength rating**
In patients with confirmed MIBC, use computed tomography (CT) of the chest, abdomen and pelvis as the optimal form of staging.	Strong
Perform a CT urography for upper tract evaluation and for staging.	Strong
For upper tract evaluation, use diagnostic ureteroscopy and biopsy only in cases where additional information will impact treatment decisions.	Strong
Use magnetic resonance urography when CT urography is contraindicated for reasons related to contrast administration or radiation dose.	Strong
Use CT or magnetic resonance imaging (MRI) for staging locally advanced or metastatic disease in patients in whom radical treatment is considered.	Strong

Use CT to diagnose pulmonary metastases. Computed tomography and MRI are generally equivalent for diagnosing local disease and distant metastases in the abdomen.	Strong

Prognosis

Recommendations for the use of comorbidity scales	Strength rating
Base the decision on bladder-sparing treatment or radical cystectomy in elderly/ geriatric patients with invasive bladder cancer on tumour stage and comorbidity.	Strong
Assess comorbidity by a validated score, such as the Charlson Comorbidity Index. The American Society of Anesthesiologists score should not be used in this setting.	Strong

Disease Management

Recommendations for treatment failure of non-muscle-invasive bladder cancer	Strength rating
Discuss immediate radical treatment in all T1 tumours at high risk of progression (i.e., high grade, multifocality, carcinoma *in situ*, and tumour size, as outlined in the EAU Guidelines for Non-muscle-invasive Bladder Cancer).	Strong
Offer radical treatment to all T1 patients failing intravesical therapy.	Strong

Neoadjuvant chemotherapy

Neoadjuvant cisplatin-containing combination chemotherapy (NAC) improves overall survival (5-8% at five years), irrespective of the type of definitive treatment used. Currently, no tools are available to select patients who have a higher probability of benefitting from NAC. However, NAC has its limitations regarding patient selection, current development of surgical techniques, and current chemotherapy combinations.

Recommendations for neoadjuvant chemotherapy	Strength rating
Offer NAC for T2-T4a, cN0M0 bladder cancer. In this case, always use cisplatin-based combination therapy.	Strong
Do not offer NAC to patients who are ineligible for cisplatin-based combination chemotherapy.	Strong

Recommendations for pre- and post-operative radiotherapy in MIBC	Strength rating
Do not offer pre-operative radiotherapy (RT) to improve survival.	Strong
Offer pre-operative RT for operable MIBC since it can result in tumour downstaging after four to six weeks.	Weak

Radical cystectomy and urinary diversion

Contraindications for orthotopic bladder substitution are positive margins at the level of urethral dissection, positive margins anywhere on the bladder specimen (in both sexes), if the primary tumour is located at the bladder neck or in the

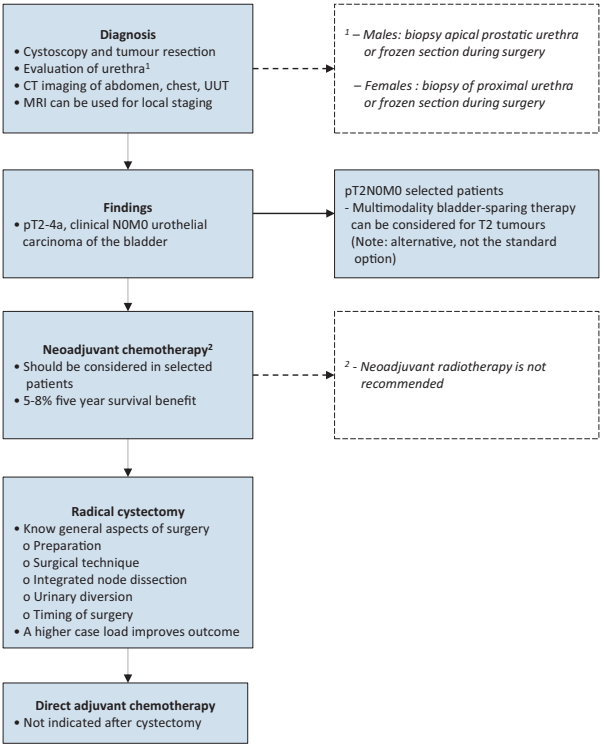
urethra (in women), or if tumour extensively infiltrates the prostate (in men).

Recommendations for radical cystectomy and urinary diversion	Strength rating
Do not delay cystectomy for > 3 months as it increases the risk of progression and cancer-specific mortality.	Strong
Before cystectomy, fully inform the patient about the benefits and potential risks of all possible alternatives. The final decision should be based on a balanced discussion between the patient and the surgeon.	Strong
Do not offer an orthotopic bladder substitute diversion to patients who have a tumour in the urethra or at the level of urethral dissection.	Strong
Do not offer pre-operative radiotherapy when subsequent cystectomy with urinary diversion is planned.	Strong
Do not offer sexual-preserving cystectomy as standard therapy for MIBC.	Strong
Offer sexual-preserving techniques to men motivated to preserve their sexual function since the majority will benefit.	Strong
Select patients based on: • organ-confined disease; • absence of any kind of tumour at the level of the prostate, prostatic urethra or bladder neck.	Strong
Do not offer pelvic organ-preserving radical cystectomy (RC) to female patients as standard therapy for MIBC.	Strong

Offer sexual-preserving techniques to female patients motivated to preserve their sexual function since the majority will benefit.	Weak
Select patients based on: • organ-confined disease; • absence of tumour in bladder neck or urethra.	Strong
Pre-operative bowel preparation is not mandatory. "Fast track" measurements may reduce the time of bowel recovery.	Strong
Offer RC in T2-T4a, N0M0, and high-risk non-MIBC.	Strong
Perform a lymph node dissection as an integral part of cystectomy.	Strong
Do not preserve the urethra if margins are positive.	Strong

Recommendations for laparoscopic/ robotic-assisted laparoscopic cystectomy	**Strength rating**
Inform the patient of the advantages and disadvantages of open radical cystectomy and robot-assisted radical cystectomy (RARC) to allow selection of the proper procedure.	Strong
Select experienced centres, not specific techniques, both for RARC and ORC.	Strong

Figure 1: Flow chart for the management of T2-T4a N0M0 urothelial bladder cancer



CT = computed tomography; MRI = magnetic resonance imaging; UUT = upper urinary tract.

Bladder-sparing treatments for localised disease

Transurethral resection of bladder tumour

Transurethral resection of bladder tumour alone is only possible as a therapeutic option if tumour growth is limited to the superficial muscle layer and if restaging biopsies are negative for residual tumour.

External beam radiotherapy

External beam radiotherapy alone should only be considered as a therapeutic option when the patient is unfit for cystectomy or a multimodality bladder-preserving approach. Radiotherapy can also be used to stop bleeding from the tumour when local control cannot be achieved by transurethral manipulation due to extensive local tumour growth.

Chemotherapy and best supportive care

Complete and partial local responses have been reported with cisplatin-based chemotherapy as primary therapy for locally advanced tumours in highly selected patients.

Multimodality treatment

In a highly selected patient population, long-term survival rates of multimodality treatment are comparable to those of early cystectomy. Delaying surgery can compromise survival rates.

Recommendations for bladder-sparing treatments for localised disease	Strength rating
Do not offer transurethral resection of bladder tumour alone as a curative treatment option as most patients will not benefit.	Strong
Do not offer radiotherapy alone as primary therapy for localised bladder cancer.	Strong

Do not offer chemotherapy alone as primary therapy for localised bladder cancer.	Strong
Offer surgical intervention or multimodality treatments (MMT) as primary curative therapeutic approaches since they are more effective than radiotherapy alone.	Strong
Offer MMT as an alternative in selected, well-informed and compliant patients, especially for whom cystectomy is not an option.	Strong

Surgically non-curable tumours

Palliative radical cystectomy for metastatic disease

Primary radical cystectomy (RC) in T4b bladder cancer is not a curative option. If there are symptoms, RC may be a therapeutic/palliative option. Intestinal or non-intestinal forms of urinary diversion can be used, with or without palliative cystectomy.

Recommendations	Strength rating
Offer radical cystectomy as a palliative treatment to patients with inoperable locally advanced tumours (T4b).	Weak
Offer palliative cystectomy in patients with symptoms.	Weak

Adjuvant Chemotherapy

Recommendations	Strength rating
Offer adjuvant cisplatin-based combination chemotherapy to patients with pT3/4 and/or pN+ disease if no neoadjuvant chemotherapy has been given.	Strong

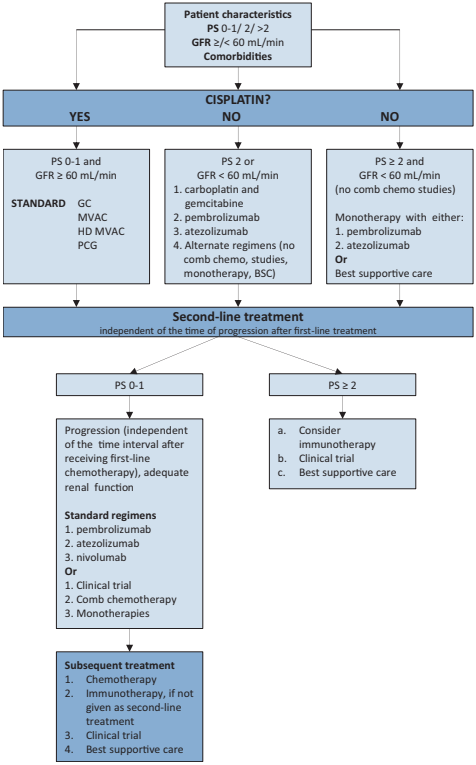
Metastatic disease

Recommendations	Strength rating
First-line treatment for fit patients	
Use cisplatin-containing combination chemotherapy with GC, MVAC, preferably with G-CSF, HD-MVAC with G-CSF or PCG.	Strong
Do not use carboplatin and non-platinum combination chemotherapy.	Strong
First-line treatment in patients ineligible (unfit) for cisplatin:	
Use checkpoint inhibitors pembrolizumab or atezolizumab.	Strong
Use carboplatin combination chemotherapy.	Weak
Second-line treatment	
Offer checkpoint inhibitors pembrolizumab or atezolizumab to patients progressing during or after platinum-based combination chemotherapy for metastatic disease. Alternatively, offer treatment within a clinical trial setting.	Strong
Offer checkpoint inhibitor nivolumab to patients progressing during or after platinum-based combination chemotherapy for metastatic disease. Alternatively, offer treatment within a clinical trial setting.	Strong
Offer zoledronic acid or denosumab to treat bone metastases.	Weak

Subsequent treatment	
Only offer vinflunine to patients for metastatic disease as second-line treatment if immunotherapy or combination chemotherapy is not feasible. Alternatively, offer vinflunine as subsequent treatment line, or offer treatment within a clinical trial setting or best supportive care.	Weak

GC = gemcitabine plus cisplatin; G-CSF = granulocyte colony-stimulating factor; HD-MVAC = high-dose methotrexate, vinblastine, adriamycin plus cisplatin; PCG = paclitaxel, cisplatin, gemcitabine.

Figure 2: Flow chart for the management of metastatic urothelial cancer



BSC = best supportive care; GC = gemcitabine plus cisplatin; GFR = glomerular filtration rate; HD MVAC = high-dose methotrexate, vinblastine, adriamycin plus cisplatin; MVAC = methotrexate, vinblastine,adriamycin plus cisplatin; PCG = paclitaxel, cisplatin, gemcitabine; PS = performance status.

Health-related quality-of-life (HRQoL)

Important determinants of (subjective) quality of life are a patient's personality, coping style and social support.

Recommendations	Strength rating
Use validated questionnaires to assess HRQoL in patients with MIBC.	Strong
Offer a continent urinary diversion unless a patient's comorbidities, tumour variables and coping abilities present clear contraindications.	Strong
Pre-operative patient information, patient selection, surgical techniques, and careful post-operative follow-up are the cornerstones for achieving good long-term results.	Strong
Provide clear and exhaustive information on all potential benefits and side-effects, allowing patients to make informed decisions. Encourage patients to actively participate in the decision-making process.	Strong

This short booklet text is based on the more comprehensive EAU Guidelines (978-94-92671-01-1), available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines/.

EAU-ESTRO-ESUR-SIOG GUIDELINES ON PROSTATE CANCER

(Text update March 2018)

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Introduction

Prostate cancer (PCa) is a complex disease, in which disease characteristics, age, comorbidities and individual patient preference will impact treatment choice. All available management options need to be discussed, in full, with the patient.

Epidemiology and Risk Prevention

Prostate cancer is the second most common cancer in males. It is a major health concern, especially in developed countries due to the greater proportion of elderly men in the general population, and the potential risk of over-treatment following early diagnosis. There are three well-established risk factors for PCa: increasing age, ethnic origin, and genetic predisposition. There is currently no high-level evidence that preventative measures may reduce the risk of PCa.

Classification and Staging Systems

The 2017 Tumour Node Metastasis (TNM) classification is used for staging (Table 1).

Table 1: 2017 TNM classification

T - Primary Tumour		
TX	Primary tumour cannot be assessed	
T0	No evidence of primary tumour	
T1	Clinically inapparent tumour that is not palpable	
	T1a	Tumour incidental histological finding in 5% or less of tissue resected
	T1b	Tumour incidental histological finding in more than 5% of tissue resected
	T1c	Tumour identified by needle biopsy (e.g. because of elevated prostate-specific antigen [PSA])
T2	Tumour that is palpable and confined within the prostate	
	T2a	Tumour involves one half of one lobe or less
	T2b	Tumour involves more than half of one lobe, but not both lobes
	T2c	Tumour involves both lobes
T3	Tumour extends through the prostatic capsule*	
	T3a	Extracapsular extension (unilateral or bilateral) including microscopic bladder neck involvement
	T3b	Tumour invades seminal vesicle(s)
T4	Tumour is fixed or invades adjacent structures other than seminal vesicles: external sphincter, rectum, levator muscles, and/or pelvic wall	
N - Regional Lymph Nodes[1]		
NX	Regional lymph nodes cannot be assessed	
N0	No regional lymph node metastasis	
N1	Regional lymph node metastasis	

M - Distant Metastasis[2]		
M0	No distant metastasis	
M1	Distant metastasis	
	M1a	Non-regional lymph node(s)
	M1b	Bone(s)
	M1c	Other site(s)

** Invasion into the prostatic apex or into (but not beyond) the prostatic capsule is not classified as T3, but as T2.*

[1] Metastasis no larger than 0.2 cm can be designated pNmi.

[2] When more than one site of metastasis is present, the most advanced category is used. (p)M1c is the most advanced category.

Pathological staging (pTNM) is based on histopathological tissue assessment and largely parallels the clinical TNM, except for clinical stage T1c and the T2 substages. All histopathologically confirmed organ-confined PCas after radical prostatectomy (RP) are pathological stage T2 and the current UICC no longer recognises pT2 substages.

Table 2: EAU risk groups for biochemical recurrence of localised and locally advanced prostate cancer

Definition			
Low-risk	**Intermediate-risk**	**High-risk**	
PSA < 10 ng/mL and GS < 7 (ISUP grade 1) and cT1-2a	PSA 10-20 ng/mL or GS 7 (ISUP grade 2/3) or cT2b	PSA > 20 ng/mL or GS > 7 (ISUP grade 4/5) or cT2c	any PSA any GS cT3-4 or cN+
Localised			**Locally advanced**

GS = Gleason score; ISUP = International Society for Urological Pathology; PSA = prostate-specific antigen.

Recommendations for screening and early detection	Strength rating
Do not subject men to prostate-specific antigen (PSA) testing without counselling them on the potential risks and benefits.	Strong
Offer an individualised risk-adapted strategy for early detection to a well-informed man with a good performance status (PS) and a life-expectancy of at least ten to fifteen years.	Strong
Offer early PSA testing in well-informed men at elevated risk of having PCa: • men > 50 years of age; • men > 45 years of age and a family history of PCa; • African-Americans > 45 years of age.	Strong
Offer a risk-adapted strategy (based on initial PSA level), with follow-up intervals of two years for those initially at risk: • men with a PSA level of > 1 ng/mL at 40 years of age; • men with a PSA level of > 2 ng/mL at 60 years of age. Postpone follow-up to eight years in those not at risk.	Weak
Stop early diagnosis of PCa based on life expectancy and PS; men who have a life-expectancy of < 15 years are unlikely to benefit.	Strong

Diagnostic Evaluation

Clinical diagnosis

Prostate cancer is usually suspected on the basis of digital rectal examination (DRE) and/or PSA levels. Definitive diagnosis depends on histopathological verification of adenocarcinoma in prostate biopsy cores or unexpected discovery in specimens from transurethral resection of the prostate (TURP) or prostatectomy for benign prostatic enlargement.

The decision whether to proceed with further diagnostic or staging work-up is guided by which treatment options are available to the patient, taking the patient's life expectancy into consideration. Diagnostic procedures that will not affect the treatment decision can usually be avoided.

A biopsy pathology report includes the type of carcinoma and parameters describing its extent (e.g. proportion of positive cores, percentage or mm of carcinoma involvement per core) as well as Gleason score (GS) per biopsy site and global GS. Reporting of a radical prostatectomy (RP) specimen includes type of carcinoma, global GS, pathological stage and surgical margin status.

The International Society of Urological Pathology (ISUP) World Health Organization (WHO) 2014 grade groups were adopted which allow patients to better understand the behaviour of their diagnosed prostate carcinoma, while separating GS 7 adenocarcinoma into two prognostically very distinct categories; grade group 2 for GS 7(3+4) and grade group 3 for GS 7(4+3) (see Table 3).

Table 3: ISUP 2014 grade groups

Gleason score	Grade group
2-6	1
7 (3+4)	2
7 (4+3)	3
8 (4+4 or 3+5 or 5+3)	4
9-10	5

Recommendations for clinical diagnosis of PCa	Strength rating
Do not use transurethral resection of the prostate as a tool for cancer detection.	Strong
Use the International Society of Urological Pathology (ISUP) 2014 Gleason grading system for grading of PCa.	Strong
In symptomatic men, base the initial decision to perform a biopsy on prostate-specific antigen testing and digital rectal examination.	Strong
Do not initially offer transition zone biopsies due to low detection rates.	Weak
For initial diagnosis, perform a core biopsy of ten to twelve systematic transrectal or transperineal peripheral zone biopsies under ultrasound guidance.	Strong
Perform transrectal prostate needle biopsies under antibiotic protection.	Strong
Use a local anaesthetic by periprostatic infiltration for transrectal prostate needle biopsies.	Strong

Ensure that prostate core biopsies from different sites are submitted separately for processing and pathology reporting.	Strong
Adhere to the 2010 ISUP Consensus Meeting Guidelines for processing and reporting of prostatectomy specimens.	Strong

Recommendations for processing prostatectomy specimens	**Strength rating**
Ensure total embedding, by conventional (quadrant) or whole-mount sectioning.	Strong
Ink the entire surface before cutting, to evaluate the surgical margin.	Strong
Examine the apex and base separately, using the cone method with sagittal or radial sectioning.	Strong

Recommendations for repeat-biopsy imaging	**Strength rating**
Before repeat biopsy, perform multiparametric magnetic resonance imaging (mpMRI) when clinical suspicion of PCa persists in spite of negative biopsies.	Strong
During repeat biopsy include systematic biopsies and targeting of any mpMRI lesions seen.	Strong

Guidelines for staging

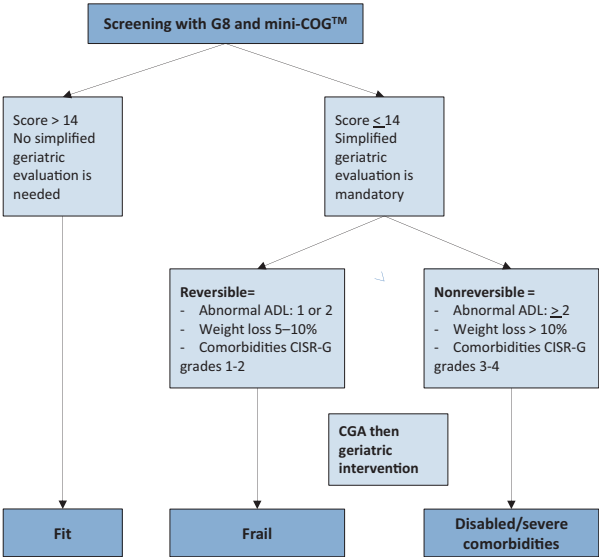
Any risk group staging	**Strength rating**
Do not use computed tomography and transrectal ultrasound for local staging.	Strong

Low-risk localised PCa	Strength rating
Do not use additional imaging for staging purposes.	Strong

Intermediate-risk PCa	Strength rating
In predominantly Gleason pattern 4 (≥ ISUP 3) use prostate multiparametric magnetic resonance imaging (mpMRI) for local staging.	Weak
In predominantly Gleason pattern 4, include at least a cross-sectional abdominopelvic imaging and bone-scan for metastatic screening.	Weak

High-risk localised PCa/locally advanced PCa	Strength rating
Use prostate mpMRI for local staging.	Strong
Perform metastatic screening including at least cross-sectional abdominopelvic imaging and a bone-scan.	Strong

Figure 1: Decision-making based on health status assessment (men > 70 years)*



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Mini-COG™ = cognitive test; ADL = activities of daily living; CIRS-G = cumulative illness rating score-geriatrics; CGA = comprehensive geriatric assessment.

Recommendations for evaluating health status and life expectancy	Strength rating
Systematically screen the health status of older (> 70 years) men with PCa (Figure 1).	Strong
Use the Geriatric-8 and mini-COG tools for health status screening.	Weak
Perform a full specialist geriatric evaluation in patients with G8 score ≤ 14.	Strong
Consider standard treatment in frail patients with reversible impairments (after resolution of geriatric problems) similar to fit patients, if life expectancy is > 10 years.	Weak
Offer adapted treatment in patients with irreversible impairment.	
Offer palliation in patients with poor health status.	

Disease Management

Deferred treatment

Many men with localised PCa will not benefit from definitive treatment, and 45% of men with PSA-detected PCa may be candidates for deferred management.

In men with comorbidity and a limited life expectancy, treatment of localised PCa may be deferred to avoid loss of quality of life (QoL).

Primary treatment of PCa

General recommendations for active treatment	Strength rating
Inform patients that no active treatment modality has shown superiority over any other management options in terms of survival.	Strong

Inform patients that all active treatments have side effects.	Strong
Surgical treatment	
Inform patients that no surgical approach (open, laparoscopic- or robotic radical prostatectomy) has clearly shown superiority in terms of functional or oncological results.	Strong
Perform an extended pelvic LND (ePLND), when a LND is deemed necessary.	Strong
Do not perform nerve-sparing surgery when there is a risk of extracapsular extension (based on cT stage, GS, nomogram, multiparametric magnetic resonance imaging).	Strong
Do not offer neoadjuvant androgen deprivation therapy before surgery.	Strong
Radiotherapeutic treatment	
Offer intensity-modulated radiation therapy (IMRT) or volumetric arc external-beam radiotherapy (VMAT) for definitive treatment of PCa by external-beam radiation therapy (EBRT).	Strong
Only offer moderate hypofractionation (HFX) with IMRT/VMAT, including image-guided radiation therapy (IGRT) to the prostate, to carefully selected patients with localised disease.	Strong
Ensure that moderate HFX adheres to radiotherapy (RT) protocols from trials with equivalent outcome and toxicity, i.e. 60 Gy/20 fractions in four weeks or 70 Gy/28 fractions in six weeks.	Strong

Active therapeutic options outside surgery and radiotherapy	
Only offer cryotherapy and high-intensity focused ultrasound within a clinical trial setting.	Strong
Only offer focal therapy within a clinical trial setting.	Strong

Guidelines for first line treatment of various disease stages		Strength rating
Low-risk disease		
Watchful waiting (WW)	Offer a WW policy to asymptomatic patients with a life expectancy < 10 years (based on comorbidities).	Strong
Active surveillance (AS)	Offer AS to patients suitable for curative treatment but with low-risk PCa.	Strong
	Perform multiparametric magnetic resonance imaging (mpMRI) before a confirmatory biopsy.	Strong
	During confirmatory biopsy include systematic and targeted biopsies.	Strong
	Base follow up on digital rectal examination, prostate-specific antigen (PSA) and repeat biopsies.	Strong
	Counsel patients about the possibility of needing further treatment in the future.	Strong

Active treatment	Offer surgery and radiotherapy (RT) as alternatives to AS to patients suitable for such treatments and who accept a trade-off between toxicity and prevention of disease progression.	Weak
Pelvic lymph node dissection (PLND)	Do not perform a PLND (estimated risk for pN+ < 5%).	Strong
Radiotherapy	Offer low-dose rate (LDR) brachytherapy to patients with low-risk PCa, without a previous transurethral resection of the prostate (TURP) and with a good International Prostatic Symptom Score (IPSS) and a prostate volume < 50 mL.	Strong
	Use intensity-modulated radiation therapy (IMRT) with a total dose of 74-80 Gy, without androgen deprivation therapy (ADT).	Strong
	Offer moderate hypofractionation (HFX) (68 Gy/20 fx in four weeks or 70 Gy/28 fractions (fx) in six weeks) as an alternative treatment option.	Strong
Other options	Only offer whole gland treatment (such as cryotherapy, HIFU, etc.) or focal treatment within a clinical trial setting.	Strong

Intermediate-risk disease		
Active surveillance	Offer AS to highly selected patients (< 10% pattern 4) accepting the potential increased risk of further metastases.	Weak
Radical prostatectomy (RP)	Offer RP to patients with intermediate-risk disease and a life expectancy > 10 years.	Strong
	Offer nerve-sparing surgery to patients with a low risk of extracapsular disease (refer to nomograms).	strong
Extended pelvic lymph node dissection (ePLND)	Perform an ePLND in intermediate-risk disease if the estimated risk for positive lymph nodes exceeds 5%.	Strong
Radiotherapy	Offer LDR brachytherapy to selected patients; patients without a previous TURP and with a good IPSS and a prostate volume < 50 mL.	Strong
	For EBRT, use a total dose of 76-78 Gy, in combination with short-term neoadjuvant plus concomitant ADT (four to six months).	Strong
	In patients not willing to undergo ADT, use an escalated dose of EBRT (76-80 Gy) or a combination with brachytherapy.	Weak

Other options	Only offer whole gland treatment (such as cryotherapy, HIFU, etc.) or focal treatment within a clinical trial setting.	Strong
High-risk localised disease		
Radical prostatectomy	Offer RP to patients with high-risk localised PCa and a life expectancy of > 10 years only as part of multi-modal therapy.	Strong
Extended pelvic lymph node dissection	Perform an ePLND in high-risk disease.	Strong
	Do not perform a frozen section of nodes during RP to decide whether to proceed with, or abandon, the procedure.	Strong
Radiotherapy	In patients with high-risk localised disease, use ERBT with 76-78 Gy in combination with long-term ADT (two to three years).	Strong
	In patients with high-risk localised disease, use EBRT with brachytherapy boost (either HDR or LDR), in combination with long-term ADT (two to three years).	Weak
Other options	Do not offer either whole gland or focal treatment to high-risk patients.	Strong
	Do not use ADT monotherapy in asymptomatic patients.	Strong

Locally-advanced disease		
Radical prostatectomy	Offer RP to highly selected patients with (cT3b-T4 N0 or any T N1) only as part of multi-modal therapy.	Strong
Extended pelvic lymph node dissection	Perform an ePLND in high-risk PCa.	Strong
	Do not perform a frozen section of nodes during RP to decide whether to proceed with, or abandon, the procedure.	Strong
Radiotherapy	In patients with locally advanced cN0 disease, offer RT in combination with long-term ADT.	Strong
	Offer long-term ADT for two to three years.	Weak
Other options	Do not offer whole gland treatment or focal treatment to high-risk patients.	Strong
	Only offer ADT monotherapy to those patients unwilling or unable to receive any form of local treatment and who are either symptomatic or asymptomatic, but with a PSA-doubling time (DT) over twelve months or a PSA > 50 ng/mL or a poorly differentiated tumour.	Strong

Adjuvant treatment after radical prostatectomy		
	Only discuss adjuvant treatment in men with a post-operative PSA < 0.1 ng/mL.	Strong
	Do not prescribe adjuvant ADT in pN0 patients.	Strong
	Offer adjuvant EBRT to the surgical field to patients at increased risk of local relapse: pT3 pN0 with positive margins (highest impact), and/or invasion of the seminal vesicles.	Strong
	Discuss three management options with patients with pN+ disease after an ePLND, based on nodal involvement characteristics: 1. Offer adjuvant ADT for node-positive (pN+). 2. Offer adjuvant ADT with additional radiotherapy. 3. Offer observation (expectant management) to a patient after eLND and ≤ 2 nodes with microscopic involvement, and a PSA < 0.1 ng/mL and absence of extranodal extension.	Weak

Non-curative or palliative treatments in a first-line setting		
Localised disease		
Watchful waiting	Offer WW to asymptomatic patients not eligible for local curative treatment and those with a short life expectancy.	Strong
	While on WW, base the decision to start non-curative treatment on symptoms and disease progression.	Strong
Locally advanced disease		
Watchful waiting	Offer a deferred treatment policy using ADT monotherapy to M0 asymptomatic patients with a PSA-DT > twelve months, a PSA < 50 ng/mL and well differentiated tumour, who are unwilling or unable to receive any form of local treatment.	Strong
Metastatic disease in a first-line setting		
Symptomatic patients	In M1 symptomatic patients, offer immediate systemic treatment to palliate symptoms and reduce the risk for potentially serious sequelae of advanced disease (spinal cord compression, pathological fractures, ureteral obstruction, and extra-skeletal metastasis).	Strong

Asymptomatic patients	In M1 asymptomatic patients, offer immediate systemic treatment to improve survival, defer progression to a symptomatic stage and prevent serious disease progression-related complications.	Strong
	In M1 asymptomatic patients, discuss deferred castration with a well-informed patient since it lowers the treatment side effects, provided the patient is closely monitored.	Weak
All M1 patients	Offer LHRH antagonists, especially to patients with an impending spinal cord compression or bladder outlet obstruction.	Weak
	In M1 patients treated with a LHRH agonist, offer short-term administration of anti-androgens to reduce the risk of the 'flare-up' phenomenon.	Weak
	Do not offer anti-androgen monotherapy for M1 disease.	Strong
	Offer castration combined with chemotherapy (docetaxel) to all patients whose first presentation is M1 disease and who are fit enough for docetaxel.	Strong

	Offer castration combined with abiraterone acetate plus prednisone to all patients whose first presentation is M1 disease and who are fit enough for the regimen.	Strong
	Offer castration alone, with or without an anti-androgen, to patients unfit for, or unwilling to consider, castration combined with docetaxel or abiraterone acetate plus prednisone.	Strong
M1 patients receiving Intermittent treatment	In asymptomatic M1 patients, only offer intermittent treatment to highly motivated men, with a major PSA response after the induction period.	Strong
	• In M1 patients, follow the schedules used in published clinical trials on timing of intermittent treatment. • Stop treatment when the PSA level is < 4 ng/mL after six to seven months of treatment. • Resume treatment when the PSA level is > 10-20 ng/mL (or returned to the initial level of < 20 ng/mL).	Weak
	Do not use castration combined with any local treatment (RT/surgery) outside an investigational setting except for symptom control.	Strong

Guidelines for second-line and palliative treatments

Biochemical recurrence after treatment with curative intent		
Biochemical recurrence after radical prostatectomy (RP)	Offer AS and possibly delayed salvage RT (SRT) to patients with a biochemical recurrence and favourable prognostic factors (≤ pT3a, time to biochemical recurrence > three year, PSA-DT > twelve months, GS ≤ 7), who may not benefit from intervention.	Strong
	Treat patients with a PSA rise from the undetectable range with SRT. The total dose of SRT should be at least 66 Gy and should be given early (PSA < 0.5 ng/mL).	Strong
Biochemical recurrence after RT	Treat highly selected patients with localised PCa and a histologically proven local recurrence with salvage RP (SRP).	Weak
	Salvage RP should only be performed in experienced centres.	Strong
	Do not offer HIFU, cryosurgical ablation and salvage brachy-therapy to patients with proven local recurrence since it is still experimental.	Strong
Systemic salvage treatment	Do not offer ADT to M0 patients with a PSA-DT > twelve months.	Strong

Life-prolonging treatments of castration-resistant disease		
	Ensure that testosterone levels are confirmed to be < 50 ng/mL, before diagnosing castration-resistant PCa (CRPC).	Strong
	Do not treat patients for non-metastatic CRPC outside of a clinical trial.	Strong
	Counsel, manage and treat patients with metastatic CRPC (mCRPC) in a multidisciplinary team.	Strong
	Treat patients with mCRPC with life-prolonging agents. Base the choice of first-line treatment on the performance status (PS), symptoms, comorbidities, location and extent of disease, patient preference, and on the previous treatment for hormone-sensitive PCa (alphabetical order: abiraterone, docetaxel, enzalutamide, radium-223, sipuleucel-T).	Strong
Cytotoxic treatments of castration-resistant disease		
	Counsel, manage and treat patients with mCRPC in a multidisciplinary team.	Strong
	Offer patients with mCRPC who are candidates for cytotoxic therapy docetaxel with 75 mg/m^2 every three weeks.	Strong

	In patients with mCRPC and progression following docetaxel chemotherapy offer further life-prolonging treatment options, which include abiraterone, cabazitaxel, enzalutamide and radium-223.	Strong
	Base second-line treatment decisions of mCRPC on pre-treatment PS, symptoms, patient preference, comorbidities and extent of disease.	Strong
Supportive care of castration-resistant disease		
	Offer bone protective agents to patients with mCRPC and skeletal metastases to prevent osseous complications.	Strong
	Offer calcium and vitamin D supplementation when prescribing either denosumab or bisphosphonates.	Strong
	Treat painful bone metastases early on with palliative measures such as EBRT, and adequate use of analgesics.	Strong
	In patients with spinal cord compression start immediate high-dose corticosteroids and assess for spinal surgery followed by irradiation. Offer radiation therapy alone if surgery is not appropriate.	Strong

Follow-up after treatment with curative intent

- After RP, PSA should be undetectable (< 0.1 ng/mL). A PSA of > 0.1 ng/mL after RP is a signal of residual prostate tumour tissue. After an undetectable PSA is obtained following RP, a PSA > 0.4 ng/mL and rising, best predicts further metastases.
- After RT, an increase in PSA > nadir + 2 ng/mL best predicts further metastases.
- Palpable nodules and increasing serum PSA are often signs of local recurrence.

Recommendations for follow-up	Strength rating
Routinely follow-up asymptomatic patients, by obtaining a disease-specific history and serum prostate-specific antigen (PSA) measurement. These should be performed at three, six and twelve months after treatment, then every six months until three years, and then annually.	Strong
During follow up, perform a systematic digital rectal examination (DRE) after surgery if unfavourable pathology (> pT3, pN1, Gleason ≥ 8).	Weak
During follow up, perform a systematic DRE after radiotherapy.	Strong
At recurrence, only image to detect local recurrence if it affects treatment planning.	Strong
Do not routinely offer bone scans and other imaging modalities to asymptomatic patients if there are no signs of biochemical relapse. In case patients have bone pain or other symptoms of possible progression, restaging should be considered irrespective of serum PSA level.	Strong

Recommendations for follow-up during hormonal treatment	Strength rating
Evaluate patients at three to six months after the initiation of treatment.	Strong
The follow-up strategy must be individualised based on stage of disease, prior symptoms, prognostic factors and the treatment given.	Strong
In patients with stage M0 disease, schedule follow-up every six months. As a minimum requirement, include a disease-specific history, DRE and serum PSA determination in the diagnostic work-up.	Strong
In patients with stage M1 disease, schedule follow-up every three to six months. As a minimum requirement, include a disease-specific history, DRE, serum PSA, haemoglobin, serum creatinine and alkaline phosphatase measurements in the diagnostic work-up. The testosterone level should be checked, especially during the first year.	Strong
Counsel patients (especially with M1b status) about the clinical signs suggestive of spinal cord compression.	Strong
When disease progression is suspected, adapt/individualise follow up.	Strong
In patients with suspected progression, assess the testosterone level. By definition, castration resistant PCa (CRPC) requires a testosterone level < 50 ng/dL (< 1 mL/L).	Strong
Do not offer routine imaging to otherwise stable asymptomatic patients.	Strong

Quality of Life

Treating PCa can affect an individual both physically and mentally, as well as his close relations and his work or vocation. These multifaceted issues all have a bearing on his perception of 'quality of life (QoL)'. Prostate cancer care should not be reduced to focusing on the organ in isolation. Taking QoL into consideration relies on understanding the patient's wishes and preferences so that optimal treatment proposals can be formulated and discussed. There is clear evidence of unmet needs and ongoing support requirements for some men after diagnosis and treatment for PCa.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-01-1), available to all members of the European Association of Urology at their website: http://www.uroweb.org/guidelines/.

EAU GUIDELINES ON RENAL CELL CARCINOMA

(Limited text update March 2018)

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Epidemiology

The use of imaging techniques such as ultrasound (US) and computerised tomography (CT) has increased the detection of asymptomatic renal cell cancer (RCC). The peak incidence of RCC occurs between 60 and 70 years of age, with a 3 : 2 ratio of men to women. Aetiological factors include lifestyle factors, such as smoking, obesity and hypertension. Having a first-degree relative with RCC is associated with a significantly increased risk of RCC.

Staging system

The current UICC 2017 TNM (Tumour Node Metastasis) classification is recommended for the staging of RCC (Table 1).

Table 1: The 2017 TNM staging classification system

T - Primary Tumour	
TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
T1	Tumour ≤ 7 cm or less in greatest dimension, limited to the kidney
	T1a Tumour ≤ 4 cm or less
	T1b Tumour > 4 cm but ≤ 7 cm
T2	Tumour > 7 cm in greatest dimension, limited to the kidney
	T2a Tumour > 7 cm but ≤ 10 cm
	T2b Tumours > 10 cm, limited to the kidney
T3	Tumour extends into major veins or perinephric tissues but not into the ipsilateral adrenal gland and not beyond Gerota fascia
	T3a Tumour grossly extends into the renal vein or its segmental (muscle-containing) branches, or tumour invades perirenal and/or renal sinus fat (peripelvic), but not beyond Gerota fascia
	T3b Tumour grossly extends into the vena cava below diaphragm
	T3c Tumour grossly extends into vena cava above the diaphragm or invades the wall of the vena cava
T4	Tumour invades beyond Gerota fascia (including contiguous extension into the ipsilateral adrenal gland)
N - Regional Lymph Nodes	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in regional lymph node(s)

M - Distant Metastasis			
M0	No distant metastasis		
M1	Distant metastasis		
TNM stage grouping			
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1, T2, T3	N1	M0
Stage IV	T4	Any N	M0
	Any T	Any N	M1

A help desk for specific questions about TNM classification is available at http://www.uicc.org/tnm.

Clinical Diagnosis

Many renal masses remain asymptomatic until late disease stages. The classic triad of flank pain, visible haematuria, and palpable abdominal mass is rare and correlates with aggressive histology and advanced disease.

Paraneoplastic syndromes are found in approximately 30% of patients with symptomatic RCCs. A few symptomatic patients present with symptoms caused by metastatic disease, such as bone pain or persistent cough.

Imaging

Computed tomography imaging, before and after intravenous contrast, can verify the diagnosis and provide information on the function and morphology of the contralateral kidney and assess tumour extension, including extra-renal spread, venous involvement, and enlargement of lymph nodes (LNs) and adrenals.

Abdominal US and magnetic resonance imaging (MRI) are supplements to CT. Contrast-enhanced US can be helpful in specific cases (e.g., chronic renal failure with a relative contraindication for iodinated or gadolinium-based

contrast media, complex cystic masses, and differential diagnosis of peripheral vascular disorders such as infarction and cortical necrosis).

Magnetic resonance imaging can be used in patients with possible venous involvement, or allergy to intravenous contrast. Chest CT is the most accurate for chest staging and is recommended in the primary work–up of patients with suspected RCC.

In patients with hereditary RCC who are worried about the radiation exposure of frequent CT scans, MRI may be offered as alternative for follow-up imaging.

Biopsy

Percutaneous renal tumour biopsies are used:

- to obtain histology of radiologically indeterminate renal masses;
- to select patients with small renal masses for active surveillance;
- to obtain histology before, or simultaneously with, ablative treatments;
- to select the most suitable form of medical and surgical strategy in the setting of metastatic disease.

In patients with any sign of impaired renal function, a renal scan and total renal function evaluation using estimated glomerular filtration rate should always be undertaken to optimise the treatment decision.

Renal biopsy is not indicated for comorbid and frail patients who can be considered only for conservative management (watchful waiting) regardless of biopsy results.

Recommendations for the diagnostic assessment of renal cell cancer	Strength rating
Use multi-phasic contrast-enhanced computed tomography (CT) of abdomen and chest for the diagnosis and staging of renal tumours.	Strong
Use magnetic resonance imaging to better evaluate venous involvement, reduce radiation or avoid intravenous CT contrast.	Weak
Use non-ionising modalities, mainly contrast enhanced ultrasound, for further characterisation of small renal masses, tumour thrombus and differentiation of unclear renal masses.	Weak
Do not routinely use bone scan and/or positron-emission tomography (PET) CT for staging of RCC.	Weak
Perform a renal tumour biopsy before ablative therapy and systemic therapy without previous pathology.	Strong
Perform a percutaneous biopsy in select patients who are considered for active surveillance.	Weak
Use a coaxial technique when performing a renal tumour biopsy.	Strong
Do not perform a renal tumour biopsy of cystic renal masses.	Strong
Use a core biopsy technique rather than fine needle aspiration for histological characterisation for solid renal tumours.	Strong

Histological diagnosis

A variety of renal tumours exist, and about 15% are benign. All kidney lesions require examination for malignant behaviour.

Histopathological classification

The new WHO/ISUP classification will replace the Fuhrman nuclear grade system in due time but will need validation.

The three most common RCC subtypes, with genetic and histological differences, are: clear cell RCC (80-90%), papillary RCC (10-15%), and chromophobe RCC (4-5%). The various RCC types have different clinical courses and responses to therapy.

Prognostic factors

In all RCC types, prognosis worsens with stage and histopathological grade. Histological factors include tumour grade, RCC subtype, sarcomatoid features, microvascular invasion, tumour necrosis, and invasion of the perirenal fat and collecting system. Clinical factors include performance status (PS), local symptoms, cachexia, anaemia, platelet count, neutrophil/lymphocyte ratio, C-reactive protein and albumin.

Recommendations	Strength rating
Use the current Tumour, Node, Metastasis classification system.	Strong
Use grading systems and classify RCC subtype.	Strong
Use prognostic systems in the metastatic setting.	Strong
In localised disease, use integrated prognostic systems or nomograms to assess risk of recurrence.	Strong

Disease Management

Treatment of localised RCC

Localised renal cancers are best managed with partial nephrectomy (PN) rather than radical nephrectomy (RN), irrespective of the surgical approach. Partial nephrectomy is unsuitable in some patients with localised RCC due to:

- locally advanced tumour growth;
- unfavourable tumour location;
- significant health deterioration.

If pre-operative imaging and intra-operative findings are normal, routine adrenalectomy is not indicated. Lymphadenectomy should be restricted to staging because the survival benefit of extended LN dissection is unclear in patients with localised disease. In patients who have RCCs with tumour thrombus and no metastatic spread, prognosis is improved after nephrectomy and complete thrombectomy.

Nephron-sparing surgery versus radical nephrectomy

Based on current available oncological and quality of life outcomes, localised renal cancers are best managed by nephron-sparing surgery (NSS) rather than RN, irrespective of the surgical approach. Before routine nephrectomy, tumour embolisation has no benefit. In patients unfit for surgery with massive haematuria or flank pain, embolisation can be a beneficial palliative approach.

Recommendations	Strength rating
Offer surgery to achieve cure in localised RCC.	Strong
Offer partial nephrectomy to patients with T1 tumours.	Strong

Do not perform ipsilateral adrenalectomy if there is no clinical evidence of invasion of the adrenal gland.	Strong
Consider an extended lymph node dissection in patients with adverse clinical features including a large diameter of the primary tumour.	Weak
Offer embolisation in patients unfit for surgery presenting with massive haematuria or flank pain.	Weak

Radical- and partial nephrectomy techniques

Summary of evidence	LE
Laparoscopic RN has lower morbidity than open surgery.	1b
Oncological outcomes for T1-T2a tumours are equivalent between laparoscopic and open RN.	2a
Partial nephrectomy can be performed, either with an open, pure laparoscopic- or robot-assisted approach, based on surgeon's expertise and skills.	2b
Partial nephrectomy is associated with a higher percentage of positive surgical margins compared with RN.	3

Recommendations	Strength rating
Offer laparoscopic radical nephrectomy (RN) to patients with T2 tumours and localised masses not treatable by partial nephrectomy.	Strong

Do not perform minimally invasive RN in patients with T1 tumours for whom a partial nephrectomy is feasible by any approach, including open.	Strong
Do not perform minimally invasive surgery if this approach may compromise oncological, functional and perioperative outcomes.	Strong

Alternatives to surgery

Surveillance

Elderly and comorbid patients with incidental small renal masses have a low RCC-specific mortality and significant competing-cause mortality. In selected patients with advanced age and/or comorbidities, active surveillance (AS) is appropriate to initially monitor small renal masses, followed, if required, by treatment for progression. The concept of AS differs from the concept of watchful waiting. Watchful waiting is reserved for patients whose comorbidities contraindicate any subsequent active treatment and who do not require follow-up imaging, unless clinically indicated.

Cryoablation and radiofrequency ablation

Currently there are no data showing oncological benefit of cryoablation or radiofrequency ablation (RFA) techniques over PN.

Recommendations	Strength rating
Offer active surveillance, radiofrequency ablation and cryoablation to elderly and/or comorbid patients with small renal masses.	Weak

Treatment of locally advanced RCC

Management of clinically positive lymph nodes (cN+)

In the presence of clinically positive LNs (cN+), LND is always justified but the extent of LND is still controversial.

Low level data suggest that tumour thrombus in the setting of non-metastatic disease should be excised. Adjunctive procedures such as tumour embolisation or inferior vena cava filter do not appear to offer any benefits in the treatment of tumour thrombus.

In patients unfit for surgery, or with non-resectable disease, embolisation can control symptoms, including visible haematuria or flank pain. At present there is no evidence for the use of adjuvant therapy following surgery.

Treatment of advanced/metastatic RCC

Management of RCC with venous tumour thrombus

Recommendations	Strength rating
In patients with clinically enlarged lymph nodes, perform lymph node dissection for staging purposes or local control.	Weak
In case of venous involvement, remove the renal tumour and thrombus.	Strong

Cytoreductive nephrectomy

Tumour nephrectomy is curative only if all tumour deposits are excised. This includes patients with the primary tumour in place and single- or oligo-metastatic resectable disease. For most patients with metastatic disease, cytoreductive nephrectomy is palliative and systemic treatments are necessary.

Summary of evidence	LE
Cytoreductive nephrectomy combined with interferon-alpha (INF-α) improves survival in patients with metastatic RCC and good performance status.	1a
Deferred cytoreductive nephrectomy with presurgical sunitinib in intermediate-risk patients with clear-cell metastatic RCC leads to a survival benefit in secondary endpoint analysis and selects out patients with inherent resistance to systemic therapy.	2b
Cytoreductive nephrectomy for patients with simultaneous complete resection of a single metastasis or oligometastases may improve survival and delay systemic therapy.	3
Patients with IMDC poor risk (≥ four risk factors) do not benefit.	2b

Recommendations	Strength rating
Offer cytoreductive nephrectomy to favourable- and intermediate-risk patients with metastatic RCC (mRCC).	Weak
Do not offer cytoreductive nephrectomy in IMDC poor-risk patients with ≥ four risk factors.	Weak
Perform immediate cytoreductive nephrectomy in patients with oligometastases when complete resection can be achieved.	Weak
Offer deferred cytoreductive nephrectomy to intermediate-risk patients with clear-cell mRCC who require systemic therapy with sunitinib.	Weak

IMDC = The Metastatic Renal Cancer Database Consortium.

Local therapy of metastases in metastatic RCC (mRCC)

A systematic review of the local treatment of metastases from RCC in any organ was undertaken. The heterogeneity of the data will only allow for cautious recommendations.

Summary of evidence	LE
All included studies were retrospective non-randomised comparative studies, resulting in a high risk of bias associated with non-randomisation, attrition, and selective reporting.	3
With the exception of brain and possibly bone metastases, metastasectomy remains by default the only local treatment for most sites.	3
Retrospective comparative studies consistently point towards a benefit of complete metastasectomy in mRCC patients in terms of overall survival, cancer-specific survival and delay of systemic therapy.	3
Radiotherapy to bone and brain metastases from RCC can induce significant relief from local symptoms (e.g. pain).	3

Recommendations	Strength rating
Offer local therapy for metastatic disease (including metastasectomy) to patients with a favourable disease profile in whom complete resection is achievable or when local symptoms need to be controlled.	Weak
Offer stereotactic radiotherapy for clinically relevant bone or brain metastases for local control and symptom relief.	Weak

Systemic therapy for advanced/metastatic RCC

Chemotherapy

Summary of evidence	LE
In metastatic RCC, 5-fluorouracil combined with immunotherapy has equivalent efficacy to INF-α.	1b
In metastatic RCC, chemotherapy is otherwise not effective with the exception of gemcitabine and doxorubicine in sarcomatoid and rapidly progressive disease.	3

Recommendation	Strength rating
Do not offer chemotherapy as first-line therapy in patients with clear-cell metastatic RCC.	Strong

Immunotherapy

Interferon-α may only be effective in some patient subgroups, including patients with clear-cell RCC (ccRCC), favourable-risk criteria, and lung metastases only. Interleukin-2 (IL-2), vaccines and targeted immunotherapy have no place in the standard treatment of advanced/mRCC.

Immune checkpoint inhibition of programmed death receptor (PD-1) and ligand (PD-L1) inhibition have been investigated in mRCC. Randomised data support the use of nivolumab (a PD-1 inhibitor) in vascular endothelial growth factor (VEGF)-refractory disease. A combination of two immune checkpoint inhibitors ipilimumab and nivolumab versus sunitinib in a phase III study on metastatic RCC showed superior survival for a combination of ipilimumab and nivolumab in intermediate- and poor-risk patients.

Summary of evidence	LE
Interferon-α monotherapy is inferior to VEGF-targeted therapy or mTOR inhibition in mRCC.	1b
Interleukin (IL)-2 monotherapy may have an effect in selected cases (good PS, ccRCC, lung metastases only).	2a
IL-2 has more side-effects than IFN-α.	2b
High-dose (HD)-IL-2 is associated with durable complete responses in a limited number of patients. However, no clinical factors or biomarkers exist to accurately predict a durable response in patients treated with HD-IL-2.	1b
Bevacizumab plus IFN-α is more effective than IFN-α in treatment-naïve, low-risk and intermediate-risk ccRCC.	1b
Vaccination therapy with tumour antigen 5T4 showed no survival benefit over first-line standard therapy.	1b
Cytokine combinations, with or without additional chemotherapy, do not improve overall survival (OS) compared with monotherapy.	1b
Nivolumab leads to superior OS compared to everolimus in patients failing one or two lines of VEGF-targeted therapy.	1b
The combination of nivolumab and ipilimumab in treatment-naïve patients with clear-cell mRCC of IMDC intermediate-and poor-risk leads to superior survival compared to sunitinib.	1b
The combination of nivolumab and ipilimumab in the intention to treat population of treatment-naïve unselected patients with clear-cell mRCC leads to superior survival compared to sunitinib.	2b

Due to the exploratory nature of PD-L1 tumour expression, the small sample size, the lack of OS data and the premature results in this subpopulation, definitive conclusions cannot be drawn.	2b
Nivolumab plus ipilimumab was associated with 15% grade 3-5 toxicity and 1.5% treatment-related deaths.	1b

Recommendations	Strength rating
Use ipilimumab plus nivolumab in treatment-naïve patients with clear-cell mRCC of IMDC intermediate and poor risk.	Strong
Offer nivolumab after one or two lines of VEGF-targeted therapy in mRCC.	Strong
Do not offer monotherapy with interferon-α or high-dose bolus interleukin-2 as first-line therapy in mRCC.	Weak
Do not use bevacizumab plus INF-α in treatment-naïve clear-cell favourable- and intermediate-risk RCC patients.	Weak
Do not use PD-L1 tumour expression as a predictive biomarker.	Weak
Administer nivolumab plus ipilimumab in centres with experience of immune combination therapy and appropriate supportive care within the context of a multidisciplinary team.	Weak
Do not rechallange patients who stop nivolumab plus ipilimumab because of toxicity with the same drugs in the future without expert guidance and support from a multidisciplinary team.	Strong

IMDC = The Metastatic Renal Cancer Database Consortium; VEGF = vascular endothelial growth factor.

Targeted therapies

At present, several targeting drugs have been approved both for the treatment of mRCC.

Summary of evidence	LE
VEGF-targeted therapies increase progression-free survival (PFS) and/or OS as both first-line and second-line treatments for patients with clear-cell mRCC.	1b
Cabozantinib in intermediate-and poor-risk treatment-naïve clear-cell RCC leads to better response rates and PFS but not OS when compared to sunitinib.	1a
Tivozanib has recently been approved but the evidence is still considered inferior over existing choices.	3
Axitinib has proven efficacy and superiority in PFS as a second-line treatment after failure of cytokines and VEGF-targeted therapy in comparison with sorafenib.	1b
Sunitinib is more effective than IFN-α in treatment-naïve patients.	1b
In treatment-naïve patients, bevacizumab in combination with INF-α has not been tested against nivolumab plus ipilimumab and the evidence for subsequent therapies is unclear.	1b
Pazopanib is superior to placebo in both treatment-naïve mRCC patients and post-cytokine patients.	1b
First-line pazopanib is not inferior to sunitinib in clear-cell mRCC patients.	1b
Temsirolimus monotherapy prolongs OS compared to IFN-α in treatment-naïve poor-risk mRCC.	1b
In treatment-naïve patients, temsirolimus has not been tested against nivolumab plus ipilimumab and the evidence for subsequent therapies is unclear.	3

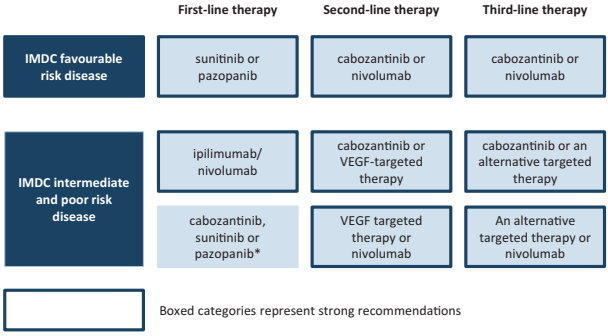
Cabozantinib is superior to everolimus in terms of PFS and OS in patients after one or more lines of VEGF-targeted therapy.	1b
Everolimus prolongs PFS after VEGF-targeted therapy when compared to placebo or when the patient cannot tolerate these therapies.	1b
Sorafenib has broad activity in a spectrum of settings in ccRCC patients previously treated with cytokine or targeted therapies. It is inferior to axitinib in both sunitinib or cytokine pre-treated patients.	4
Both mTOR inhibitors (everolimus and temsirolimus) and VEGF-targeted therapies (sunitinib or sorafenib) have limited oncological efficacy in non-clear cell RCC. There is a non-significant trend for improved oncological outcomes for sunitinib, over everolimus.	2a
Lenvatinib in combination with everolimus modestly improved PFS over everolimus alone.	2a

Recommendations	**Strength rating**
Use sunitinib or pazopanib in treatment-naïve patients with clear-cell mRCC of IMDC favourable risk.	Strong
Use cabozantinib in treatment-naïve patients with clear-cell mRCC of IMDC intermediate and poor risk.	Weak
Do not use bevacizumab plus INF-α in treatment-naïve clear-cell favourable- and intermediate-risk RCC patients.	Weak
Do not use tivozanib in treatment-naïve clear-cell mRCC patients.	Weak
Do not use temsirolimus in treatment-naïve clear-cell poor-risk RCC patients.	Weak

Use VEGF-TKIs in second-line in patients refractory to nivolumab plus ipilimumab.	Weak
Offer cabozantinib for ccRCC after one or two lines of VEGF-targeted therapy in mRCC.	Strong
Offer axitinib, everolimus or lenvatinib plus everolimus to ccRCC patients who failed VEGF-targeted therapy, and when nivolumab or cabozantinib are not safe, tolerable or available.	Strong
Sequence systemic therapy in treating mRCC.	Strong
Offer sunitinib as first-line therapy for non-clear cell mRCC.	Weak
Do not offer sorafenib as second-line treatment to patients with mRCC.	Weak

IMDC = The Metastatic Renal Cancer Database Consortium; VEGF = vascular endothelial growth factor.

Figure 1: Updated EAU Guidelines recommendations for the treatment of first-line clear-cell metastatic renal cancer.



IMDC = The International Metastatic Renal Cell Carcinoma Database Consortium; VEGF = vascular endothelial growth factor.
**pazopanib for intermediate-risk disease only.*

Recurrent RCC

Locally recurrent disease can occur either after nephrectomy, PN, or after ablative therapy. After nephron-sparing treatment approaches the recurrence may be intra-renal or regional, e.g. venous tumour thrombi or retroperitoneal LN metastases. Isolated local recurrence in the true renal fossa is rare. Patients can benefit from a complete surgical resection of local recurrent disease. In cases where complete surgical removal is not feasible due to advanced tumour growth and pain, palliative treatments including radiation treatment can be considered.

Surveillance following surgery for RCC

The aim of surveillance is to detect either local recurrence or metastatic disease while the patient is still surgically curable. Surveillance after treatment for RCC allows the urologist to identify:

- postoperative complications;
- renal function;
- local recurrence;
- recurrence in the contralateral kidney;
- development of metastases.

Depending on the availability of new effective treatments, more intensive follow-up schedules may be required, particularly as there is a higher local recurrence rate after cryotherapy and RFA. At present there is no evidence-based standard for the follow-up of patients with RCC, or for the optimal duration of follow-up. An example of a surveillance algorithm monitoring patients after treatment for RCC that recognises not only the patient's risk profile but also treatment efficacy is provided in Table 2. For patients with metastatic disease, individualised follow-up is indicated.

Table 2: Proposed surveillance schedule following treatment for RCC, taking into account patient risk profile and treatment efficacy

Risk profile	Surveillance				
	6 mo	1 y	2 y	3 y	> 3 y
Low	US	CT	US	CT	CT once every 2 years; counsel about recurrence risk of ~10%
Intermediate	CT	CT	CT	CT	CT once every 2 years

CT = computed tomography of chest and abdomen, alternatively use magnetic resonance imaging for the abdomen; US = ultrasound of abdomen, kidneys and renal bed.

Summary of evidence and recommendations for surveillance following RN or PN orablative therapies in RCC

Summary of evidence	LE
Surveillance can detect local recurrence or metastatic disease while the patient is still surgically curable.	4
After NSS, there is an increased risk of recurrence for larger (> 7 cm) tumours, or when there is a positive surgical margin.	3
Patients undergoing surveillance have a better overall survival than patients not undergoing surveillance.	3
Repeated CT scans do not reduce renal function in chronic kidney disease patients.	3

Recommendations	Strength rating
Base follow-up after RCC on the risk of recurrence.	Strong
Intensify follow-up in patients after NSS for tumours > 7 cm or in patients with a positive surgical margin.	Weak
Base risk stratification on pre-existing classification systems such as the University of California Los Angeles integrated staging system integrated risk assessment score (http://urology.ucla.edu/body.cfm?id=443).	Strong

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN: 978-94-92671-01-1), available to all members of the European Association of Urology at their website: http://www.uroweb.org/guidelines/.

EAU GUIDELINES ON TESTICULAR CANCER

(Limited text update March 2018)

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Introduction

Compared with other types of cancer, testicular cancer is relatively rare accounting for approximately 1-1.5% of all cancers in men. Nowadays, testicular tumours show excellent cure rates, mainly due to early diagnosis and their extreme chemo- and radiosensitivity.

Staging and Classification

Staging

Postorchiectomy half-life kinetics of serum tumour markers

For an accurate staging the following steps are necessary (see Table 1):

The persistence of elevated serum tumour markers after orchiectomy may indicate the presence of disease, while their normalisation does not necessarily mean absence of tumour. Tumour markers should be assessed until they are normal, as long as they follow their half-life kinetics and no metastases are revealed. A chest computed tomography (CT) scan should be routinely performed in patients diagnosed with non-seminomatous germ cell tumours (NSGCT), because in up to 10% of cases, small subpleural nodes may be present that are not visible radiologically.

Table 1: Recommended tests for staging at diagnosis

Tests	Recommendations	Strength rating
Serum tumour markers	- Alpha-fetoprotein - human chorionic gonadotrophin (hCG) - Lactate dehydrogenase	Strong
Abdominopelvic computed tomography (CT)	All patients	Strong
Chest CT	All patients	Strong
Testis ultrasound (bilateral)	All patients	Strong
Bone scan or magnetic resonance imaging (MRI) columna	In case of symptoms	Strong
Brain scan (CT/MRI)	In case of symptoms and patients with metastatic disease with multiple lung metastases and/ or high beta-hCG values.	Strong
Further investigations		
Fertility investigations: • total testosterone • luteinising hormone • follicle-stimulating hormone • semen analysis		Weak
Discuss sperm banking with all men prior to starting treatment for testicular cancer.		Strong

Staging system

The Tumour, Node, Metastasis (TNM 2017) staging system is endorsed (Table 2).

Table 2: TNM classification for testicular cancer

pT - Primary Tumour[1]	
pTX	Primary tumour cannot be assessed (see note 1)
pT0	No evidence of primary tumour (e.g. histological scar in testis)
pTIS	Intratubular germ cell neoplasia (carcinoma *in situ*)
pT1	Tumour limited to testis and epididymis without vascular/lymphatic invasion; tumour may invade tunica albuginea but not tunica vaginalis*
pT2	Tumour limited to testis and epididymis with vascular/lymphatic invasion, or tumour extending through tunica lbuginea with involvement of tunica vaginalis
pT3	Tumour invades spermatic cord with or without vascular/lymphatic invasion
pT4	Tumour invades scrotum with or without vascular/ lymphatic invasion
N - Regional Lymph Nodes - Clinical	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis with a lymph node mass 2 cm or less in greatest dimension and 5 or fewer positive nodes, none more than 2 cm in greatest dimension
N2	Metastasis with a lymph node mass more than 2 cm but not more than 5 cm in greatest dimension; or more than 5 nodes positive, none more than 5 cm; or evidence of extranodal extension of tumour

N3	Metastasis with a lymph node mass more than 5 cm in greatest dimension		
Pn - Regional Lymph Nodes - Pathological			
pNX	Regional lymph nodes cannot be assessed		
pN0	No regional lymph node metastasis		
pN1	Metastasis with a lymph node mass 2 cm or less in greatest dimension and 5 or fewer positive nodes, none more than 2 cm in greatest dimension		
pN2	Metastasis with a lymph node mass more than 2 cm but not more than 5 cm in greatest dimension; or more than 5 nodes positive, none more than 5 cm; or evidence or extranodal extension of tumour		
pN3	Metastasis with a lymph node mass more than 5 cm in greatest dimension		
M - Distant Metastasis			
MX	Distant metastasis cannot be assessed		
M0	No distant metastasis		
M1	Distant metastasis		
	M1a	Non-regional lymph node(s) or lung metastasis	
	M1b	Distant metastasis other than non-regional lymph nodes and lung	
S - Serum tumour markers			
SX	Serum marker studies not available or not performed		
S0	Serum marker study levels within normal limits		
	LDH (U/l)	**hCG (mIU/mL)**	**AFP (ng/mL)**
S1	< 1.5 x N and	< 5,000 and	< 1,000
S2	1.5-10 x N or	5,000-50,000 or	1,000-10,000
S3	> 10 x N or	> 50,000 or	> 10,000

N indicates the upper limit of normal for the LDH assay.

LDH = lactate dehydrogenase; hCG = human chorionic gonadotrophin; AFP = alpha-fetoprotein.

[1]*Except for pTis and pT4, where radical orchidectomy is not always necessary for classification purposes, the extent of the primary tumour is classified after radical orchidectomy; see pT. In other circumstances, TX is used if no radical orchidectomy has been performed.*

The International Germ Cell Cancer Collaborative Group (IGCCCG) defined a prognostic factor-based staging system for metastatic germ cell cancer that includes good and intermediate prognosis seminoma and good, intermediate, and poor prognosis NSGCT (Table 3).

Table 3: Prognostic-based staging system for metastatic germ cell cancer (IGCCCG)*

Good-prognosis group	
Non-seminoma (56% of cases) 5-year PFS 89% 5-year survival 92%	*All of the following criteria:* • Testis/retro-peritoneal primary • No non-pulmonary visceral metastases • AFP < 1,000 ng/mL • hCG < 5,000 IU/L (1,000 ng/mL) • LDH < 1.5 x ULN
Seminoma (90% of cases) 5-year PFS 82% 5-year survival 86%	*All of the following criteria:* • Any primary site • No non-pulmonary visceral metastases • Normal AFP • Any hCG • Any LDH

Intermediate-prognosis group	
Non-seminoma (28% of cases) 5-year PFS 75% 5-year survival 80%	*Any of the following criteria:* • Testis/retro-peritoneal primary • No non-pulmonary visceral metastases • AFP 1,000 - 10,000 ng/mL or • hCG 5,000 - 50,000 IU/L or • LDH 1.5 - 10 x ULN
Seminoma (10% of cases) 5-year PFS 67% 5-year survival 72%	*All of the following criteria:* • Any primary site • Non-pulmonary visceral metastases • Normal AFP • Any hCG • Any LDH
Poor-prognosis group	
Non-seminoma (16% of cases) 5-year PFS 41% 5-year survival 48%	*Any of the following criteria:* • Mediastinal primary • Non-pulmonary visceral metastases • AFP > 10,000 ng/mL or • hCG > 50,000 IU/L (10,000 ng/mL) or • LDH > 10 x ULN
Seminoma	No patients classified as poor prognosis

** Pre-chemotherapy serum tumour markers should be assessed immediately prior to the administration of chemotherapy (same day).*

PFS = progression-free survival; AFP = alpha-fetoprotein; hCG = human chorionic gonadotrophin; LDH = lactate dehydrogenase.

Diagnostic evaluation

The diagnosis of testicular cancer is based on:
Clinical examination of the testis and general examination to rule out enlarged nodes or abdominal masses. Ultrasound (US) of both testes should be performed whenever a testicular tumour is suspected. An additional US of the retroperitoneum is recommended to screen for extensive retroperitoneal metastasis. Ultrasound of both testes should also be performed in patients with a retroperitoneal mass and/or elevated tumour serum markers without a palpable scrotal mass.

Serum tumour markers, both before, and five to seven days after orchiectomy (AFP and hCG) and LDH. The latter is mandatory in advanced tumours.

Inguinal exploration and orchiectomy with *en bloc* removal of testis, tunica albuginea, and spermatic cord. If the diagnosis is not clear, a testicular biopsy (tumour enucleation) is to be taken for histopathological frozen section.

Organ-sparing surgery can be attempted in special cases (bilateral tumour or solitary testes). Routine contralateral biopsy for diagnosis of carcinoma *in situ* should be discussed with the patient and is recommended in 'high-risk' patients (testicular volume < 12 mL, a history of cryptorchidism and age < 40 years).

Pathological examination of the testis

Following orchiectomy, the pathological examination of the testis should include a number of investigations.

1. macroscopic features: side, testis size, maximum tumour size, and macroscopic features of the epididymis, spermatic cord, and tunica vaginalis;

2. sampling: a 1 cm^2 section for every centimetre of maximum tumour diameter, including normal macroscopic parenchyma (if present), albuginea and epididymis, with selection of suspected areas;
3. at least one proximal and one distal section of spermatic cord plus any suspected area;
4. microscopic features and diagnosis: histological type (specify individual components and estimate amount as percentage) according to WHO 2004;
5. presence or absence of peri-tumoural venous and/or lymphatic invasion;
6. presence or absence of albuginea, tunica vaginalis, rete testis, epididymis or spermatic cord invasion; presence or absence of germ cell neoplasia *in situ* (GCNIS) in non-tumour parenchyma;
7. pT category according to TNM 2016;
8. immunohistochemical studies: in seminoma and mixed germ cell tumour, AFP and hCG.

Diagnosis and treatment of testicular intraepithelial neoplasia

Diagnosis and treatment of testicular intraepithelial neoplasia (TIN) Biopsy should be offered to patients at high risk for contralateral TIN (testicular volume < 12 mL, history of cryptorchidism or poor spermatogenesis). If performed, a double biopsy is preferred. In the case of TIN, local radiotherapy is indicated following counselling on impaired testosterone production and infertility.

Recommendations for the diagnosis and staging of testicular cancer	Strength rating
Perform testicular ultrasound in all patients with suspicion of testicular cancer.	Strong
Offer biopsy of the contralateral testis and discuss its consequences with patients at high risk for contralateral germ cell neoplasia *in situ*.	Strong
Perform orchiectomy and pathological examination of the testis to confirm the diagnosis and to define the local extension (pT category). In a life-threatening situation due to extensive metastasis, start chemotherapy before orchiectomy.	Strong
Perform serum determination of tumour markers (alpha-fetoprotein, human chorionic gonadotrophin, and lactate dehydrogenase), both before, and five to seven days after orchiectomy, for staging and prognostic reasons.	Strong
Assess the state of the retroperitoneal, mediastinal and supraclavicular nodes and viscera in testicular cancer.	Strong
Advise patients with a familiar history of testis cancer, as well as their family members, to perform regular testicular self-examination.	Strong

Prognosis

Risk factors for occult metastatic disease in stage I testicular cancer		
	For seminoma	**For non-seminoma**
Pathological (for stage I)		
Histopathological type	• Tumour size (> 4 cm) • Invasion of the rete testis	• Vascular/lymphatic or peri-tumoural invasion • Proliferation rate > 70% • Percentage of embryonal carcinoma > 50%

Disease management

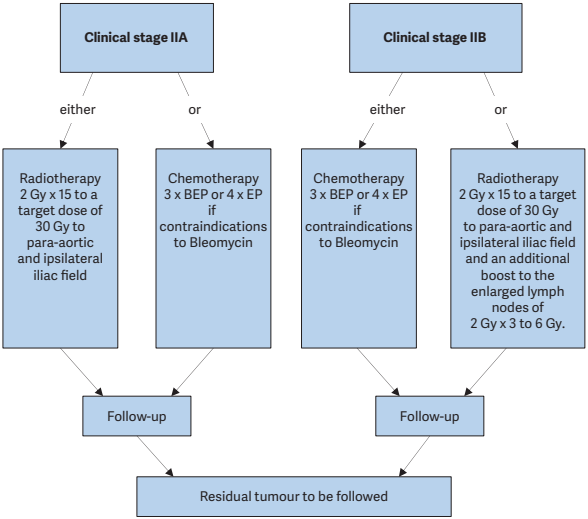
Recommendations for the treatment of stage I seminoma	Strength rating
Fully inform the patient about all available management options, including surveillance or adjuvant chemotherapy after orchiectomy, as well as treatment-specific recurrence rates and acute and long-term side effects.	Strong
Offer surveillance as a management option if facilities are available and the patient is compliant.	Strong
Offer one course at area under curve (AUC) 7, if carboplatin chemotherapy is considered.	Strong
Do not perform adjuvant treatment in patients at very low risk (no risk factors).	Strong

Do not perform radiotherapy as adjuvant treatment.	Strong

Recommendations for the treatment of stage 1 non-seminomatous germ cell tumour	**Strength rating**
Inform patients with stage 1 non-seminomatous germ cell tumour (NSGCT) about all adjuvant treatment options after orchiectomy (surveillance, adjuvant chemotherapy, and retroperitoneal lymph node dissection [RPLND]) including treatment-specific recurrence rates as well as acute and long-term side effects.	Strong
In patients with stage 1 NSGCT, offer surveillance or risk-adapted treatment based on vascular invasion (see below).	Strong
If patients are not willing to undergo surveillance, offer one course of cisplatin, etoposide, bleomycin (BEP) as an adjuvant treatment alternative since it has proven to be superior to RPLND in terms of recurrence rates.	Strong
In patients with marker-positive recurrent and/or progressing lesion during surveillance, perform salvage treatment consisting of three or four courses of BEP chemotherapy according to the International Germ Cell Cancer Collaborative Group classification, followed by post-chemotherapy RPLND, if necessary.	Strong

Recommendations for risk-adapted treatment for clinical stage 1 based on vascular invasion	Strength rating
Stage IA (pT1, no vascular invasion): low risk	
Offer surveillance if the patient is willing and able to comply.	Strong
In low-risk patients not willing (or unsuitable) to undergo surveillance, offer adjuvant chemotherapy with one course of cisplatin, etoposide, bleomycin (BEP).	Strong
Stage IB (pT2-pT4): high risk	
Offer primary chemotherapy with one course of BEP, or surveillance.	Strong
Inform patients having adjuvant chemotherapy about the advantages and disadvantages of one vs. two cycles of BEP.	Strong
Offer surveillance to patients not willing to undergo adjuvant chemotherapy.	Strong
Offer nerve-sparing retroperitoneal lymph node dissection to highly selected patients only; those with contraindication to adjuvant chemotherapy and unwilling to accept surveillance.	Strong

Figure 1: Treatment options in patients with seminoma clinical stage IIA and B



BEP = cisplatin, etoposide, bleomycin; EP = etoposide and cisplatin.

Recommendations for the treatment of metastatic germ cell tumours	Strength rating
Treat low volume non-seminomatous germ cell tumour (NSGCT) stage IIA/B with elevated markers like 'good- or intermediate-prognosis' advanced NSGCT, with three or four cycles of cisplatin, etoposide, bleomycin (BEP).	Strong

In stage IIA/B NSGCT without marker elevation, exclude marker negative embryonal carcinoma by obtaining histology by either retroperitoneal lymph node dissection (RPLND) or biopsy. If not possible, repeat staging after six weeks of surveillance before making a final decision on further treatment.	Strong
In metastatic NSGCT with an intermediate prognosis, treat with four courses of standard BEP.	Strong
In metastatic NSGCT with a poor prognosis, treat with one cycle of BEP, or cisplatin, etoposide and ifosfamide (PEI) in case of poor lung function, followed by tumour marker assessment after three weeks. In case of a favourable marker decline, continue BEP (or PEI) up to a total of four cycles. In case of an unfavourable decline, initiate chemotherapy intensification.	Strong
Perform surgical resection of residual masses after chemotherapy in NSGCT in the case of visible residual masses and when serum levels of tumour markers are normal or normalising.	Strong
In CS IIA seminoma, offer radiotherapy or chemotherapy and inform the patient of possible undesirable long-term side effects of both management options.	Strong
Initially offer chemotherapy in seminoma stage CS IIB (BEP x 3 or EP x 4, in good prognosis) as an alternative to radiotherapy.	Strong

Treat seminoma stage IIC and higher, with primary chemotherapy according to the same principles used for NSGCT.	Strong

Relapse after chemotherapy

The treatment of relapsed GCT after chemotherapy is typically salvage chemotherapy. For patients at first relapse with good prognostic features (initial achievement of CR/PRM- and gonadal primary tumour) four cycles of standard-dose salvage chemotherapy are proposed. For patients with poor prognostic factors (extragonadal primary and/or incomplete response to first-line chemotherapy) and for all patients with subsequent (> first) relapse, high-dose chemotherapy with autologous stem cell support is recommended.

Follow-up

The primary aim of follow-up in the first five years is the timely diagnosis of recurrent disease in order to be able to treat the patient with curative intent with the least aggressive therapy.

a) Interval between examinations and duration of follow-up should be consistent with the time of maximal risk of recurrence;
b) Tests should be directed at the most likely sites of recurrence and have a good accuracy;
c) The increased risk of second malignancy (in the primary site and in other tissues that may have been exposed to the same carcinogens, or in which there is epidemiological evidence of increased risk) should also guide the selection of tests;
d) Non-malignant complications of therapy must also be considered.

Table 4: Recommended minimal follow-up for seminoma stage I on active surveillance or after adjuvant treatment (carboplatin or radiotherapy)

Modality	Year 1	Year 2	Year 3	Years 4 & 5	After 5 years
Tumour markers ± doctor visit	2 times	2 times	2 times	once	Further management according to survivorship care plan
Chest X-ray	-	-	-	-	
Abdominopelvic computed tomography/ magnetic resonance imaging	2 times	2 times	Once at 36 months	Once at 60 months	

Table 5: Recommended minimal follow-up for non-seminoma stage I on active surveillance

Modality	Year 1	Year 2	Year 3	Years 4 & 5	After 5 years
Tumour markers ± doctor visit	4 times**	4 times	2 times	1-2 times	Further management according to survivorship care plan
Chest X-ray	2 times	2 times	Once, in case of LVI+	At 60 months if LVI+	
Abdominopelvic computed tomography/magnetic resonance imaging	2 times	At 24 months ***	Once at 36 months*	Once at 60 months*	

**Recommended by 50% of the consensus group members.*

***In case of high risk (LVI+) a minority of the consensus group members recommended six times.*

****In case of high risk (LVI+) a majority of the consensus group members recommended an additional CT at eighteen months.*

Table 6: Recommended minimal follow up after adjuvant treatment or complete remission for advanced disease (excluded: poor prognosis and no remission)

Modality	Year 1	Year 2	Year 3	Years 4 & 5	After 5 years
Tumour markers ± doctor visit	4 times	4 times	2 times	2 times	Further management according to survivorship care plan**
Chest X-ray	1-2 times	Once	Once	Once	
Abdominopelvic computed tomography/ magnetic resonance imaging	1-2 times	At 24 months	Once at 36 months	Once at 60 months	
Thorax CT	*	*	*	*	

**Same time points as abdomino-pelvic CT/MRI in case of pulmonary metastases at diagnosis.*

***In case of teratoma in resected residual disease: the patient should remain with the uro-oncologist.*

Quality of life and long-term toxicities after cure

Patients diagnosed with TC are usually between 18 and 40 years at diagnosis and life expectancy after cure extends over several decades. Before any treatment is planned, patients should be informed of common long-term toxicities.

During follow-up, patients should be screened and treated for known risk factors such as high blood pressure, hyperlipidaemia and testosterone deficiency. When follow up by the clinical expert is discontinued, a written cancer survivorship plan addressing late toxic effects, lifestyle recommendations, recurrence risk, and cancer-specific follow-up might be helpful.

Testicular Stromal Tumours

Testicular stromal tumours are rare, however, Leydig cell and Sertoli cell tumours are of clinical relevance.

Leydig cell tumours

Approximately 10% of Leydig tumours are malignant presenting the following features:

- large size (> 5 cm);
- cytologic atypia and DNA aneuploidy;
- increased mitotic activity and increased MIB-1 expression;
- necrosis;
- vascular invasion infiltrative margins;
- extension beyond the testicular parenchyma.

The tumour presents as a painless enlarged testis or as an incidental US finding accompanied in up to 80% of cases by hormonal disorders. Serum tumour markers are negative and approximately 30% of patients present with gynaecomastia. These tumours are often treated by inguinal orchiectomy because they are misinterpreted as germ cell tumours. In patients with symptoms of gynaecomastia or hormonal disorders or typical imaging on US, until final histology is available, a partial orchiectomy (+ frozen section) should be considered. In the case of histological signs of malignancy, orchiectomy and RPLND are the treatment of choice.

Sertoli cell tumours

Sertoli cell tumours are malignant in 10-22% of cases. Morphological signs of malignancy are:

- large size (> 5 cm);
- pleomorphic nuclei with nucleoli;
- increased mitotic activity;
- necrosis and vascular invasion.

They present either as an enlarged testis or as incidental US finding. Hormonal disorders are infrequent and serum tumour markers are negative. Ultrasonographically, they generally appear as hypoechoic and cannot be safely distinguished from germ-cell tumour except for the subtype large cell calcifying form which is usually associated with genetic syndromes (Carney's complex, Peutz-Jeghers syndrome). Sertoli cell tumours are often interpreted as germ-cell tumours and an orchiectomy is performed.

Organ-sparing surgery should be considered (with caution) but, in the case of histological signs of malignancy, orchiectomy and RPLND are the treatment of choice.

Conclusions

Most testis tumours are diagnosed at an early stage. Staging is the cornerstone.

Following orchiectomy, excellent cure rates are achieved for those early stages irrespective of the treatment policy adopted, although pattern and relapse rates are closely linked to the treatment modality chosen. In metastatic disease a multidisciplinary therapeutic approach offers an acceptable survival. Follow-up schedules should be tailored to initial staging and treatment.

This short booklet text is based on the more comprehensive EAU Guidelines (978-94-92671-01-1), available to all members of the European Association of Urology at their website: http://www.uroweb.org/guidelines/.

EAU GUIDELINES ON PENILE CANCER

(Text update March 2018)

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Introduction and epidemiology

The incidence of penile cancer increases with age, peaking during the sixth decade of life. However, the disease does occur in younger men. There are significant geographical variations within Europe as well as worldwide. Penile cancer is common in regions with a high prevalence of human Papilloma virus (HPV), which may account for the global incidence variation, as the worldwide HPV prevalence varies considerably. There is at present no recommendation for the use of HPV vaccination in boys.

Risk factors

Recognised aetiological and epidemiological risk factors for penile cancer are:

Risk factors	Relevance
Phimosis	Odds ratio 11-16 vs. no phimosis
Chronic penile inflammation (balanoposthitis related to phimosis), lichen sclerosus	Risk
Sporalene and ultraviolet A phototherapy for various dermatological conditions such as psoriasis	Incidence rate ratio 9.51 with > 250 treatments
Smoking	Five-fold increased risk (95% Confidence interval: 2.0-10.1) vs. non-smokers
HPV infection, condylomata acuminata	22.4% in verrucous squamous cell carcinoma 36-66.3% in basaloid-warty
Rural areas, low socio-economic status, unmarried	
Multiple sexual partners, early age of first intercourse	Three to five-fold increased risk of penile cancer

Pathology

Different variants of squamous cell carcinoma (SCC) accounts for more than 95% of cases of malignant penile disease. Table 1 lists premalignant lesions and Table 2 lists the pathological subtypes of penile carcinomas.

Table 1: Premalignant penile lesions (precursor lesions)

Lesions sporadically associated with squamous cell carcinoma (SCC) of the penis: • Bowenoid papulosis of the penis (HPV related) • Lichen sclerosus
Premalignant lesions (up to one-third transform to invasive SCC): • Penile intraepithelial lesions • Giant condylomata (Buschke-Löwenstein) • Bowen's disease • Paget's disease (intradermal ADK)

Table 2: Histological subtypes of penile carcinomas, their frequency and outcome

Subtype	Frequency (% of cases)	Prognosis
Common squamous cell carcinoma (SCC)	48-65	Depends on location, stage and grade
Basaloid carcinoma	4-10	Poor prognosis, frequently early inguinal nodal metastasis
Warty carcinoma	7-10	Good prognosis, metastasis rare
Verrucous carcinoma	3-8	Good prognosis, no metastasis
Papillary carcinoma	5-15	Good prognosis, metastasis rare
Sarcomatoid carcinoma	1-3	Very poor prognosis, early vascular metastasis
Mixed carcinoma	9-10	Heterogeneous group

Pseudohyperplastic carcinoma	< 1	Foreskin, related to lichen sclerosis, good prognosis, metastasis not reported
Carcinoma cuniculatum	< 1	Variant of verrucous carcinoma, good prognosis, metastasis not reported
Pseudoglandular carcinoma	< 1	High-grade carcinoma, early metastasis, poor prognosis
Warty-basaloid carcinoma	9-14	Poor prognosis, high metastatic potential (higher than in warty, lower than in basaloid SCC)
Adenosquamous carcinoma	< 1	Central and peri-meatal glans, high-grade carcinoma, high metastatic potential but low mortality
Mucoepidermoid carcinoma	< 1	Highly aggressive, poor prognosis
Clear cell variant of penile carcinoma	1-2	Exceedingly rare, associated with human papilloma virus, aggressive, early metastasis, poor prognosis, outcome is lesion-dependent, frequent lymphatic metastasis

Biopsy

Doubtful penile lesions should be biopsied and histological verification obtained before local treatment. Histological confirmation is necessary to guide management when:

- there is doubt about the exact nature of the lesion (e.g. carcinoma *in situ*, metastasis or melanoma);
- treatment with topical agents, radiotherapy or laser surgery is planned.

Recommendations for the pathological assessment of tumour specimens	Strength rating
The pathological evaluation of penile carcinoma specimens must include an assessment of the HPV status.	Strong
The pathological evaluation of penile carcinoma specimens must include a diagnosis of the squamous cell carcinoma subtype.	Strong
The pathological evaluation of penile carcinoma surgical specimens must include an assessment of surgical margins including the width of the surgical margin.	Strong

Staging and classification systems

The 2016 UICC, Tumour Node Metastasis (TNM) classification should be used for staging and classification (Table 3). The T1 category is stratified into two prognostically different risk groups. The classification T2 denotes invasion of the corpus spongiosum and T3 invasion of the corpora cavernosa, recognising that these two invasion patterns differ prognostically. The current pN1 group consists of one or two inguinal lymph node metastases, pN2 is more than two uni- or bilateral metastatic nodes, and pN3 any pelvic nodes, uni- or bilateral and any extranodal extension.

Table 3: 2016 TNM clinical and pathological classification of penile cancer

Clinical classification		
T - Primary tumour		
TX	Primary tumour cannot be assessed	
T0	No evidence of primary tumour	
Tis	Carcinoma *in situ*	
Ta	Non-invasive verrucous carcinoma*	
T1	Tumour invades subepithelial connective tissue	
	T1a	Tumour invades subepithelial connective tissue without lymphovascular invasion and is not poorly differentiated
	T1b	Tumour invades subepithelial connective tissue with lymphovascular invasion or is poorly differentiated
T2	Tumour invades corpus spongiosum with or without invasion of the urethra	
T3	Tumour invades corpus cavernosum with or without invasion of the urethra	
T4	Tumour invades other adjacent structures	
N - Regional lymph nodes		
NX	Regional lymph nodes cannot be assessed	
N0	No palpable or visibly enlarged inguinal lymph nodes	
N1	Palpable mobile unilateral inguinal lymph node	
N2	Palpable mobile multiple or bilateral inguinal lymph nodes	
N3	Fixed inguinal nodal mass *or* pelvic lymphadenopathy, unilateral or bilateral	
M - Distant metastasis		
M0	No distant metastasis	
M1	Distant metastasis	

Pathological classification	
The pT categories correspond to the clinical T categories	
The pN categories are based upon biopsy or surgical excision	
pN - Regional Lymph Nodes	
pNX	Regional lymph nodes cannot be assessed
pN0	No regional lymph node metastasis
pN1	Metastasis in one or two inguinal lymph nodes
pN2	Metastasis in more than two unilateral inguinal nodes or bilateral inguinal lymph nodes
pN3	Metastasis in pelvic lymph node(s), unilateral *or* bilateral or extranodal extension of regional lymph node metastasis
pM - Distant Metastasis	
pM1	Distant metastasis microscopically confirmed
G - Histopathological Grading	
GX	Grade of differentiation cannot be assessed
G1	Well differentiated
G2	Moderately differentiated
G3	Poorly differentiated
G4	Undifferentiated

**Verrucous carcinoma not associated with destructive invasion.*

Diagnostic evaluation and staging

Penile cancer can be cured in over 80% of all cases if diagnosed early. Once metastatic spread has occurred, it is a life-threatening disease with poor prognosis. Local treatment, although potentially life-saving, can be mutilating and devastating for the patient's psychological well-being.

Physical Examination

Careful palpation of both groins for enlarged inguinal lymph nodes must be part of the initial physical examination of patients with penile cancer.

Imaging

- Ultrasound (US) can give information about infiltration of the corpora.
- Magnetic resonance imaging (MRI) with an artificially induced erection can help to exclude tumour invasion of the corpora cavernosa if preservation of the penis is planned.
- In case of non-palpable inguinal nodes, current imaging techniques are not reliable in detecting micrometastases.
- A pelvic computed tomography (CT) scan can be used to assess pelvic lymph nodeIn case of positive inguinal nodes, CT of the abdomen and pelvis and a chest X-ray are recommended; a thoracic CT will be more sensitive than an X-ray.

Recommendations for the diagnosis and staging of penile cancer	**Strength rating**
Primary tumour	
Perform a physical examination, record morphology, extent and invasion of penile structures.	Strong
Obtain a penile Doppler ultrasound or MRI with artificial erection in cases with intended organ-sparing surgery.	Weak

Inguinal lymph nodes	
Perform a physical examination of both groins, record the number, laterality and characteristics of inguinal nodes and: • If nodes are not palpable, offer invasive lymph node staging in intermediate- and high-risk patients; • If nodes are palpable, stage with a pelvic computed tomography (CT) or positron emission tomography (PET)/CT.	Strong
Distant metastases	
In N+ patients, obtain an abdominopelvic CT scan and chest X-ray/thoracic CT for systemic staging. Alternatively, stage with a PET/CT scan.	Strong
In patients with systemic disease or with relevant symptoms, obtain a bone scan.	

Disease management

Treatment of the primary penile cancer lesion aims to remove the tumour completely while preserving as much of the penis as possible without compromising radicality.

Recommendations for stage-dependent local treatment of penile carcinoma		
Primary tumour	**Use organ-preserving treatment whenever possible**	**Strength rating**
Tis	Topical treatment with 5-fluorouracil or imiquimod for superficial lesions with or without photodynamic control.	Strong
	Laser ablation with carbon dioxide (CO_2) or neodymium: yttrium-aluminium-garnet (Nd:YAG) laser.	
	Glans resurfacing.	
Ta, T1a (G1, G2)	Wide local excision with circumcision, CO_2 or Nd:YAG laser with circumcision.	Strong
	Laser ablation with CO_2 or Nd:YAG laser.	
	Glans resurfacing.	
	Glansectomy with reconstruction.	
	Radiotherapy for lesions < 4 cm.	
T1b (G3) and T2	Wide local excision plus reconstruction.	Strong
	Glansectomy with circumcision and reconstruction.	
	Radiotherapy for lesions < 4 cm in diameter.	
T3	Partial amputation with reconstruction or radiotherapy for lesions < 4 cm in diameter.	Strong

T3 with invasion of the urethra	Partial penectomy or total penectomy with perineal urethrostomy.	Strong
T4	Neoadjuvant chemotherapy followed by surgery in responders or palliative radiotherapy.	Weak
Local recurrence	Salvage surgery with penis-sparing in small recurrences or partial amputation.	Weak
	Large or high-stage recurrence: partial or total amputation.	

Management of inguinal lymph nodes

The treatment of regional lymph nodes is crucial for the survival of the patient. A surveillance strategy carries considerable risk as regional lymph node recurrence dramatically reduces the chance of long-term survival. Invasive staging by modified inguinal lymphadenectomy or dynamic sentinel node biopsy is recommended for penile cancers pT1G1 and higher.

Recommendations for treatment strategies for nodal metastases		
Regional lymph nodes	**Management of regional lymph nodes is fundamental in the treatment of penile cancer**	**Strength rating**
No palpable inguinal nodes (cN0)	Tis, Ta G1, T1G1: surveillance.	Strong
	> T1G2: invasive lymph node staging by either bilateral modified inguinal lymphadenectomy or dynamic sentinel node biopsy.	Strong
Palpable inguinal nodes (cN1/cN2)	Radical inguinal lymphadenectomy.	Strong
Fixed inguinal lymph nodes (cN3)	Neoadjuvant chemotherapy followed by radical inguinal lymphadenectomy in responders.	Weak
Pelvic Lymph nodes	Ipsilateral pelvic lymphadenectomy if two or more inguinal nodes are involved on one side (pN2) or if extracapsular nodal metastasis (pN3) reported.	Strong
Adjuvant chemotherapy	In pN2/pN3 patients after radical lymphadenectomy.	Strong
Radiotherapy	Not recommended for nodal disease except as a palliative option.	Strong

Recommendations for chemotherapy in penile cancer patients	Strength rating
Offer patients with pN2-3 tumours adjuvant chemotherapy after radical lymphadenectomy (three to four cycles of cisplatin, a taxane and 5-fluorouracil or ifosfamide).	Strong
Offer patients with non-resectable or recurrent lymph node metastases neoadjuvant chemotherapy (four cycles of a cisplatin- and taxane-based regimen) followed by radical surgery.	Weak
Offer palliative chemotherapy to patients with systemic disease.	Weak

Follow-up

Follow-up after curative treatment in penile carcinoma, as in any malignant disease, is important for two reasons:

- early detection of recurrence allows for potentially curative treatment;
- the detection and management of treatment-related complications.

Local recurrence does not significantly reduce long-term survival if successfully treated, while inguinal nodal recurrence leads to a drastic reduction in the probability of long-term disease-specific survival.

Recommendations for follow-up in penile cancer					
	Interval of follow-up		Examinations and investigations	Minimum duration of follow-up	Strength rating
	Years one to two	Years three to five			
Recommendations for follow-up of the primary tumour					
Penile-preserving treatment	Three months	Six months	Regular physician or self-examination. Repeat biopsy after topical or laser treatment for penile intraepithelial neoplasia.	Five years	Strong
Amputation	Three months	One year	Regular physician or self-examination.	Five years	Strong
Recommendations for follow-up of the inguinal lymph nodes					
Surveillance	Three months	Six months	Regular physician or self-examination.	Five years	Strong
pN0 at initial treatment	Three months	One year	Regular physician or self-examination. Ultrasound with fine-needle aspiration biopsy optional.	Five years	Strong
pN+ at initial treatment	Three months	Six months	Regular physician or self-examination. Ultrasound with fine-needle aspiration cytology optional, computed tomography/magnetic resonance imaging optional.	Five years	Strong

Quality of life

Overall, nearly 80% of penile cancer patients of all stages can be cured. Partial penectomy has negative consequences for the patients' self-esteem and sexual function. Organ preserving treatment allows for better quality of life and sexual function and should be offered to all patients whenever feasible. Referral to centres with experience is recommended and psychological support is very important for penile cancer patients.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-01-1), available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines/.

EAU GUIDELINES ON NON-NEUROGENIC MALE LUTS INCLUDING BENIGN PROSTATIC OBSTRUCTION

(Text update March 2018)

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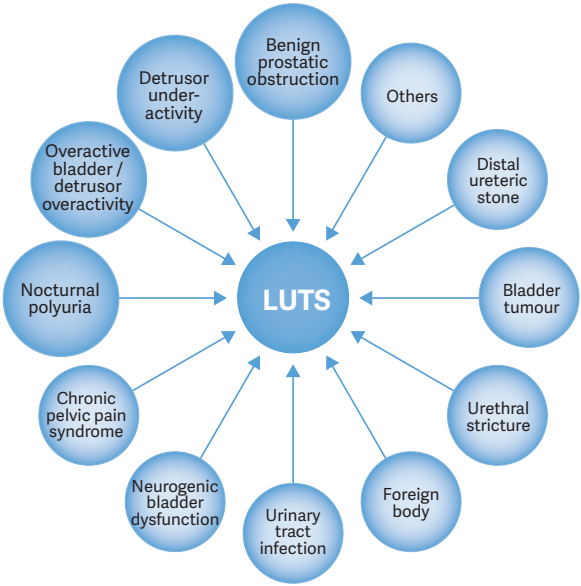
Introduction

The EAU Guidelines on Male Lower Urinary Tract Symptoms (LUTS) is a symptom-orientated guideline that mainly reviews LUTS secondary to benign prostatic obstruction (BPO), detrusor overactivity/overactive bladder (OAB), or nocturnal polyuria in men ≥ 40 years. The multifactorial aetiology of LUTS is illustrated in Figure 1.

Figure 1: Causes of male lower urinary tract symptoms (LUTS)



Diagnostic Evaluation

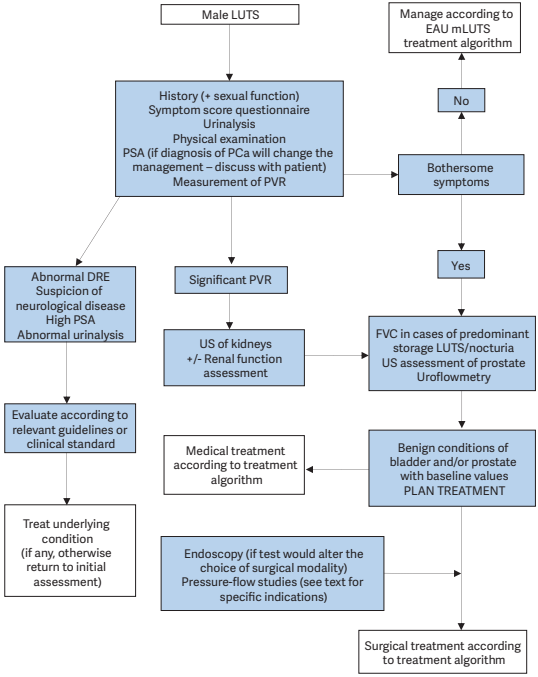
The high prevalence and the underlying multifactorial pathophysiology of male LUTS mean that an accurate assessment of LUTS is critical to provide best evidence-based care. Clinical assessment of LUTS aims to differentially diagnose and to define the clinical profile. A practical algorithm has been developed (Figure 2).

Recommendations for the diagnostic evaluation of male LUTS	Strength rating
Take a complete medical history from men with LUTS.	Strong
Use a validated symptom score questionnaire including bother and quality of life assessment during the assessment of male LUTS and for re-evaluation during and/or after treatment.	Strong
Use a bladder diary to assess male LUTS with a prominent storage component or nocturia.	Strong
Tell the patient to complete a bladder diary for the duration of at least three days.	Strong
Perform a physical examination including digital rectal examination in the assessment of male LUTS.	Strong
Urinalysis and prostate-specific antigen (PSA)	
Use urinalysis (by dipstick or urinary sediment) in the assessment of male LUTS.	Strong
Measure PSA if a diagnosis of prostate cancer will change management.	Strong
Measure PSA if it assists in the treatment and/or decision making process.	Strong
Renal function, post-void residual and uroflowmetry	
Assess renal function if renal impairment is suspected based on history and clinical examination, or in the presence of hydronephrosis, or when considering surgical treatment for male LUTS.	Strong
Measure post-void residual in the assessment of male LUTS.	Weak

Perform uroflowmetry in the initial assessment of male LUTS.	Weak
Perform uroflowmetry prior to medical or invasive treatment.	Strong
Imaging and urethrocystoscopy	
Perform ultrasound of the upper urinary tract in men with LUTS.	Weak
Perform imaging of the prostate when considering medical treatment for male LUTS, if it assists in the choice of the appropriate drug.	Weak
Perform imaging of the prostate when considering surgical treatment.	Strong
Perform urethrocystoscopy in men with LUTS prior to minimally invasive/surgical therapies if the findings may change treatment.	Weak
Pressure-flow studies (PFS)	
Perform PFS only in individual patients for specific indications prior to invasive treatment or when evaluation of the underlying pathophysiology of LUTS is warranted.	Weak
Perform PFS in men who have had previous unsuccessful (invasive) treatment for LUTS.	Weak
Perform PFS in men considering invasive treatment who cannot void > 150 mL.	Weak
Perform PFS when considering surgery in men with bothersome predominantly voiding LUTS and Q_{max} > 10 mL/s.	Weak

Perform PFS when considering invasive therapy in men with bothersome, predominantly voiding LUTS with a post-void residual > 300 mL.	Weak
Perform PFS when considering invasive treatment in men with bothersome, predominantly voiding LUTS aged > 80 years.	Weak
Perform PFS when considering invasive treatment in men with bothersome, predominantly voiding LUTS aged < 50 years.	Weak
Non-invasive tests in diagnosing bladder outlet obstruction	
Do not offer non-invasive tests, as an alternative to PFS, for diagnosing bladder outlet obstruction in men.	Strong

Figure 2: Assessment algorithm of LUTS in men aged 40 years or older



DRE = digital-rectal examination; FVC = frequency volume chart; LUTS = lower urinary tract symptoms; PCa = prostate cancer; PSA = prostate specific antigen; PVR = post-void residual; US = ultrasound.

Notice: Readers are strongly recommended to read the full text that highlights the current position of each test in detail.

Disease Management

Conservative and pharmacological treatment

Watchful waiting is suitable for mild-to-moderate uncomplicated LUTS. It includes education, re-assurance, lifestyle advice, and periodic monitoring.

Recommendation for the conservative and pharmacological management of male LUTS.	**Strength rating**
Conservative management	
Offer men with mild/moderate symptoms, minimally bothered by their symptoms, watchful waiting.	Strong
Offer men with LUTS lifestyle advice prior to, or concurrent with, treatment.	Strong
Pharmacological management	
Offer α1-blockers to men with moderate-to-severe LUTS.	Strong
Use 5α-reductase inhibitors (5-ARIs) in men who have moderate-to-severe LUTS and an increased risk of disease progression (e.g. prostate volume > 40 mL).	Strong
Counsel patients about the onset of action (3-6 months) of 5-ARIs.	Strong
Use muscarinic receptor antagonists in men with moderate-to-severe LUTS who mainly have bladder storage symptoms.	Strong
Do not use antimuscarinic overactive bladder medications in men with a post-void residual (PVR) volume > 150 mL.	Weak
Use phosphodiesterase type 5 inhibitors in men with moderate-to-severe LUTS with or without erectile dysfunction.	Strong

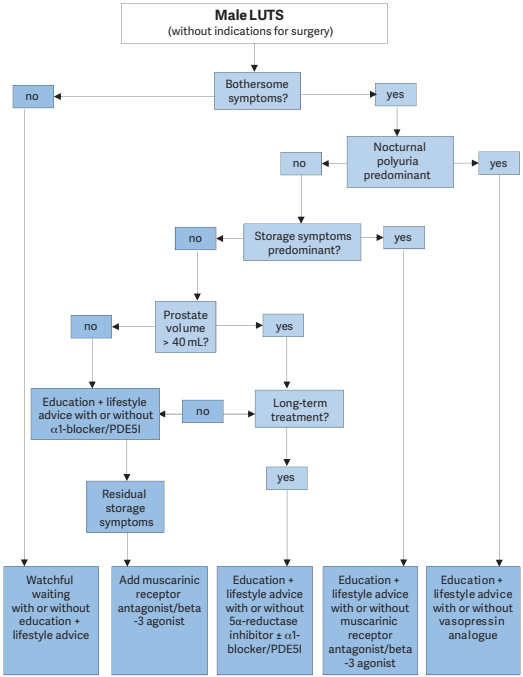
Use beta-3 agonists in men with moderate-to-severe LUTS who mainly have bladder storage symptoms.	Weak
Offer combination treatment with an α1-blocker and a 5-ARI to men with moderate-to-severe LUTS and an increased risk of disease progression (e.g. prostate volume > 40 mL).	Strong
Use combination treatment of a α1-blocker with a muscarinic receptor antagonist in patients with moderate-to-severe LUTS if relief of storage symptoms has been insufficient with monotherapy with either drug.	Strong
Do not prescribe combination treatment in men with a PVR volume > 150 mL.	Weak

Summary conservative and/or medical treatment

First choice of therapy is behavioural modification, with or without pharmacological treatment. A flowchart illustrating conservative and pharmacological treatment choices according to evidence-based medicine and patients' profiles is provided in Figure 3.

Figure 3: Treatment algorithm of male LUTS using medical and/or conservative treatment options.

Treatment decisions depend on results assessed during initial evaluation. Note that patients' preferences may result in different treatment decisions.



LUTS = lower urinary tract symptoms;
PDE5I = phosphodiesterase type 5 inhibitor.
Notice: Readers are strongly recommended to read the full text that highlights the current position of each treatment in detail.

Surgical treatment

Prostate surgery is usually required when patients have experienced recurrent or refractory urinary retention, overflow incontinence, recurrent urinary tract infections, bladder stones or diverticula, treatment-resistant macroscopic haematuria due to BPH/BPE, or dilatation of the upper urinary tract due to BPO, with or without renal insufficiency (absolute operation indications, need for surgery). Surgery is usually needed when patients have had insufficient relief of LUTS or post-void residual after conservative or pharma-cological treatments (relative operation indications).

Recommendations for surgical treatment of male LUTS	Strength rating
Offer transurethral incision of the prostate to surgically treat moderate-to-severe LUTS in men with prostate size < 30 mL, without a middle lobe.	Strong
Offer bipolar- or monopolar- transurethral resection of the prostate (TURP) to surgically treat moderate-to-severe LUTS in men with prostate size of 30-80 mL.	Strong
Offer plasma bipolar transurethral vaporisation of the prostate as an alternative to TURP to surgically treat moderate-to-severe LUTS in men with prostate size of 30-80 mL.	Strong
Offer endoscopic enucleation of the prostate or open prostatectomy to treat moderate-to-severe LUTS in men with prostate size > 80 mL.	Strong

Offer open prostatectomy in the absence of endoscopic enucleation to treat moderate-to-severe LUTS in men with prostate size > 80 mL.	Strong
Laser treatments of the prostate	
Offer laser enucleation of the prostate using holmium:yttrium-aluminum-garnet laser (HoLEP) to men with moderate-to-severe LUTS as an alternative to TURP or open prostatectomy.	Strong
Offer 80 Watt 532-nm Kalium-Titanyl-phosphate (KTP) laser vaporisation of the prostate to men with moderate-to-severe LUTS as an alternative to TURP.	Strong
Offer 120 Watt 532-nm Lithium Borat (LBO) laser vaporisation of the prostate to men with moderate-to-severe LUTS as an alternative to TURP.	Strong
Offer 180 Watt 532-nm LBO laser vaporisation of the prostate to men with moderate-to-severe LUTS as an alternative to TURP.	Strong
Offer laser vaporisation of the prostate using 80 Watt KTP, 120 or 180 Watt LBO for the treatment of patients receiving antiplatelet or anticoagulant therapy with a prostate volume < 80 mL.	Weak
Offer 120 Watt 980 nm diode laser vaporisation of the prostate to men with moderate-to-severe LUTS as a comparable alternative to TURP.	Weak

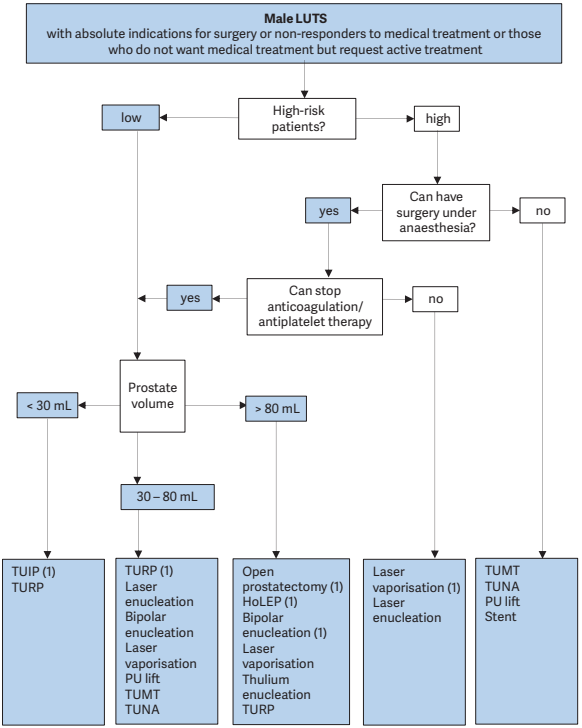
Offer 120 Watt 980 nm or 1,318 nm diode laser enucleation of the prostate to men with moderate-to-severe LUTS as a comparable alternative to TURP.	Weak
Offer laser enucleation of the prostate using Tm:YAG vapoenucleation (ThuVEP) and Tm:YAG laser assisted anatomical enucleation (ThuLEP) to men with moderate-to-severe LUTS as alternatives to TURP and HoLEP.	Weak
Offer ThuVEP to patients receiving anticoagulant or antiplatelet therapy.	Weak
Offer laser resection of the prostate using Tm:YAG laser (ThuVARP) as an alternative to TURP.	Strong
Offer ThuVARP to patients receiving anticoagulant or antiplatelet therapy.	Weak
Prostatic stents and prostatic urethral lift	
Offer prostatic stents as an alternative to catheterisation in men unfit for invasive procedures requiring spinal or general anaesthesia.	Weak
Offer Prostatic urethral lift (Urolift®) to men with LUTS interested in preserving ejaculatory function, with prostates < 70 mL and no middle lobe.	Strong
Novel interventions	
Do not offer intraprostatic Botulinum toxin injection treatment to patients with male LUTS.	Strong

Summary surgical treatment

The choice of the surgical technique depends on prostate size, co-morbidities, ability to undergo anaesthesia, patient's preference/willingness to accept surgery-associated side effects, availability of the surgical armamentarium, and experience of the surgeon. Figure 4 illustrates surgical treatment choices according to the patient's profile.

Figure 4: Treatment algorithm of bothersome LUTS refractory to conservative/medical treatment or in cases of absolute operation indications.

The flowchart is stratified by the patient's ability to have anaesthesia, cardiovascular risk, and prostate size.



(1) Current standard/first choice. The alternative treatments are presented in alphabetical order.
Notice: Readers are strongly recommended to read the full text that highlights the current position of each treatment in detail.

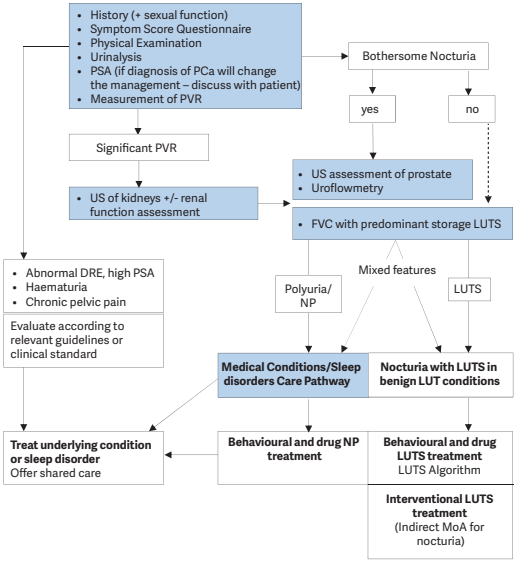
Laser vaporisation includes GreenLight, thulium, and diode laser vaporisation; Laser enucleation includes holmium and thulium laser enucleation.
HoLEP = holmium laser enucleation; TUIP = transurethral incision of the prostate; TUMT = transurethral microwave therapy; TUNA = transurethral needle ablation; TURP = transurethral resection of the prostate.

Management of Nocturia in Men with LUTS

Diagnostic assessment

Evaluation is outlined in Figure 5.

Figure 5: Evaluation of nocturia in non-neurogenic male LUTS



Assessment must establish whether the patient has polyuria, LUTS, sleep disorder or a combination. Therapy may be driven by the bother it causes, but non-bothersome nocturia may warrant assessment of a frequency volume chart (FVC), (indicated by the dotted line), depending on history and clinical examination since potential presence of a serious underlying medical condition must be considered.
DRE = digital rectal examination; NP = nocturnal polyuria; MoA = mechanism of action; PVR = post-void residual; PSA = prostate-specific antigen; US = ultrasound.

Figure 6: Shared care pathway for nocturia, highlighting the need to manage potentially complex patients using relevant expertise for the causative factors.

UROLOGICAL CONTRIBUTION	SHARED CARE	MEDICAL CONTRIBUTION
Diagnosis of LUTD • Urological/LUTS evaluation • Nocturia symptom scores • Bladder diary		**Diagnosis of conditions causing NP** • Evaluate patient's known conditions • Screening for sleep disorders • Screening for potential causes of polyuria*
Conservative management Behavioural therapy • Fluid/sleep habits advice • Drugs for storage LUTS • (Drugs for voiding LUTS) • ISC/catherisation	**Conservative management** • Antidiuretic • Diuretics • Drugs to aid sleep	**Management** • Initiation of therapy for new diagnosis • Optimised therapy of known conditions
Interventional therapy • Therapy of refractory storage LUTS • Therapy of refractory voiding LUTS		

* Potential causes of polyuria

NEPHROLOGICAL DISEASE
- Tubular dysfunction
- Global renal dysfunction

CARDIOVASCULAR DISEASE
- Cardiac disease
- Vascular disease

ENDOCRINE DISEASE
- Diabetes insipidus/mellitus
- Hormones affecting diuresis/natriuresis

NEUROLOGICAL DISEASE
- Pituitary and renal innervation
- Autonomic dysfunction

RESPIRATORY DISEASE
- Obstructive sleep apnoea

BIOCHEMICAL
- Altered blood oncotic pressure

Recommendations for treatment of nocturia	Strength rating
Treat underlying causes of nocturia, including behavioural, systemic condition(s), sleep disorders, lower urinary tract dysfunction, or a combination of factors.	Weak
Discuss behavioural changes with the patient to reduce nocturnal urine volume and episodes of nocturia, and improve sleep quality.	Weak
Offer desmopressin to decrease nocturia due to nocturnal polyuria in men < 65. Screen for hyponatremia at baseline, during dose titration and during treatment.	Strong
Offer α1-adrenergic antagonists for treating nocturia in men who have nocturia associated with LUTS.	Weak
Offer antimuscarinic drugs for treating nocturia in men who have nocturia associated with overactive bladder.	Weak
Offer 5α-reductase inhibitors for treating nocturia in men who have nocturia associated with LUTS and an enlarged prostate (> 40 mL).	Weak
Do not offer phosphodiesterase type 5 inhibitors for the treatment of nocturia.	Weak

Follow-up

Recommended follow-up strategy:

- Patients managed with watchful waiting should be reviewed at six months and then annually, provided symptoms do not deteriorate or absolute indications develop for surgical treatment.
- Patients receiving α1-blockers, muscarinic receptor

antagonists, beta-3 agonists, phospodiesterase 5 inhibitors, or a combination should be reviewed four to six weeks after drug initiation. If patients gain symptomatic relief, without troublesome side effects, drug therapy may be continued. Patients should be reviewed at six months and then annually, provided symptoms do not deteriorate or absolute indications develop for surgical treatment.

- Patients receiving 5α-reductase inhibitor should be reviewed after twelve weeks and six months to determine their response and adverse events.
- Patients receiving desmopressin: serum sodium concentration should be measured at day three and seven and after one month and, if serum sodium concentration has remained normal, every three months subsequently; the follow-up sequence should be restarted after dose escalation.
- Patients after prostate surgery should be reviewed four to six weeks after catheter removal to evaluate treatment response and side effects. If patients have symptomatic relief and there are no side effects, further assessment is not necessary.

Recommendations for follow-up	Strength rating
Follow-up all patients who receive conservative, medical or surgical management.	Weak
Define follow-up intervals and examinations according to the specific treatment.	Weak

Readers are strongly recommended to read the full version of the Guidelines where the efficacy, safety and considerations for each treatment are presented.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-01-1) available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines.

EAU GUIDELINES ON URINARY INCONTINENCE

(Limited text update March 2018)

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Introduction

This pocket version aims to synthesise the important clinical messages described in the full text and is presented as a series of 'action based recommendations' with a strength rating.

Diagnostic Evaluation

History and physical examination

The history should include details of the type, timing and severity of urinary incontinence (UI), associated voiding and other urinary symptoms. The history should allow UI to be categorised into stress urinary incontinence (SUI), urgency urinary incontinence (UUI) or mixed urinary incontinence (MUI).

It should also identify patients who need rapid referral to an appropriate specialist. These include patients with associated pain, haematuria, a history of recurrent urinary tract infection (UTI), pelvic surgery (particularly prostate surgery) or radiotherapy, constant leakage suggesting a fistula, voiding difficulty or suspected neurological disease. The patient should also be asked about other ill health and for the details of current medications, as these may impact on symptoms of UI.

Questionnaires

Recommendation	Strength rating
Use a validated and appropriate questionnaire when standardised assessment is required.	Strong

Voiding diaries

Recommendations	Strength rating
Ask patients with UI to complete a voiding diary.	Strong
Use a diary duration of at least three days.	Strong

Urinalysis and urinary tract infection

Recommendations	Strength rating
Perform urinalysis as a part of the initial assessment of a patient with UI.	Strong
If a symptomatic urinary tract infection is present with UI, reassess the patient after treatment.	Strong
Do not routinely treat asymptomatic bacteriuria in elderly patients to improve UI.	Strong

Post-voiding residual volume

Recommendations	Strength rating
When measuring post-void residual (PVR) urine volume, use ultrasound.	Strong
Measure (PVR) in patients with UI who have voiding symptoms.	Strong

Measure (PVR) when assessing patients with complicated UI.	Strong
Monitor PVR in patients receiving treatments that may cause or worsen voiding dysfunction, including surgery for SUI.	Strong

Urodynamics

Recommendations	Strength rating
(NB: Concerning only neurologically intact adults with UI)	
When performing urodynamics in patients with UI adhere to 'Good Urodynamic Practice' standards as described by the International Continence Society: • attempt to replicate the patient's symptoms; • check recordings for quality control; • interpret results in the context of the clinical problem; • remember there may be physiological variability within the same individual.	Strong
Do not routinely carry out urodynamics when offering treatment for uncomplicated SUI.	Strong
Perform urodynamics if the findings may change the choice of invasive treatment.	Weak
Do not use urethral pressure profilometry or leak point pressure to grade severity of incontinence.	Strong

Pad testing

Recommendations	Strength rating
Use a pad test of standardised duration and activity protocol.	Strong
Use a pad test when quantification of UI is required.	Weak

Imaging

Recommendation	Strength rating
Do not routinely carry out imaging of the upper or lower urinary tract as part of the assessment of UI.	Strong

Disease Management

Conservative management

In clinical practice, it is a convention that non-surgical therapies are tried first because they usually carry the least risk of harm. Conventional medical practice encourages the use of simple, relatively harmless, interventions before resorting to those associated with higher risks.

Simple medical interventions

Correction of underlying disease/cognitive impairment

Urinary incontinence, especially in the elderly, has been associated with multiple comorbid conditions including:

- cardiac failure;
- chronic renal failure;
- diabetes;
- chronic obstructive pulmonary disease;
- neurological disease including stroke and multiple sclerosis;
- general cognitive impairment;
- sleep disturbances, e.g. sleep apnoea;

- depression;
- metabolic syndrome.

Adjustment of medication

Although changing drug regimens for underlying disease may be considered as a possible early intervention for UI, there is very little evidence of benefit. There is also a risk that stopping or altering medication may result in more harm than benefit.

Recommendations	Strength rating
Take a drug history from all patients with UI.	Strong
Review any new medication associated with the development or worsening of UI.	Weak

Constipation

Studies have shown strong associations between constipation and UI. Constipation can be improved by behavioural, physical and medical treatments.

Recommendation	Strength rating
Advise adults with UI who also suffer from constipation about bowel management, in line with good medical practice.	Strong

Containment (pads etc.)

Recommendations	Strength rating
Inform adults with UI and/or their carers regarding available treatment options before deciding on containment alone.	Strong
Offer incontinence pads and/or containment devices for management of UI.	Strong

Lifestyle interventions

Examples of lifestyle factors that may be associated with UI

include obesity, smoking, level of physical activity and diet. Modification of these factors may improve UI.

Recommendations	Strength rating
Encourage overweight and obese adults with UI to lose weight and maintain weight loss.	Strong
Advise adults with UI that reducing caffeine intake may improve symptoms of urgency and frequency but not incontinence.	Strong
Review type and amount of fluid intake in patients with UI.	Weak
Provide smoking cessation strategies to patients with UI who smoke.	Strong

Behavioural and physical therapies

Recommendations	Strength rating
Offer prompted voiding for adults with incontinence, who are cognitively impaired.	Strong
Offer bladder training as a first-line therapy to adults with UUI or MUI.	Strong
Offer supervised intensive pelvic floor muscle training (PFMT), lasting at least three months, as a first-line therapy to women with SUI or MUI (including the elderly and post-natal).	Strong
Offer instruction on PFMT to men undergoing radical prostatectomy to speed-up recovery from UI.	Strong
Ensure that PFMT programmes are as intensive as possible.	Strong

Do not offer electrical stimulation with surface electrodes (skin, vaginal, anal) alone for the treatment of SUI.	Strong
Do not offer magnetic stimulation for the treatment of UI or overactive bladder in women.	Strong
Consider percutaneous tibial nerve stimulation as an option for improvement of UUI in women who have not benefited from antimuscarinic medication.	Strong

Conservative therapy in MUI

Recommendation	Strength rating
Treat the most bothersome symptom first in patients with MUI.	Weak

Pharmacological Management

Antimuscarinics

Recommendations	Strength rating
Offer antimuscarinic drugs for adults with UUI who failed conservative treatment.	Strong
Consider extended release formulations of antimuscarinics drugs, whenever possible.	Strong
If an antimuscarinic treatment proves ineffective, consider dose escalation or offering an alternative antimuscarinic formulation, or mirabegron, or a combination.	Strong

Encourage early review (of efficacy and side effects) of patients on antimuscarinic medication for UUI.	Strong

Mirabegron

Recommendation	Strength rating
Offer antimuscarinic drugs or mirabegron to adults with UUI who failed conservative treatment.	Strong

Antimuscarinic drugs in the elderly

Recommendation	Strength rating
Use long-term antimuscarinic treatment with caution in elderly patients especially those who are at risk of, or have, cognitive dysfunction.	Strong

Drugs for SUI

Recommendations	Strength rating
Offer Duloxetine in selected patients with symptoms of SUI when surgery is not indicated.	Strong
Initiate and withdraw duloxetine using dose titration because of high risk of adverse events.	Strong

Oestrogen

Recommendations	Strength rating
Offer long-term vaginal oestrogen therapy to post-menopausal women with UI and symptoms of vulvo-vaginal atrophy.	Strong
In women with a history of breast cancer, the treating oncologist should be consulted.	Weak
Discuss alternative hormone replacement therapies with women taking oral conjugated equine oestrogen as hormone replacement therapy who develop or experience worsening UI.	Strong
Advise women who are taking systemic oestradiol who suffer from UI that stopping the oestradiol is unlikely to improve their UI.	Strong

Desmopressin

Recommendations	Strength rating
Consider offering desmopressin to patients requiring occasional short-term relief from daytime UI and inform them that this drug is not licensed for this indication.	Strong
Monitor plasma sodium levels in patients on desmopressin.	Strong
Do not use desmopressin for long-term control of UI.	Strong

Drug treatment in MUI

Recommendations	Strength rating
Treat the most bothersome symptom first in patients with MUI.	Weak
Offer antimuscarinic drugs or beta 3 agonists to patients with urgency-predominant MUI.	Strong
Consider offering duloxetine to patients with MUI unresponsive to other conservative treatments and who are not seeking cure.	Strong

Surgical Management

The section considers surgical options for the following situations:

- Women with uncomplicated SUI; this means no history of previous surgery, no neurological lower urinary tract dysfunction (LUTD), no bothersome genitourinary prolapse, and those not considering further pregnancy.
- Women with complicated SUI. Neurogenic LUTD is reviewed in the EAU Guidelines on Neuro-urology.
- Associated genitourinary prolapse has been included in these Guidelines in terms of treating the incontinence, but no attempt has been made to comment on treatment of prolapse itself.
- Men with SUI, mainly those with post-prostatectomy incontinence without neurological disease affecting the lower urinary tract.
- Patients with refractory DO (detrusor overactivity) incontinence.

Women with uncomplicated SUI

Recommendations	Strength rating
Offer a mid-urethral sling to women with uncomplicated SUI.	Strong
Inform women of the unique complications associated with each individual procedure.	Strong
Inform women who are being offered a single-incision sling that long-term efficacy remains uncertain.	Strong
Inform women undergoing colposuspension that there is a longer duration of surgery, hospital stay and recovery, as well as a high risk of development of pelvic organ prolapse and voiding dysfunction post-operatively.	Strong
Inform older women with SUI about the increased risks associated with surgery, including the lower probability of success.	Weak
Inform women that any vaginal surgery may have an impact on sexual function, which is generally positive.	Weak
Only offer new devices, for which there is no level 1 evidence base, as part of a structured research programme.	Strong
Only offer adjustable mid-urethral sling as a primary surgical treatment for SUI as part of a structured research programme.	Strong
Offer bulking agents to women with SUI who request a low-risk procedure with the understanding that repeat injections are likely and long-term durability is not established.	Strong

Women with complicated SUI

Recommendations	Strength rating
Management of complicated SUI should only be offered in expert centres*.	Weak
Base the choice of surgery for recurrent SUI on careful evaluation of the individual patient including multichannel urodynamics and imaging as appropriate.	Weak
Inform women with recurrent SUI that the outcome of a surgical procedure, when used as a second-line treatment, is generally inferior to its use as a first-line treatment, both in terms of reduced efficacy and increased risk of complications.	Weak
Consider secondary synthetic sling, colposuspension or autologous sling as first options for women with complicated SUI.	Weak
Inform women receiving artificial urinary sphincter (AUS) or Adjustable Compression device (ACT©) that although cure is possible, even in expert centres, there is a high risk of complications, mechanical failure, or a need for explantation.	Weak

** Expert centres refers to the comments on surgeon volume in the introduction to the surgical chapter.*

Women with both stress urinary incontinence and pelvic organ prolapse

Recommendations for women requiring surgery for bothersome pelvic organ prolapse who have symptomatic or unmasked SUI.	**Strength rating**
Offer simultaneous surgery for pelvic organ prolapse and SUI.	Strong
Inform women of the increased risk of adverse events with combined surgery compared to prolapse surgery alone.	Strong
Recommendations for women requiring surgery for bothersome pelvic organ prolapse without symptomatic or unmasked SUI.	
Inform women that there is a risk of developing *de novo* SUI after prolapse surgery.	Strong
Warn women that the benefit of surgery for SUI may be outweighed by the increased risk of adverse events with combined surgery compared to prolapse surgery alone.	Strong

Urethral diverticulum

Recommendation	Strength rating
Symptomatic urethral diverticula should be completely surgically removed.	Strong

Men with SUI

Recommendations	Strength rating
Offer duloxetine only to hasten recovery of continence after prostate surgery but inform the patient about the possible adverse events and that its use is off label for this indication in most European countries.	Weak
Only offer bulking agents to men with mild post-prostatectomy UI who desire temporary relief of UI symptoms.	Weak
Do not offer bulking agents to men with severe post-prostatectomy UI.	Weak
Offer fixed slings to men with mild-to-moderate* post-prostatectomy UI.	Weak
Warn men that severe UI, prior pelvic radiotherapy or urethral stricture surgery, may worsen the outcome of fixed male sling surgery.	Weak
Offer artificial urinary sphincter (AUS) to men with moderate-to-severe post-prostatectomy incontinence.	Weak
Implantation of AUS or ProACT® for men should only be offered in expert centres.	Weak

Warn men receiving AUS or ProACT® that, although cure can be achieved, even in expert centres, there is a high risk of complications, mechanical failure or a need for explantation.	Weak
Do not offer non-circumferential compression device (ProACT®) to men who have had pelvic radiotherapy.	Weak

** The terms mild and moderate post-prostatectomy UI remain undefined.*

Surgical interventions for refractory detrusor overactivity

Intravesical injection of botulinumtoxin A

Recommendations	Strength rating
Offer bladder wall injections of onabotulinum toxin A (100 U) to patients with UUI refractory to conservative therapy (such as pelvic floor muscle training and/or drug treatment).	Strong
Warn patients of the limited duration of response, risk of urinary tract infection and the possible prolonged need to self-catheterise (ensure that they are willing and able to do so).	Strong

Sacral nerve stimulation (neuromodulation)

Recommendation	Strength rating
Offer sacral nerve modulation to patients who have UUI refractory to antimuscarinic therapy.	Strong

Cystoplasty/urinary diversion

Recommendations	Strength rating
Offer augmentation cystoplasty to patients with UI who have failed all other treatment options.	Weak
Inform patients undergoing augmentation cystoplasty of the high risk of having to perform clean intermittent self-catheterisation (ensure they are willing and able to do so) and that they need lifelong surveillance.	Weak
Do not offer detrusor myectomy as a treatment for UI.	Weak
Only offer urinary diversion to patients who have failed less invasive therapies for the treatment of UI and who will accept a stoma and have been warned about the possible small risk of malignancy.	Weak

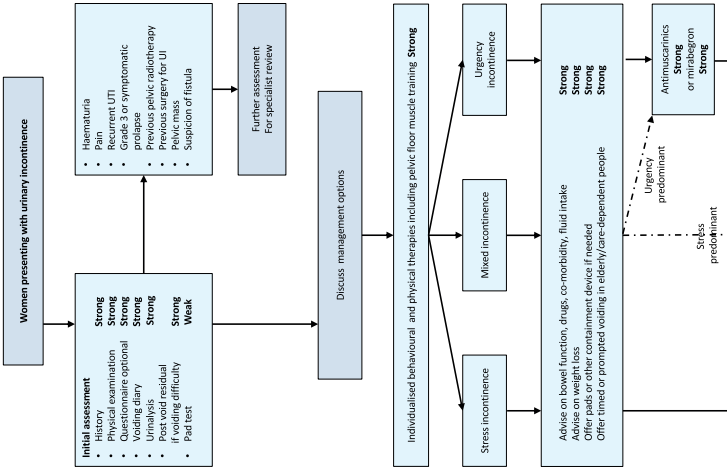
Surgery in patients with MUI

Recommendations	Strength rating
Treat the most bothersome symptom first in patients with MUI.	Weak
Warn patients with MUI that surgery is less likely to be successful than surgery for SUI alone.	Strong
Inform women with MUI that one single treatment may not cure UI; it may be necessary to treat other components of the incontinence problem as well as the most bothersome symptom.	Strong

Surgery for UI in the elderly

Recommendation	Strength rating
Inform older women with UI about the increased risks associated with surgery (including onabotulinum toxin A injection), together with the lower probability of benefit.	Weak

Figure 1: Women presenting with urinary incontinence



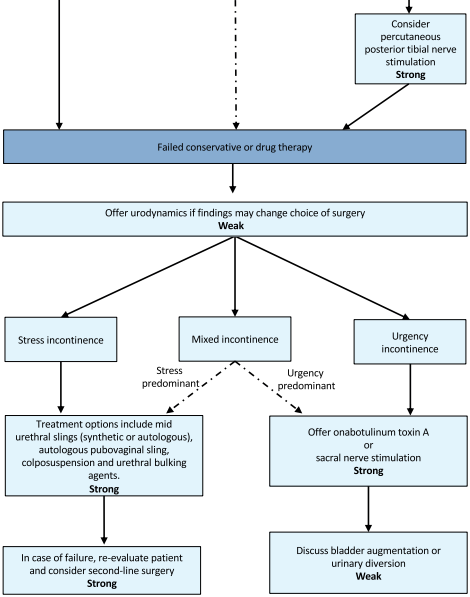
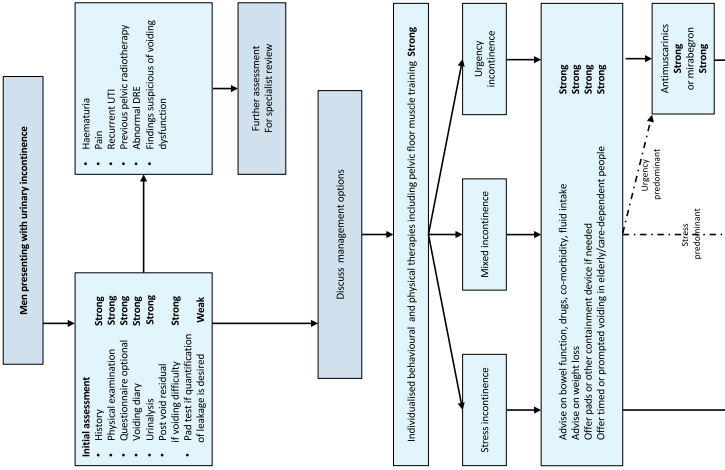
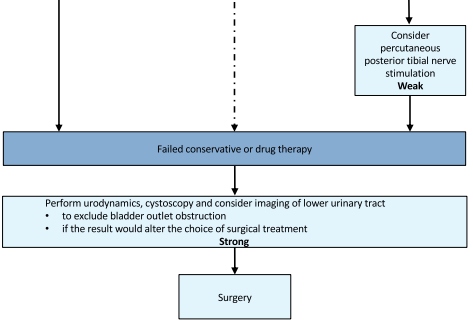

Consider percutaneous posterior tibial nerve stimulation
Strong
Failed conservative or drug therapy
Offer urodynamics if findings may change choice of surgery
Weak
Stress incontinence
Mixed incontinence
Urgency incontinence
Stress predominant
Urgency predominant
Treatment options include mid urethral slings (synthetic or autologous), autologous pubovaginal sling, colposuspension and urethral bulking agents.
Strong
Offer onabotulinum toxin A or sacral nerve stimulation
Strong
In case of failure, re-evaluate patient and consider second-line surgery
Strong
Discuss bladder augmentation or urinary diversion
Weak

Figure 2: Men presenting with urinary incontinence




Consider percutaneous posterior tibial nerve stimulation
Weak
Failed conservative or drug therapy
Perform urodynamics, cystoscopy and consider imaging of lower urinary tract
• to exclude bladder outlet obstruction
• if the result would alter the choice of surgical treatment
Strong
Surgery

Non Obstetric Urinary Fistula*

Recommendations	Strength rating
General	
Surgeons undertaking complex pelvic surgery should be competent at identifying, preserving and repairing the ureter.	Weak
Do not routinely use ureteric stents as prophylaxis against injury during routine gynaecological surgery.	Weak
Suspect ureteric injury or fistula in patients following pelvic surgery if a fluid leak or pelvicalyceal dilatation occurs post-operatively or if drainage fluid contains high levels of creatinine.	Weak
Suspect uretero-arterial fistula in patients presenting with haematuria with a history of relevant surgery.	Weak
Use three dimensional imaging techniques to diagnose and localise urinary fistulae.	Weak
Manage upper urinary tract fistulae by conservative or endoluminal technique where such expertise and facilities exists.	Weak
Surgical principles	
Surgeons involved in fistula surgery should have appropriate training, skills, and experience to select an appropriate procedure for each patient.	Weak
Attention should be given as appropriate to skin care, nutrition, rehabilitation, counselling and support prior to, and following, fistula repair.	Weak

If a vesicovaginal fistula is diagnosed within six weeks of surgery, consider indwelling catheterisation for a period of up to twelve weeks after the causative event.	Weak
Tailor the timing of fistula repair to the individual patient and surgeon requirements once any oedema, inflammation, tissue necrosis, or infection, are resolved.	Weak
Where concurrent ureteric re-implantation or augmentation cystoplasty are required, the abdominal approach is necessary.	Weak
Ensure that the bladder is continuously drained following fistula repair until healing is confirmed (expert opinion suggests: 10-14 days for simple and/or post-surgical fistulae; 14-21 days for complex and/or post-radiation fistulae).	Weak
Where urinary and/or faecal diversions are required, avoid using irradiated tissue for repair.	Weak
Use interposition grafts when repair of radiation associated fistulae is undertaken.	Weak
In patients with intractable UI from radiation-associated fistula, where life expectancy is very short, consider performing ureteric occlusion.	Weak
Repair persistent ureterovaginal fistula by an abdominal approach using open, laparoscopic or robotic techniques according to availability and competence.	Weak

Consider palliation by nephrostomy tube diversion and endoluminal distal ureteric occlusion for patients with ureteric fistula associated with advanced pelvic cancer and poor performance status.	Weak
Urethrovaginal fistulae should preferably be repaired by a vaginal approach.	Weak

** These recommendations are derived from the ICUD 2013 review and have not been fully validated by the EAU Guidelines Office methodology.*

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-01-1), available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines/.

EAU GUIDELINES ON NEURO-UROLOGY

(Limited text update March 2018)

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Introduction

Neuro-urological disorders can cause a variety of long-term complications; the most dangerous being damage of renal function. Treatment and intensity of follow-up examinations are based on the type of neuro-urological disorder and the underlying cause.

Terminology

The terminology used and the diagnostic procedures outlined in this document follow those published by the International Continence Society (ICS).

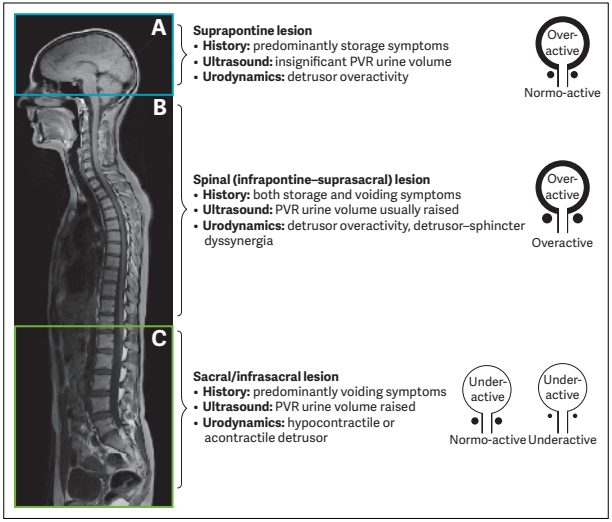
Risk factors and epidemiology

All central and peripheral neurological disorders carry a high risk of causing functional disturbances of the urinary tract.

Classification

The pattern of lower urinary tract (LUT) dysfunction following neurological disease is determined by the site and nature of the lesion. A very simple classification system, for use in daily clinical practice, to decide on the appropriate therapeutic approach is provided in Figure 1.

Figure 1: Patterns of lower urinary tract dysfunction following neurological disease



The pattern of LUT dysfunction following neurological disease is determined by the site and nature of the lesion. Panel A denotes the region above the pons, panel B the region between the pons and sacral cord and panel C the sacral cord and infrasacral region. Figures on the right show the expected dysfunctional states of the detrusor-sphincter system. Figure adapted from Panicker et al. with permission from Elsevier. PVR = post-void residual.

Diagnostic evaluation

Early diagnosis and treatment are essential in both congenital and acquired neuro-urological disorders, even in the presence

of normal neurological reflexes. Neuro-urological disorders can be the presenting feature of neurological pathology and early intervention can prevent irreversible deterioration of the lower and upper urinary tract.

Patient assessment

Diagnosis of neuro-urological disorders should be based on a comprehensive assessment of neurological and non-neurological conditions. Initial assessment should include a detailed history, physical examination, and urinalysis.

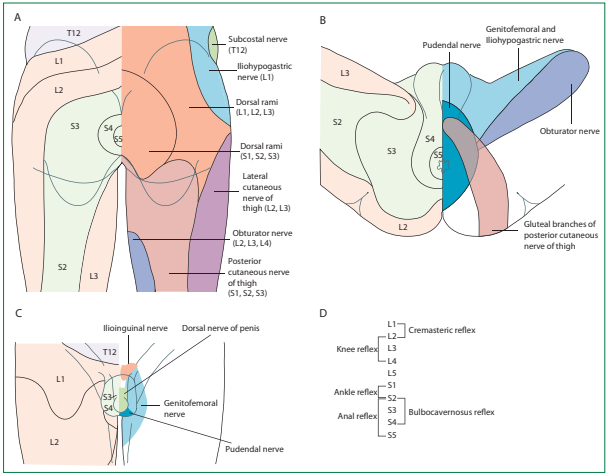
History

An extensive general and specific history is mandatory and should concentrate on past and present symptoms, disorders of the urinary tract as well as bowel, sexual and neurological function. Special attention should be paid to possible warning signs and symptoms (e.g. pain, infection, haematuria, fever) that warrant further investigation.

Physical examination

The neurological status should be described as completely as possible. All sensations and reflexes in the urogenital area must be tested, including detailed testing of the anal sphincter and pelvic floor functions (Figure 2). Availability of this clinical information is essential for the reliable interpretation of subsequent diagnostic investigations.

Figure 2: Lumbosacral dermatomes, cutaneous nerves, and reflexes



The physical examination includes testing sensations and reflexes mediated through the lower spinal cord. Abnormal findings would suggest a lesion affecting the lumbosacral segments; mapping out distinct areas of sensory impairment helps to further localise the site of lesion. Distribution of dermatomes (areas of skin mainly supplied by a single spinal nerve) and cutaneous nerves over the perianal region and back of the upper thigh (A), the perineum (B), male external genitalia (C) and root values of lower spinal cord reflexes (D). Figure adapted from Panicker et al., with parts A-C adapted from Standring, both with permission from Elsevier.

Recommendations for history taking and physical examination

Recommendations	Strength rating
History taking	
Take an extensive general history, concentrating on past and present symptoms.	Strong
Take a specific history for each of the four mentioned functions - urinary, bowel, sexual and neurological.	Strong
Pay special attention to the possible existence of alarm signs (e.g. pain, infection, haematuria, fever) that warrant further specific diagnosis.	Strong
Assess quality of life when evaluating and treating the neuro-urological patient.	Strong
Use available validated tools including the Qualiveen and I-QoL for urinary symptoms and the QoL-BM for bowel dysfunction in multiple sclerosis and spinal cord injury patients. In addition, generic (SF-36 or KHQ) questionnaires can be used.	Strong
Use MSISQ-15 and MSISQ-19 to evaluate sexual function in multiple sclerosis patients.	Strong
Physical examination	
Acknowledge individual patient disabilities when planning further investigations.	Strong
Describe the neurological status as completely as possible, sensations and reflexes in the urogenital area must all be tested.	Strong
Test the anal sphincter and pelvic floor functions.	Strong

Perform urinalysis, blood chemistry, bladder diary, residual and free flowmetry, incontinence quantification and urinary tract imaging.	Strong

I-QoL = Incontinence Quality of Life Instrument; OoL-BM = Quality of Life Bowel Management scoring tool; KHQ = King's Health Questionnaire; SF-36 = Short Form 36-item Health Survey Questionnaires; MSISQ 15/19 = Multiple Sclerosis Intimacy and Sexuality Questionnaire 15/19 question version.

Urodynamic tests

Bladder diaries are considered a valuable diagnostic tool in patients with neuro-urological disorders. A bladder diary should be recorded for at least two to three days. Uroflowmetry and ultrasound assessment of post-void residual should be repeated at least two or three times in patients able to void. Invasive urodynamic studies comprise mandatory assessment tools to determine the exact type of neuro-urological disorder. Video-urodynamics combines filling cystometry and pressure flow studies with radiological imaging. Currently, video-urodynamics is considered to provide the most comprehensive information for evaluating neuro-urological disorders.

Recommendations for urodynamics and uro-neurophysiology

Recommendations	Strength rating
Perform a urodynamic investigation to detect and specify lower urinary tract (dys-)function, use same session repeat measurement as it is crucial in clinical decision making.	Strong

Non-invasive testing is mandatory before invasive urodynamics is planned.	Strong
Use video-urodynamics for invasive urodynamics in neuro-urological patients. If this is not available, then perform a filling cystometry continuing into a pressure flow study.	Strong
Use a physiological filling rate and body-warm saline.	Strong

Treatment

The primary aims and their prioritisation when treating neuro-urological disorders are:

1. protection of the upper urinary tract;
2. improvement of urinary continence;
3. restoration of (parts of) LUT function;
4. improvement of the patient's QoL.

Further considerations are the patient's disability, cost-effectiveness, technical complexity, and possible complications.

Conservative treatment

Assisted bladder emptying

Triggered reflex voiding is not recommended as there is a risk of pathologically elevated bladder pressures. Only in the case of absence, or surgically reduced outlet obstruction it may be an option.

Caution: bladder compression techniques to expel urine (Credé) and voiding by abdominal straining (Valsalva manoeuvre) create high pressures and are potentially hazardous, and their use should be discouraged.

Rehabilitation

In selected patients, pelvic floor muscle exercises, pelvic floor electro-stimulation, and biofeedback might be beneficial.

External appliances

Social continence for the incontinent patient can be achieved using an appropriate method of urine collection.

Medical therapy

A single, optimal, medical therapy for patients with neuro-urological symptoms is not yet available. Muscarinic receptor antagonists are the first-line choice for treating neuro-urological disorders.

Recommendations on drug treatment

Recommendations	Strength rating
Use antimuscarinic therapy as the first-line medical treatment for neurogenic detrusor overactivity.	Strong
Offer intravesical oxybutynin to neurogenic detrusor overactivity patients with poor tolerance to the oral route.	Strong
Prescribe α-blockers to decrease bladder outlet resistance.	Strong
Do not prescribe parasympathomimetics for underactive detrusor.	Strong

Recommendations for catheterisation

Recommendations	Strength rating
Use intermittent catheterisation, whenever possible aseptic technique, as a standard treatment for patients who are unable to empty their bladder.	Strong
Thoroughly instruct patients in the technique and risks of intermittent catheterisation.	Strong
Avoid indwelling transurethral and supra-pubic catheterisation whenever possible.	Strong

Recommendations for minimal invasive treatment

Recommendations	Strength rating
Use botulinum toxin injection in the detrusor to reduce neurogenic detrusor overactivity in multiple sclerosis or spinal cord injury patients if antimuscarinic therapy is ineffective.	Strong
Bladder neck incision is effective in a fibrotic bladder neck.	Strong

Recommendations for surgical treatment

Recommendations	Strength rating
Perform bladder augmentation in order to treat refractory neurogenic detrusor overactivity.	Strong
Place an autologous urethral sling in female patients with neurogenic stress urinary incontinence who are able to self-catheterise.	Strong
Insert an artificial urinary sphincter in male patients with neurogenic stress urinary incontinence.	Strong

Urinary tract infections (UTI)

Patients with neuro-urological disorders, especially those with spinal cord injury, may have other signs and symptoms in addition to, or instead of, traditional signs and symptoms of a UTI in able-bodied individuals.

Recommendations for the treatment of UTI

Recommendations	Strength rating
Do not screen for or treat asymptomatic bacteriuria in patients with neuro-urological disorders.	Strong
Avoid the use of long-term antibiotics for recurrent urinary tract infections (UTIs).	Strong
In patients with recurrent UTI, optimise treatment of neuro-urological symptoms and remove foreign bodies (e.g. stones, indwelling catheters) from the urinary tract.	Strong

Individualise UTI prophylaxis in patients with neuro-urological disorders as there is no optimal prophylactic measure available.	Strong

Sexual (dys)function and fertility

Patients with neurological disease often suffer from sexual dysfunction, which frequently impairs QoL.

Recommendations for erectile dysfunction and male fertility

Recommendations	Strength rating
Prescribe oral phosphodiesterase type 5 inhibitors as first-line medical treatment in neurogenic erectile dysfunction.	Strong
Give intracavernous injections of vasoactive drugs (alone or in combination) as second-line medical treatment in neurogenic erectile dysfunction.	Strong
Offer mechanical devices such as vacuum devices and rings to patients with neurogenic erectile dysfunction.	Strong
Perform vibrostimulation and transrectal electroejaculation for sperm retrieval in men with spinal cord injury.	Strong
Perform microsurgical epididymal sperm aspiration, testicular sperm extraction and intracytoplasmic sperm injection after failed vibrostimulation and/or transrectal electroejaculation in men with spinal cord injury.	Strong

Counsel men with spinal cord injury at or above Th 6 and fertility clinics about the potentially life-threatening condition of autonomic dysreflexia.	Strong

Recommendations on female sexuality and fertility

Recommendations	Strength rating
Do not offer medical therapy for the treatment of neurogenic sexual dysfunction in women.	Strong
Take a multidisciplinary approach, tailored to individual patient's needs and preferences, in the management of fertility, pregnancy and delivery in women with neurological diseases.	Strong

Follow-up

Neuro-urological disorders are often unstable and the symptoms may vary considerably, even within a relatively short period. Regular follow-up is therefore necessary.

Recommendations for follow-up

Recommendations	Strength rating
Assess the upper urinary tract at regular intervals in high risk patients.	Strong
Perform a physical examination and urine laboratory every year in high risk patients.	Strong
Any significant clinical changes should instigate further, specialised, investigation.	Strong
Perform urodynamic investigation as a mandatory baseline diagnostic intervention in high-risk patients at regular intervals.	Strong

Summary

Neuro-urological disorders present a multifaceted pathology. Extensive investigation and a precise diagnosis are required before the clinician can initiate individualised therapy. Treatment must take into account the patient's medical and physical condition and expectations with regard to his/her future social, physical, and medical situation.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-02-8) available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines.

EAU GUIDELINES ON MALE SEXUAL DYSFUNCTION: Erectile Dysfunction and Premature Ejaculation

(Limited text update March 2018)

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ERECTILE DYSFUNCTION

Introduction

Erectile dysfunction (ED) is defined as the persistent inability to attain and maintain an erection sufficient to permit satisfactory sexual performance. Erectile dysfunction may affect physical and psychosocial health and may have a significant impact on the quality of life (QoL) of sufferers and their partners. There is increasing evidence that ED can also be an early manifestation of coronary artery and peripheral vascular disease; therefore, ED should not be regarded only as a QoL issue, but also as a potential warning sign of cardiovascular disease (CVD).

Table 1: Pathophysiology of erectile dysfunction

Vasculogenic
Recreational habits (e.g. cigarette smoking)
Lack of regular physical exercise
Obesity
Cardiovascular diseases (e.g. hypertension, coronary artery disease; peripheral vasculopathy, etc.)
Type 1 and 2 diabetes mellitus; hyperlipidaemia; metabolic syndrome; hyperhomocysteinemia, etc.
Major pelvic surgery (radical prostatectomy) or radiotherapy (pelvis or retroperitoneum)
Neurogenic
Central causes
Degenerative disorders (e.g., multiple sclerosis, Parkinson's disease, multiple atrophy, etc.)
Spinal cord trauma or diseases
Stroke
Central nervous system tumours
Peripheral causes
Type 1 and 2 diabetes mellitus
Chronic renal failure; chronic liver failure
Polyneuropathy
Surgery (major surgery of pelvis/retroperitoneum) or radiotherapy (pelvis or retroperitoneum)
Surgery of the urethra (urethral stricture, urethroplasty, etc.)
Anatomical or structural
Hypospadias; epispadias; micropenis
Phimosis
Peyronie's disease
Penile cancer (other tumors of the external genitalia)

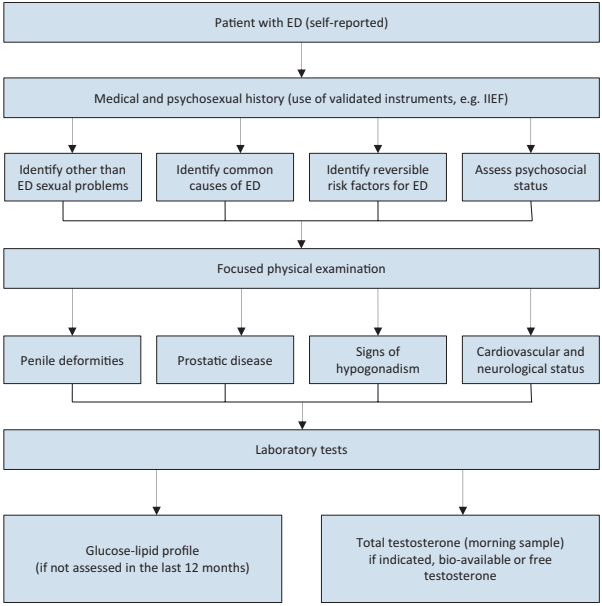
Hormonal
Diabetes Mellitus; Metabolic Syndrome;
Hypogonadism (any type)
Hyperprolactinaemia
Hyper- and hypothyroidism
Hyper- and hypocortisolism (Cushing's disease, etc.)
Panhypopituitarism and multiple endocrine disorders
Mixed pathophysiology pathways
Chronic systemic diseases (e.g., diabetes mellitus; hypertension; metabolic syndrome; chronic renal failure; chronic liver disorders; hyperhomocysteinemia; obstructive sleep apnoea; etc.)
Psoriasis; gouty arthritis; ankylosing spondylitis; non-alcoholic fatty liver; chronic periodontitis; open-angle glaucoma; inflammatory bowel disease
Iatrogenic causes (e.g. transrectal ultrasonography-guided prostate biopsy, etc.)
Drug-induced
Antihypertensives (e.g., thiazide diuretics, beta-blockers, etc.)
Antidepressants (selective serotonin re-uptake inhibitors, tricyclics)
Antipsychotics (e.g., neuroleptics, etc.)
Antiandrogens (GnRH analogues and antagonists; 5-ARIs)
Recreational drugs (e.g., alcohol, heroin, cocaine, marijuana, methadone, synthetic drugs, anabolic steroids, etc.)
Psychogenic
Generalised type (e.g., lack of arousability and disorders of sexual intimacy)
Situational type (e.g., partner-related, performance-related issues or due to distress)

Trauma
Penile fracture
Pelvic fractures

GnRH = Gonadotropin-releasing hormone;
5-ARIs = 5α-Reductase inhibitors

Diagnostic evaluation

Figure 1: Minimal diagnostic evaluation (basic work-up) in patients with erectile dysfunction



ED = erectile dysfunction; IIEF = International Index of Erectile Function.

Table 2: Cardiac risk stratification (based on 2nd Princeton Consensus)

Low-risk category	Intermediate-risk category	High-risk category
Asymptomatic, < 3 risk factors for CAD (excluding sex)	≥ 3 risk factors for CAD (excluding sex)	High-risk arrhythmias
Mild, stable angina (evaluated and/or being treated)	Moderate, stable angina	Unstable or refractory angina
Uncomplicated previous MI	Recent MI (> 2, < 6 weeks)	Recent MI (< 2 weeks)
LVD/CHF (NYHA class I or II)	LVD/CHF (NYHA class III)	LVD/CHF (NYHA class IV)
Post-successful coronary revascularisation	Non-cardiac sequelae of atherosclerotic disease (e.g., stroke, peripheral vascular disease)	Hypertrophic obstructive and other cardiomyopathies
Controlled hypertension		Uncontrolled hypertension
Mild valvular disease		Moderate-to-severe valvular disease

CAD = coronary artery disease; CHF = congestive heart failure; LVD = left ventricular dysfunction; MI = myocardial infarction; NYHA = New York Heart Association.

Table 3: Indications for specific diagnostic tests

Primary ED (not caused by organic disease or psychogenic disorder).
Young patients with a history of pelvic or perineal trauma, who could benefit from potentially curative revascularisation surgery or angioplasty.
Patients with penile deformities which might require surgical correction (e.g., Peyronie's disease, congenital penile curvature).
Patients with complex psychiatric or psychosexual disorders.
Patients with complex endocrine disorders.
Specific tests may be indicated at the request of the patient or his partner.
Medico-legal reasons (e.g., implantation of penile prosthesis to document end stage ED, sexual abuse).

Table 4: Specific diagnostic tests

Nocturnal Penile Tumescence and Rigidity using Rigiscan®.
Vascular studies: - Intracavernous vasoactive drug injection. - Penile Dynamic Duplex Ultrasonography. - Penile Dynamic Infusion Cavernosometry and Cavernosography. - Internal pudendal arteriography.
Neurological studies (e.g., bulbocavernosus reflex latency, nerve conduction studies).
Endocrinological studies.
Specialised psychodiagnostic evaluation.

Recommendations for the diagnosis of erectile dysfunction	Strength rating
Take a comprehensive medical and sexual history in every patient.	Strong
Use a validated questionnaire related to erectile dysfunction to assess all sexual function domains and the effect of a specific treatment modality.	Strong
Include a physical examination in the initial assessment of men with erectile dysfunction (ED) to identify underlying medical conditions and comorbid genital disorders that may be associated with ED.	Strong
Assess routine laboratory tests, including glucose-lipid profile and total testosterone, to identify and treat any reversible risk factors and lifestyle factors that can be modified.	Strong
Include specific diagnostic tests in the initial evaluation only in the presence of the conditions presented in Table 3.	Strong

Figure 2: Management algorithm for erectile dysfunction

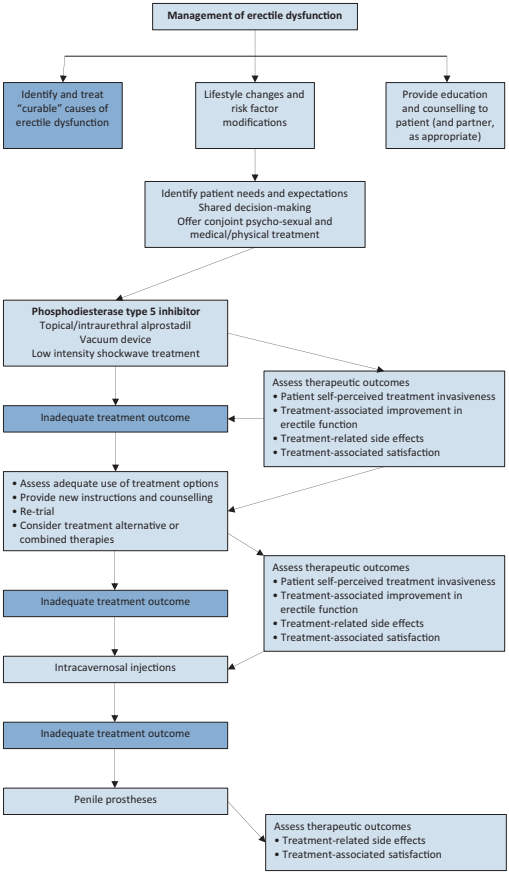


Table 5: Summary of the key pharmacokinetic data for the four PDE5 inhibitors currently EMA-approved to treat erectile dysfunction*

Parameter	Sildenafil, 100 mg	Tadalafil, 20 mg	Vardenafil, 20 mg	Avanafil 200mg
C_{max}	560 µg/L	378 µg/L	18.7 µg/L	5.2 µg/L
T_{max} (median)	0.8-1 hours	2 hours	0.9 hours	0.5-0.75 hours
T1/2	2.6-3.7 hours	17.5 hours	3.9 hours	6-17 hours
AUC	1,685 µg.h/L	8,066 µg.h/L	56.8 µg.h/L	11.6 µg.h/L
Protein binding	96%	94%	94%	99%
Bioavailability	41%	NA	15%	8-10%

** Fasted state, higher recommended dose. Data adapted from EMA statements on product characteristics.*
C_{max}: maximal concentration, T_{max}: time-to-maximum plasma concentration; T1/2: plasma elimination half-time; AUC: area under curve or serum concentration time curve.

Table 6: Common adverse events of the four PDE5 inhibitors currently EMA-approved to treat erectile dysfunction*

Adverse event	Sildenafil	Tadalafil	Vardenafil	Avanafil 200mg
Headache	12.8%	14.5%	16%	9.3%
Flushing	10.4%	4.1%	12%	3.7%
Dyspepsia	4.6%	12.3%	4%	uncommon
Nasal congestion	1.1%	4.3%	10%	1.9%
Dizziness	1.2%	2.3%	2%	0.6%
Abnormal vision	1.9%		< 2%	none
Back pain		6.5%		< 2%
Myalgia		5.7%		< 2%

** Adapted from EMA statements on product characteristics.*

Table 7: Penile prostheses models available on the market

Semi-rigid prostheses	Inflatable prostheses	
	Two-piece	Three piece
Spectra ™ [AMS]	Ambicor™ [AMS]	Titan OTR ™ (One Touch Release) [Coloplast]
Genesis ™ [Mentor]		Titan OTR NB ™ (Narrow base) [Coloplast]
		Titan Zero Degree ™
Tube ™ [Promedon]		AMS 700 CX ™ [Boston Scientific]
ZSI 100 ™ [Zephyr]		AMS 700 LGX ™ [Boston Scientific]
Virilis II ™ [Subrini]		AMS 700 CXR ™ [Boston Scientific]
		ZSI 475 ™ [Zephyr]

Recommendations for the treatment of erectile dysfunction	Strength rating
Enact lifestyle changes and risk factor modification prior to or accompanying erectile dysfunction (ED) treatment.	Strong
Support the resumption of sexual activity through pro-erectile treatments at the earliest opportunity after radical prostatectomy.	Strong
Treat a curable cause of ED first, when found.	Weak
Use phosphodiesterase type 5 inhibitors (PDE5Is) as first-line therapy.	Strong

Assess all patients for inadequate/incorrect information about the mechanism of action and the ways in which drugs should be taken, since they are the main causes of a lack of response to PDE5Is.	Weak
Use vacuum erection devices as a first-line therapy in well-informed older patients with infrequent sexual intercourse and comorbidity requiring non-invasive, drug-free management of ED.	Weak
Use low intensity shockwave therapy in mild organic ED patients or poor responders to PDE5Is.	Weak
Use topical/intraurethral Alprostadil as an alternative to intracavernous injections in patients who prefer a less-invasive therapy.	Weak
Use intracavernous injections as second-line therapy.	Strong
Use implantation of a penile prosthesis as third-line therapy.	Strong

PREMATURE EJACULATION (PE)

Introduction

Although PE is a common male sexual dysfunction, it is poorly understood. Patients are often unwilling to discuss their symptoms and many physicians do not know about effective treatments. As a result, patients may be misdiagnosed or mistreated.

PE (lifelong and acquired) is a male sexual dysfunction characterised by the following:

1. Ejaculation that always or nearly always occurs prior to or within about 1 minute of vaginal penetration (lifelong PE) or

a clinically significant and bothersome reduction in latency time, often to about 3 minutes or less (acquired PE);
2. The inability to delay ejaculation on all or nearly all vaginal penetrations;
3. Negative personal consequences, such as distress, bother, frustration and/or the avoidance of sexual intimacy.

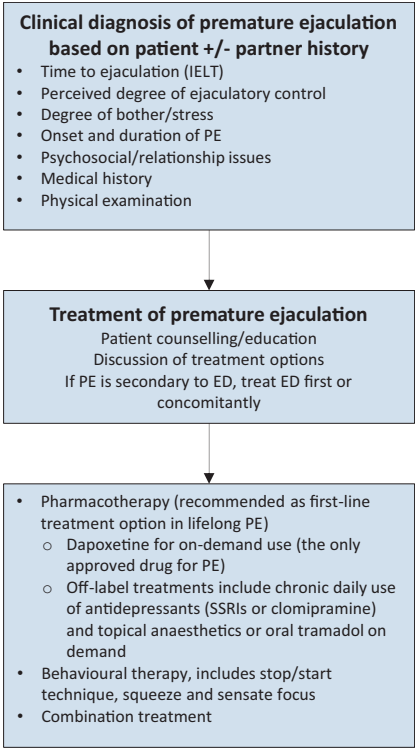
Diagnostic evaluation

Recommendations for the diagnostic evaluation of premature ejaculation	Strength rating
Perform the diagnosis and classification of premature ejaculation (PE) based on medical and sexual history, which should include assessment of intravaginal ejaculatory latency time (IELT) (self-estimated), perceived control, distress and interpersonal difficulty due to the ejaculatory dysfunction.	Strong
Do not use stopwatch-measured IELT in clinical practice.	Weak
Use patient-reported outcomes in daily clinical practice.	Weak
Include physical examination in the initial assessment of PE to identify anatomical, abnormalities that may be associated with PE or other sexual dysfunctions, particularly erectile dysfunction.	Strong
Do not perform routine laboratory or neurophysiological tests. They should only be directed by specific findings from history or physical examination.	Strong

Disease management

Recommendations for the treatment of premature ejaculation	Strength rating
Treat ED, other sexual dysfunction or genitourinary infection (e.g. prostatitis) first.	Strong
Use pharmacotherapy as first-line treatment of lifelong premature ejaculation (PE).	Strong
Use off-label topical anaesthetic agents as a viable alternative to oral treatment with selective serotonin re-uptake inhibitors (SSRIs).	Strong
Use tramadol on demand as a weak alternative to SSRIs.	Strong
Use PDE5Is alone or in combination with other therapies in patients with PE (without ED).	Strong
Use psychological/behavioural therapies in combination with pharmacological treatment in the management of acquired PE.	Weak

Figure 3: Management of premature ejaculation*



** Adapted from Lue et al. 2004.*
ED = erectile dysfunction; PE = premature ejaculation; IELT = intravaginal ejaculatory latency time; SSRI = selective serotonin receptor inhibitor.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-01-1), available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines.

EAU GUIDELINES ON PRIAPISM

(Limited text update March 2018)

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Guideline Associates: A. Parnham, E.C. Serefoglu

Introduction

Priapism is a pathological condition representing a true disorder of penile erection that persists for more than four hours and is beyond or unrelated to sexual interest or stimulation. Erections lasting up to four hours are defined by consensus as 'prolonged'. Priapism may occur at all ages.

Classification

Ischaemic priapism is a persistent erection marked by rigidity of the corpora cavernosa and by little or no cavernous arterial inflow, although often proximally there is a compensated high velocity picture with little blood flow distally. The patient typically complains of penile pain and clinical examination reveals a rigid erection.

Non-ischaemic priapism is a persistent erection caused by unregulated cavernous arterial inflow. The patient typically reports an erection that is not fully rigid and is not associated with pain although fully rigid erections may still occur with sexual stimulation.

Stuttering (recurrent or intermittent) priapism is a distinct condition that is characterised by repetitive and painful episodes of prolonged erections. Erections are often

self-limited with intervening periods of detumescence. These are analogous to repeated episodes of ischaemic (or low flow) priapism. The duration of the erectile episodes is generally shorter than in ischaemic priapism. The frequency and/or duration of these episodes is variable and a single episode can sometimes progress into a full-blown ischaemic priapism.

Ischaemic (Low-Flow or Veno-Occlusive) Priapism

Diagnostic Evaluation

Table 1: Key points when taking the history of priapism

Duration of erection
Presence and severity of pain
Previous episodes of priapism and method of treatment
Current erectile function, especially the use of any erectogenic therapies prescription or nutritional supplements
Medications and recreational drug use
Sickle cell disease, haemoglobinopathies, hypercoagulable states
Trauma to the pelvis, perineum, or penis

Table 2: Key findings in priapism

	Ischaemic priapism	Non-ischaemic priapism
Corpora cavernosa fully rigid	Usually	Seldom
Penile pain	Usually	Seldom
Abnormal penile blood gas	Usually	Seldom
Haematological abnormalities	Sometimes	Seldom
Recent intracavernosal injection	Sometimes	Sometimes
Perineal trauma	Seldom	Usually

Table 3: Typical blood gas values

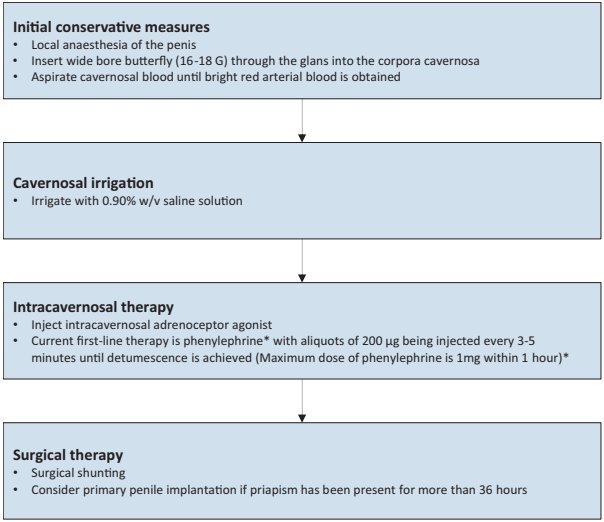
Source	pO_2 (mmHg)	pCO_2 (mmHg)	pH
Normal arterial blood (room air) [similar values are found in arterial priapism]	> 90	< 40	7.40
Normal mixed venous blood (room air)	40	50	7.35
Ischaemic priapism (first corporal aspirate)	< 30	> 60	< 7.25

Recommendations for the diagnosis of ischaemic priapism	Strength rating
Take a comprehensive history to establish the diagnosis which can help to determine the priapism subtype.	Strong
Include a physical examination of the genitalia, the perineum and the abdomen in the diagnostic evaluation.	Strong
For laboratory testing, include complete blood count, white blood count with blood cell differential, platelet count and coagulation profile. Direct further laboratory testing based on history, clinical and laboratory findings. In children with priapism, perform a complete evaluation of all possible causes.	Strong
Analyse the blood gas parameters from blood aspirated from the penis to differentiate between ischaemic and non-ischaemic priapism.	Strong
Perform colour duplex ultrasound of the penis and perineum for the differentiation between ischaemic and non-ischaemic priapism as an alternative or adjunct to blood gas analysis.	Strong
In cases of prolonged ischaemic priapism, use magnetic resonance imaging of the penis to predict smooth muscle viability and confirm erectile function restoration.	Strong
Perform selected pudendal arteriogram when embolisation is planned for the management of non-ischaemic priapism.	Strong

Disease Management

The treatment is sequential and the physician should move on to the next stage if the treatment fails.

Figure 1: Treatment of ischaemic priapism



** The dose of phenylephrine should be reduced in children. It can result in significant hypertension and should be used with caution in men with cardiovascular disease. Monitoring of pulse, blood pressure and electrocardiogram (ECG) is advisable in all patients during administration and for 60 minutes afterwards. Its use is contraindicated in men with a history of cerebro-vascular disease and significant hypertension.*

Table 4: Medical treatment of ischaemic priapism

Drug	Dosage/Instructions for use
Phenylephrine	• Intracavernous injection of 200 µg every three to five minutes. • Maximum dosage is 1 mg within one hour. • Lower doses are recommended in children and patients with severe cardiovascular disease.
Etilephrine	• Intracavernosal injection at a concentration of 2.5 mg in 1-2 mL normal saline.
Methylene blue	• Intracavernous injection of 50-100 mg, left for five minutes. It is then aspirated and the penis compressed for an additional five minutes.
Adrenaline	• Intracavernous injection of 2 mL of 1/100,000 adrenaline solution up to five times over a twenty minute period.
Terbutaline	• Oral administration of 5 mg for prolonged erections lasting more than 2.5 hours, after intracavernous injection of vasoactive agents.

Recommendations for the treatment of ischaemic priapism	Strength rating
Start management of ischaemic priapism as early as possible (within four to six hours) and follow a stepwise approach.	Strong

First, decompress the corpora cavernosa by penile aspiration until fresh red blood is obtained.	Weak
In priapism secondary to intracavernous injections of vasoactive agents, replace blood aspiration with intracavernous injection of a sympathomimetic drug as the first step.	Strong
In priapism that persists despite aspiration, proceed to the next step, which is intra-cavernous injection of a sympathomimetic drug.	Strong
In cases that persist despite aspiration and intracavernous injection of a sympathomi-metic drug, repeat these steps several times before considering surgical intervention.	Strong
Treat ischaemic priapism due to sickle cell anaemia in the same fashion as idiopathic ischaemic priapism. Provide other supportive measures (intravenous hydration, oxygen administration with alkalisation with bicarbonates, blood exchange transfusions), but do not delay initial treatment to the penis.	Strong
Proceed to surgical treatment only when blood aspiration and intracavernous injection of sympathomimetic drugs have failed or for priapism events lasting < 72 hours.	Strong
Perform distal shunt surgical procedures first followed by proximal procedures in case of failure.	Strong
Consider insertion of a penile prosthesis if priapism episode is > 36 hours after onset, or in cases for which all other interventions have failed.	Strong

Non-ischaemic (High-Flow or Arterial) Priapism

Diagnostic Evaluation

History

A comprehensive history is also mandatory in the diagnosis of non-ischaemic priapism and follows the same principles as described in Table 1.

Recommendations for the diagnosis of non-ischaemic priapism

The same recommendations as for ischaemic priapism apply.

Disease Management

Recommendations for the treatment of non-ischaemic priapism	Strength rating
Because non-ischaemic priapism is not an emergency, perform definitive management at the discretion of the treating physician.	Weak
Manage conservatively with the use of site specific perineal compression as the first step, especially in children. Consider androgen deprivation therapy only in adults.	Weak
Perform superselective arterial embolisation, using temporary material.	Strong
Repeat the procedure with temporary or permanent material for recurrent non-ischaemic priapism following selective arterial embolisation.	Weak
Reserve selective surgical ligation of a fistula as a final treatment option when embolisation has failed.	Weak

Stuttering (Recurrent or Intermittent) Priapism

Diagnostic Evaluation

History

A comprehensive history is mandatory and follows the same principles as described in Table 1.

Disease Management

Recommendations for the treatment of stuttering priapism	Strength rating
Manage each acute episode similar to that for ischaemic priapism.	Weak
Use hormonal therapies (mainly gonadotropin-receptor hormone agonists or antagonists) and/or anti-androgens for the prevention of future episodes in patients with frequent relapses. Do not use them before sexual maturation is reached.	Weak
Initiate treatment with phosphodiesterase type 5 inhibitors only when the penis is in its flaccid state.	Strong
Use digoxin, α-adrenergic agonists, baclofen, gabapentin or terbutaline only in patients with very frequent and uncontrolled relapses.	Weak
Use intracavernous self-injections at home of sympathomimetic drugs for the treatment of acute episodes on an interim basis until ischaemic priapism has been alleviated.	Weak

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EAU GUIDELINES ON PENILE CURVATURE

(Limited text update March 2018)

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Guideline Associates: A. Parnham, E.C. Serefoglu

Introduction

Congenital penile curvature results from disproportionate development of the tunica albuginea of the corporal bodies and is not associated with urethral malformation. In the majority of the cases the curvature is ventral but, can be lateral though rarely dorsal.

Diagnostic evaluation

Taking a medical and sexual history is usually sufficient to establish the diagnosis of congenital penile curvature. Patients usually present after reaching puberty as the curvature becomes more apparent with erections, and severe curvature can make intercourse difficult or impossible. Physical examination during erection (autophotograph or after intracavernosal injection of vasoactive drugs) is useful to document curvature and exclude other pathologies.

Disease management

The treatment of this disorder is surgical correction deferred until after puberty. Surgical treatments for congenital penile curvature generally share the same principles as in Peyronie's disease (presented in detail in the next section). Nesbit procedure with excision of an ellipse of the tunica albuginea is the gold standard of treatment but many other techniques have

been described and employed. Plication techniques are widely used including techniques producing a de-rotation of the corporal bodies. Most of the time, dissection and mobilisation of the penile dorsal neurovascular bundle are required in order to avoid loss of sensation and ischaemia to the glans penis.

Peyronie's disease

An insult (repetitive microvascular injury or trauma) to the tunica albuginea is the most widely accepted hypothesis on the aetiology of the disease. A prolonged inflammatory response will result in the remodelling of connective tissue into a fibrotic plaque. Penile plaque formation can result in curvature which, if severe, may prevent vaginal intromission.

The most commonly associated comorbidities and risk factors are diabetes, hypertension, lipid abnormalities, ischaemic cardiopathy, erectile dysfunction (ED), smoking, and excessive consumption of alcohol.

Two phases of the disease can be distinguished. The first is the acute inflammatory phase, which may be associated with pain in the flaccid state or painful erections and a palpable nodule or plaque in the tunica of the penis; typically a penile curvature begins to develop. The second is the fibrotic phase with the formation of hard palpable plaques that can be calcified, which also results in disease stabilisation.

Diagnostic evaluation

The aim of the initial evaluation is to provide information on the presenting symptoms and their duration (erectile pain, palpable nodules, curvature, length, rigidity, and girth) and erectile function status. It is mandatory to obtain information on the distress provoked by the symptoms and the potential risk factors for ED and Peyronie's disease.

Major attention should be given to whether the disease is still active, as this will influence medical treatment or the timing of surgery. Patients who are still likely to have an active disease are those with short symptom duration, pain during erection, or a recent change in penile curvature.

The examination should start with a routine genito-urinary assessment, which is then extended to the hands and feet for detecting possible Dupuytren's contracture or Ledderhose scarring of the plantar fascia. Penile examination consists generally of a palpable node or plaque. The extent of curvature must be evaluated with self-photograph, vacuum-assisted erection test or pharmacological-induced erection test. Measurement of length during erection is important because it may have an impact on treatment decisions.

Erectile dysfunction is common in patients with Peyronie's disease (> 50%) but it is important to define whether it pre- or post-dates the onset of Peyronie's disease.

Recommendations for the diagnostic evaluation of Peyronie's disease	**Strength rating**
In the medical and sexual history of patients with Peyronie's disease, include duration of the disease, penile pain, change of penile deformity, difficulty in vaginal intromission due to deformity, and erectile dysfunction (ED).	Strong
In the physical examination, include assessment of palpable plaques, penile length, extent of curvature (self-photograph, vacuum-assisted erection test or pharmacological-induced erection) and any other possibly related diseases (Dupuytren's contracture, Ledderhose disease).	Strong

Do not use Peyronie's disease specific questionnaire in everyday clinical practice.	Weak
Do not use ultrasound (US) measurement of plaque size in everyday clinical practice.	Weak
Use Doppler US only in the case of diagnostic evaluation of ED, to ascertain vascular parameters associated with ED.	Weak

Disease management

Non-operative treatment

Clostridium collagenase is the only drug approved for the treatment of Peyronie's disease by the FDA. No single drug has been approved by the European Medicines Agency (EMA) for the treatment of Peyronie's disease at this time.

Table 1: Non-operative treatments for Peyronie's disease

Oral treatments
Vitamin E
Potassium para-aminobenzoate (Potaba)
Tamoxifen
Colchicine
Acetyl esters of carnitine
Pentoxifylline
Phosphodiesterase type 5 inhibitors
Intralesional treatments
Steroids
Verapamil
Clostridium collagenase
Interferon

Topical treatments
Verapamil
Iontophoresis
H-100 gel
Extracorporeal shockwave treatment
Traction devices

Recommendations for the non-operative treatment of Peyronie's disease	Strength rating
Use conservative treatment in patients not fit for surgery or when surgery is not acceptable to the patient.	Weak
Do not use extracorporeal shockwave treatment to improve penile curvature and reduce plaque size.	Weak
Use penile traction devices and vacuum devices to reduce penile deformity and increase penile length.	Weak
Do not use intralesional treatment with steroids to reduce penile curvature, plaque size or pain.	Weak
Do not use oral treatment with vitamin E and tamoxifen for significant reduction in penile curvature or plaque size.	Weak
Do not offer other oral treatments (acetyl esters of carnitine, pentoxifylline, colchicine).	Weak

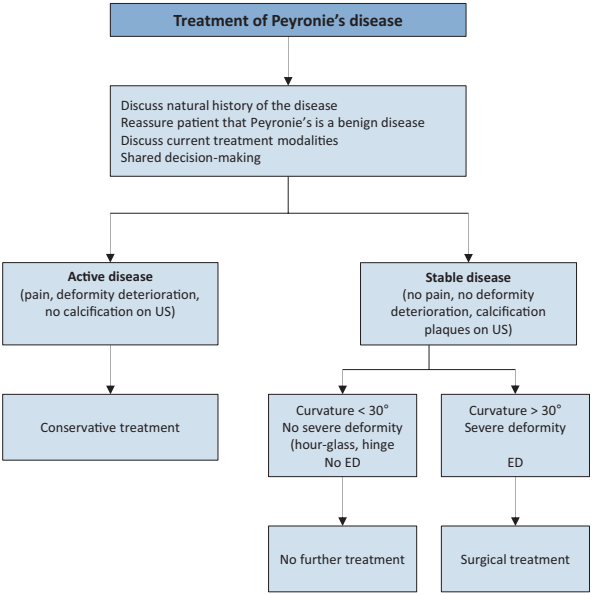
Surgical treatment

Recommendations	Strength rating
Perform surgery only when Peyronie's disease has been stable for at least three months (without pain or deformity deterioration), which is usually the case after twelve months from the onset of symptoms, and intercourse is compromised due to deformity.	Strong
Prior to surgery, assess penile length, curvature severity, erectile function (including response to pharmacotherapy in case of ED) and patient expectations.	Strong
Use tunical shortening procedures, especially plication techniques as the first treatment option for congenital penile curvature and for Peyronie's disease with adequate penile length, curvature < 60° and absence of special deformities (hour-glass, hinge).	Strong
Use grafting techniques for patients with Peyronie's disease and normal erectile function, with no adequate penile length, curvature > 60º and presence of special deformities (hour-glass, hinge).	Weak
Use penile prosthesis implantation, with or without any additional procedure (modelling, plication or grafting), in Peyronie's disease patients with ED not responding to pharmacotherapy.	Strong

Table 2: Types of grafts used in Peyronie's disease surgery

Autologous grafts
Dermis
Vein grafts
Tunica albuginea
Tunica vaginalis
Temporalis fascia
Buccal mucosa
Allografts
Cadaveric pericardium
Cadaveric fascia lata
Cadaveric dura matter
Cadaveric dermis
Xenografts
Porcine small intestinal submucosa
Bovine pericardium
Porcine dermis
Synthetic grafts
Gore-Tex®
Dacron®
Collagen fleece (TachoSil®)

Figure 1: Treatment algorithm for Peyronie's disease



ED = erectile dysfunction; US = Ultrasound.

This short booklet text is based on the more comprehensive EAU Guidelines (978-94-92671-01-1), available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines.

EAU GUIDELINES ON MALE INFERTILITY

(Limited text update March 2018)

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Introduction

'Infertility is the inability of a sexually active, non-contracepting couple to achieve spontaneous pregnancy in one year.' (World Health Organization 2000).

Epidemiology and aetiology

About 15% of couples do not achieve pregnancy within one year and seek medical treatment for infertility.

Male fertility can be impaired as a result of:

- congenital or acquired urogenital abnormalities;
- malignancies;
- urogenital tract infections;
- increased scrotal temperature (e.g. as a consequence of varicocele);
- endocrine disturbances;
- genetic abnormalities;
- immunological factors.

Prognostic factors

The main factors influencing the prognosis in infertility are:

- duration of infertility;
- primary or secondary infertility;
- results of semen analysis;
- age and fertility status of the female partner.

Diagnostic evaluation

The diagnosis of male fertility should focus on a number of prevalent disorders (Table 1). Simultaneous assessment of the female partner is preferable, even if abnormalities are found in the male, since data show that in one out of four couples both male and female partners have pathological findings.

Semen analysis

A comprehensive andrological examination is indicated if semen analysis shows abnormalities compared with reference values (Table 1).

Table 1: Lower reference limits (5th centiles and their 95% CIs) for semen characteristics

Parameter	Lower reference limit (range)
Semen volume (mL)	1.5 (1.4-1.7)
Total sperm number (10^6/ejaculate)	39 (33-46)
Sperm concentration (10^6/mL)	15 (12-16)
Total motility (PR + NP)	40 (38-42)
Progressive motility (PR, %)	32 (31-34)
Vitality (live spermatozoa, %)	58 (55-63)
Sperm morphology (normal forms, %)	4 (3.0-4.0)
Other consensus threshold values	
pH	> 7.2
Peroxidase-positive leukocytes (10^6/mL)	< 1.0
Optional investigations	
MAR test (motile spermatozoa with bound particles, %)	< 50
Immunobead test (motile spermatozoa with bound beads, %)	< 50
Seminal zinc (µmol/ejaculate)	≥ 2.4
Seminal fructose (µmol/ejaculate)	≥ 13
Seminal neutral glucosidase (mU/ejaculate)	≤ 20

Recommendations	Strength rating
Include the fertility status of the female partner in the diagnosis and management of male sub-fertility because this might determine the final outcome.	Strong
Perform semen analyses according to the guidelines of the WHO Laboratory Manual for the Examination and Processing of Human Semen (5th edn).	Strong
Perform further andrological assessment when semen analysis is abnormal in at least two tests.	Strong
Adhere to the 2000 WHO Manual for the standardised investigation, diagnosis and management of the infertile male for diagnosis and evaluation of male sub-fertility.	Weak

Primary Spermatogenic Failure

Diagnostic evaluation

Routine investigations include semen analysis and hormonal determinations. Other investigations may be required depending on the individual situation.

Semen analysis

In non-obstructive azoospermia (NOA), semen analysis shows normal ejaculate volume and azoospermia after centrifugation. A recommended method is semen centrifugation at 3000 g for 15 minutes and a thorough microscopic examination by phase contrast optics at x 200 magnification of the pellet. All samples can be stained and re-examined microscopically.

Hormonal determinations

In men with testicular deficiency, hypergonadotropic hypogonadism is usually present, with elevated levels of follicle stimulating hormone (FSH) and luteinising hormone (LH), and with or without low levels of testosterone. Generally, the levels of FSH correlate with the number of spermatogonia and are elevated when spermatogonia are absent or markedly diminished. Spermatogenic arrest is typically associated with normal FSH.

Testicular biopsy

Testicular biopsy and simultaneous testicular sperm extraction (TESE) is a therapeutic option in couples considering assisted reproductive techniques (ART) in men with NOA.

Recommendations	Strength rating
For men who are candidates for sperm retrieval, give appropriate genetic counselling even when testing for genetic abnormalities was negative.	Strong
Perform multiple testicular biopsies (TESE or micro-TESE) in men with non-obstructive azoospermia, to define spermatogenesis, cryopreserve sperm and diagnose germ cell neoplasia *in situ*.	Strong

Genetic Disorders in Infertility

Current routine clinical practice is based on the screening of genomic DNA from peripheral blood samples, however, screening of chromosomal anomalies in spermatozoa is also feasible and can be performed in selected cases.

Recommendations	Strength rating
Obtain standard karyotype analysis in all men with damaged spermatogenesis (spermatozoa < 10 million/mL) for diagnostic purposes.	Strong
Provide genetic counselling in all couples with a genetic abnormality found on clinical or genetic investigation and in patients who carry a (potential) inheritable disease.	Strong
For all men with Klinefelter's syndrome, provide long-term endocrine follow-up and appropriate medical treatment, if necessary.	Strong
Do not test for microdeletions in men with obstructive azoospermia (OA) since spermatogenesis should be normal.	Strong
Inform men with Yq microdeletion and their partners who wish to proceed with intracytoplasmic sperm injection that microdeletions will be passed to sons, but not to daughters.	Strong
In men with structural abnormalities of the vas deferens (unilateral or bilateral absence with no renal agenesis), test the man and his partner for cystic fibrosis transmembrane conductance regulator gene mutations.	Strong

Obstructive Azoospermia

Obstructive azoospermia (OA) is the absence of spermatozoa and spermatogenetic cells in semen and post-ejaculate urine due to obstruction. Sometimes, the vas deferens is absent as in Congenital Bilateral Absence of the Vas Deferens (CBAVD) or Congenital Unilateral Absence of the Vas Deferens (CUAVD).

Obstruction in primary infertile men is frequently present at the epididymal level.

Diagnostic evaluation

Clinical examination should follow the investigation and diagnostic evaluation of infertile men. The following findings indicate OA:

- at least one testis with a volume > 15 mL, although a smaller volume may be found in some patients with OA and concomitant partial testicular failure;
- enlarged and dilated epididymis;
- nodules in the epididymis or vas deferens;
- absence or partial atresia of the vas.

Semen analysis

At least two examinations must be carried out at an interval of one to two months, according to the WHO. When semen volume is low, a search must be made for spermatozoa in urine after ejaculation. Absence of spermatozoa and immature germ cells in semen smears suggest complete seminal duct obstruction.

Hormone levels

Serum FSH and Inhibin B levels may be normal, but do not exclude a testicular cause of azoospermia (e.g. spermatogenic arrest).

Ultrasonography

In addition to physical examination, a scrotal ultrasound may be helpful in finding signs of obstruction (e.g. dilatation of rete testis, enlarged epididymis with cystic lesions, or absent vas deferens) and may demonstrate signs of testicular dysgenesis (e.g., non-homogeneous testicular architecture and microcalcifications) or testis tumours.

Testicular biopsy

In selected cases, testicular biopsy is indicated to exclude spermatogenic failure. Testicular biopsy should be combined with extraction of testicular spermatozoa (i.e. TESE) for cryopreservation.

Recommendations	Strength rating
Perform microsurgical vasovasostomy or tubulovasostomy for azoospermia caused by vasal or epididymal obstruction.	Strong
Use sperm retrieval techniques, such as microsurgical epididymal sperm aspiration, testicular sperm extraction and percutaneous epididymal sperm aspiration only when facilities for cryostorage are available.	Strong

Varicocele

Varicocele is a common genital abnormality which may be associated with the following andrological conditions:

- failure of ipsilateral testicular growth and development;
- symptoms of pain and discomfort;
- male sub-fertility;
- hypogonadism.

Diagnostic evaluation

The diagnosis of varicocele is made by clinical examination and should be confirmed by colour Duplex analysis. In centres where treatment is carried out by antegrade or retrograde sclerotherapy or embolisation, diagnosis is additionally confirmed by X-ray.

Disease management

Several treatments are available for varicoceles. Current evidence indicates that microsurgical varicocelectomy is the

most effective with the lowest complication rate among the varicocelectomy techniques.

Recommendations	Strength rating
Treat varicoceles in adolescents with ipsilateral reduction in testicular volume and evidence of progressive testicular dysfunction.	Weak
Do not treat varicoceles in infertile men who have normal semen analysis and in men with a subclinical varicocele.	Strong
Treat men with a clinical varicocele, oligo-zoospermia and otherwise unexplained infertility in the couple.	Weak

Hypogonadism

Idiopathic hypogonadotropic hypogonadism

Idiopathic hypogonadotropic hypogonadism is characterised by low levels of gonadotropins and sex steroid in the absence of anatomical or functional abnormalities of the hypothalamic-pituitary-gonadal axis. Stimulation of sperm production requires treatment with human chorionic gonadotropin (hCG) combined with recombinant FSH or urinary FSH or human menopausal gonadotropins (hMGs).

Hypergonadotropic hypogonadism

Many conditions in men are associated with hypergonado-tropic hypogonadism and impaired fertility (e.g. anorchia, maldescended testes, Klinefelter's syndrome, trauma, orchitis, systemic diseases, testicular tumour, varicocele etc).

Recommendations	Strength rating
Provide testosterone replacement therapy for symptomatic patients with primary and secondary hypogonadism who are not considering parenthood.	Strong
In men with hypogonadotropic hypogonadism, induce spermatogenesis by an effective drug therapy (human chorionic gonadotropin, human menopausal gonadotropins, recombinant follicle-stimulating hormone (rFSH), highly purified FSH (hpFSH)).	Strong
Do not use testosterone replacement for the treatment of male infertility.	Strong

Cryptorchidism

The aetiology of cryptorchidism is multifactorial, involving disrupted endocrine regulation and several gene defects. It has been postulated that cryptorchidism may be a part of the so-called testicular dysgenesis syndrome (TDS), which is a developmental disorder of the gonads caused by environmental and/or genetic influences early in pregnancy. Besides cryptorchidism, TDS may include hypospadias, reduced fertility, increased risk of malignancy, and Leydig cell dysfunction.

Recommendations	Strength rating
Do not use hormonal treatment of cryptorchidism in adults.	Strong
If undescended testes are corrected in adulthood, perform simultaneous testicular biopsy for detection of intratubular germ cell neoplasia *in situ* (formerly carcinoma *in situ*).	Weak
Provide medical treatment for male infertility in patients with of hypogonadotropic hypogonadism.	Strong
No clear recommendation can be made for treatment of patients with idiopathic infertility using gonadotropins, anti-oestrogens, and antioxidants.	Strong

Male Contraception

Recommendations	Strength rating
Use cauterisation and fascial interposition as they are the most effective techniques for the prevention of early recanalisation.	Strong
Inform patients seeking vasectomy about the surgical technique, risk of failure, potential irreversibility, the need for post-procedure contraception until clearance, and the risk of complications.	Strong
In order to achieve pregnancy, microsurgical epididymal sperm aspiration/ percutaneous epididymal sperm aspiration/ testicular sperm extraction - together with intracytoplasmic sperm injection is a second-line option for men who decline a vasectomy reversal and those with failed vasectomy reversal surgery.	Weak

Male Accessory Gland Infections and Infertility

Diagnostic evaluation

Ejaculate analysis

Ejaculate analysis according to WHO criteria, might indicate persistent inflammatory activity. It clarifies whether the prostate is involved as part of a generalised male accessory gland infection and provides information about sperm quality.

Microbiological findings

After exclusion of urethritis and bladder infection, $>10^6$ peroxidase-positive white blood cells (WBCs) per millilitre of ejaculate indicate an inflammatory process. In this case, a culture should be performed for common urinary tract pathogens.

Disease management

Antibiotic therapy is not indicated before culture results are available.

Recommendation	Strength rating
Instruct patients with epididymitis that is known or suspected to be caused by *N. gonorrhoeae* or *C. trachomatis* to refer their sexual partners for evaluation and treatment.	Strong

Germ Cell Malignancy and Testicular Microcalcification (TM)

Recommendations	Strength rating
Encourage men with testicular microcalcification (TM) to perform self-examination even without additional risk factors as this may result in early detection of testicular germ cell tumour (TGCT).	Weak
Do not perform testicular biopsy, follow-up scrotal ultrasound, routine use of biochemical tumour markers, or abdominal or pelvic computed tomography, in men with isolated TM without associated risk factors (e.g. infertility, cryptorchidism, testicular cancer, and atrophic testis).	Strong
Perform testicular biopsy for men with TM, who belong to one of the following high-risk groups: spermatogenic failure, bilateral TM, atrophic testes (less than 12cc), history of undescended testes and TGCT.	Strong
If there are suspicious findings on physical examination or ultrasound in patients with TM and associated lesions, perform surgical exploration with testicular biopsy or orchidectomy.	Strong
Follow men with TGCT because they are at increased risk of developing hypogonadism and sexual dysfunction.	Strong

Disorders of Ejaculation

Disorders of ejaculation are uncommon, but important causes of male infertility.

Diagnostic evaluation

Diagnostic management includes the following recommended procedures:

- clinical history;
- physical examination;
- post-ejaculatory urinalysis;
- microbiological examination;
- optional diagnostic work-up.

This diagnostic work-up can include:

- neurophysiological tests (bulbocavernosus evoked response and dorsal nerve somatosensory evoked potentials);
- tests for autonomic neuropathy;
- psychosexual evaluation;
- videocystometry;
- cystoscopy;
- transrectal ultrasonography;
- uroflowmetry;
- vibratory stimulation of the penis.

Disease management

The following aspects must be considered when selecting treatment:

- age of patient and his partner;
- psychological problems of the patient and his partner;
- couple's willingness and acceptance of different fertility procedures;
- associated pathology;
- psychosexual counselling.

Recommendations	Strength rating
Offer specific treatments for ejaculatory disorders before performing sperm collection and assisted reproduction technique. Premature ejaculation can be treated using dapoxetine (short acting selective serotonin reuptake inhibitor) and/or topical anaesthetics.	Strong

Semen cryopreservation

Recommendations	Strength rating
Offer cryopreservation of semen to all men who are candidates for chemotherapy, radiation or surgical interventions that might interfere with spermatogenesis or cause ejaculatory disorders.	Strong
Offer simultaneous sperm cryopreservation if testicular biopsies will be performed for fertility diagnosis.	Strong
If cryopreservation is not available locally, inform patients about the possibility of visiting, or transferring to a cryopreservation unit before therapy starts.	Strong
Take precautions to prevent transmission of viral, sexually transmitted or any other infection by cryostored materials from donor to recipient, and to prevent contamination of stored samples. These precautions include testing of the patient and the use of rapid testing and quarantine of samples until test results are known. Do not store samples from men who are positive for hepatitis virus or HIV in the same container as samples from men who have been tested and are free from infection.	Strong

This short booklet text is based on the more comprehensive EAU Guidelines ISBN 978-94-92671-02-8), available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines.

EAU GUIDELINES ON MALE HYPOGONADISM

(Limited text update March 2018)

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Introduction

Male hypogonadism is a clinical syndrome caused by androgen deficiency which may adversely affect multiple organ functions and quality of life. Androgen deficiency increases slightly with age. In middle-aged men the incidence is 6%. Hypogonadism is more prevalent in older men, in men with obesity, those with comorbidities, and in men with a poor health status.

Aetiology and classification

Male hypogonadism can be classified in accordance with disturbances at the level of:

- the testes (primary hypogonadism);
- the hypothalamus and pituitary (secondary hypogonadism);
- the hypothalamus/pituitary and gonads (common in adult onset hypogonadism);
- androgen target organs (androgen insensitivity/resistance).

Table 1: Most common forms of primary hypogonadism

Disease	Pathophysiology
Maldescended or ectopic testes	Failure of testicular descent, maldevelopment of the testis
Klinefelter syndrome 47,XXY	Sex-chromosomal non-disjunction in germ cells
Germ Cell Tumour	Testicular maldevelopment
Orchitis	Viral or unspecific orchitis
Acquired anorchia	Trauma, tumour, torsion, inflammation, iatrogenic, surgical removal
Secondary testicular dysfunction	Medication, drugs, toxins, systemic diseases
(Idiopathic) testicular atrophy/testicular dysgenesis	Male infertility (idiopathic or specific causes)
Congenital anorchia (bilateral in 1 in 20,000 males, unilateral 4 times as often)	Intra-uterine torsion is the most probable cause

Table 2: Most common forms of secondary hypogonadism

Disease	Pathophysiology
Hyperprolactinemia	Prolactin-secreting pituitary adenomas (prolactinomas) or drug-induced
Isolated (congenital) hypogonadotropic hypogonadism (IHH/CHH) (formerly termed idiopathic hypogonadotropic hypogonadism)	Specific (or unknown) mutations affecting GnRH synthesis or action

Kallmann's syndrome (hypogonadotropic hypogonadism with anosmia) (prevalence 1 in 10,000)	GnRH deficiency and anosmia, genetically determined
Secondary GnRH deficiency	Medication, drugs, toxins, systemic diseases
Hypopituitarism	Radiotherapy, trauma, infections, haemo-chromatosis and vascular insufficiency or congenital
Pituitary adenomas	Hormone-secreting adenomas; hormone-inactive pituitary adenomas; metastases to the pituitary or pituitary stalk

Recommendation	Strength rating
Differentiate the two forms of hypogonadism (primary and secondary hypogonadism) by determining luteinising hormone and follicle-stimulating hormone levels, as this has implications for patient evaluation and treatment and makes it possible to identify patients with associated health problems and infertility.	Strong

Diagnostic evaluation

Table 3: Signs and symptoms suggesting prepubertal-onset hypogonadism

Delayed puberty
Small testes
Cryptorchidism
Gynaecomastia
High-pitched voice
Unclosed epiphyses
Linear growth into adulthood
Eunuchoid habitus
Sparse body hair/facial hair
Infertility
Low bone mass
Sarcopenia
Reduced sexual desire/activity

Table 4: Signs and symptoms associated with adult-onset hypogonadism

Loss of libido
Erectile dysfunction
Fewer and decreased morning erections
Overweight or obesity
Sarcopenia
Low bone mass
Depressive thoughts
Fatigue
Loss of body hair

Hot flushes
Loss of vigour

Recommendations for diagnostic evaluation	**Strength rating**
Restrict the diagnosis of testosterone deficiency to men with persistent symptoms suggesting hypogonadism (Tables 3 and 4).	Strong
Measure testosterone in the morning before 11.00 hours, preferably in the fasting state.	Strong
Repeat total testosterone on at least two occasions with a reliable method. In addition, measure the free testosterone level in men with: - Total testosterone levels close to the lower normal range (8-12 nmol/L), to strengthen the laboratory assessment. - Suspected or known abnormal sex hormone-binding globulin levels.	Strong

Consider assessing testosterone in men with a disease or treatment in which testosterone deficiency is common and in whom treatment may be indicated. This includes men with: - Sexual dysfunction. - Type 2 diabetes. - Metabolic syndrome. - Obesity. - Pituitary mass, following radiation involving the sellar region and other diseases in the hypothalamic and sellar region. - Treatment with medications that cause suppression of testosterone levels - e.g. corticosteroids and opiates. - Moderate to severe chronic obstructive lung disease. - Infertility. - Osteoporosis or low-trauma fractures. - HIV infection with sarcopenia.	Strong
Analyse LH and FSH serum levels to differentiate between primary and secondary forms of hypogonadism.	Strong

HIV = human immunodeficiency virus;
LH = luteinizing hormone; FHS = follicle stimulating hormone.

Recommendations for screening men with adult-onset hypogonadism	**Strength rating**
Screen for testosterone deficiency only in adult men with consistent and multiple signs and symptoms listed in Table 3.	Weak

Young men with testicular dysfunction and men older than 50 years of age with low testosterone should additionally be screened for osteoporosis.	Strong

Disease management

Table 5: Indications for testosterone treatment

Delayed puberty (constitutional or congenital forms (hypogonadotropic hypogonadism, Kallmann's syndrome))
Klinefelter syndrome with hypogonadism
Sexual dysfunction and low testosterone
Low bone mass in hypogonadism
Adult men with low testosterone and consistent and preferably multiple signs and symptoms of hypogonadism following unsuccessful treatment of obesity and comorbidities (listed in Table 4)
Hypopituitarism

Table 6: Contraindications against testosterone treatment

Locally advanced or metastatic prostate cancer
Male breast cancer
Men with an active desire to have children
Haematocrit > 0.54%
Severe chronic cardiac failure/New York Heart Association Class IV

Table 7: Testosterone preparations for replacement therapy

Formulation	Administration	Advantages	Disadvantages
Testosterone undecanoate	Oral; 2-6 cps every 6 hours	Absorbed through the lymphatic system, with consequent reduction of liver involvement.	Variable levels of testosterone above and below the mid-range. Need for several doses per day with intake of fatty food.
Testosterone cypionate	Intramuscular; one injection every two to three weeks	Short-acting preparation that allows drug withdrawal in case of onset of side-effects.	Possible fluctuation of testosterone levels.
Testosterone enanthate	Intramuscular; one injection every two to three weeks	Short-acting preparation that allows drug withdrawal in case of onset of side-effects.	Fluctuation of testosterone levels.
Testosterone undecanoate	Intramuscular; one injection every ten to fourteen weeks	Steady-state testosterone levels without fluctuation.	Long-acting preparation that cannot allow drug withdrawal in case of onset of side-effects.

Transdermal testosterone	Gel; daily application	Steady-state testosterone level without fluctuation.	Risk of interpersonal transfer.
Subdermal depots	Subdermal implant every five to seven months	Long duration and constant serum testosterone level.	Risk of infection and extrusion of the implants.

Recommendations for testosterone replacement therapy	**Strength rating**
Fully inform the patient about expected benefits and side-effects of the treatment option. Select the preparation with a joint decision by an informed patient and the physician.	Strong
Use short-acting preparations rather than long-acting depot administration when starting the initial treatment, so that therapy can be adjusted or stopped in case of adverse side-effects.	Weak
Do not use testosterone therapy in patients with male infertility or active child wish since it may suppress spermatogenesis.	Strong
Only use human chorionic gonadotropin treatment for (hypogonadotrophic) hypogonadal patients with simultaneous fertility treatment.	Strong
In patients with adult-onset hypogonadism, only prescribe testosterone treatment in men with multiple symptoms and if weight loss, lifestyle modification and good treatment balance of comorbidities have proven unsuccessful.	Strong

Recommendations on risk factors in testosterone treatment	Strength rating
Perform haematological, cardiovascular, breast and prostatic assessment before the start of treatment.	Strong
Monitor testosterone, haematocrit, haemoglobin and prostate-specific antigen (PSA) during testosterone treatment.	Strong
Offer testosterone treatment cautiously in symptomatic hypogonadal men who have been surgically treated for localised prostate cancer and who are currently without evidence of active disease (i.e. measurable PSA, abnormal rectal examination, evidence of bone/visceral metastasis): treatment should be restricted to those patients with a low risk for recurrent prostate cancer (i.e. Gleason score < 8; pathological stage pT1-2; pre-operative PSA < 10 ng/mL) and should not start before one year of follow-up.	Weak
Assess for cardiovascular risk factors before commencing testosterone treatment and optimise secondary prevention in men with pre-existing cardiovascular disease.	Strong
Treat men with hypogonadism and either pre-existing cardiovascular disease, venous thromboembolism or chronic cardiac failure who require testosterone treatment with caution by carefully monitoring with clinical assessment, haematocrit (not exceeding 0.54%) and testosterone levels maintained as best possible for age within the mid-normal healthy range.	Strong

Recommendations for follow-up	Strength rating
Assess the response to testosterone treatment at three, six and twelve months after the onset of treatment, and thereafter annually.	Strong
Monitor testosterone, haematocrit at three, six and twelve months and thereafter annually. Decrease the testosterone dosage or switch testosterone preparation from intramuscular to topical or venesection, if haematocrit is above 0.54%. If haematocrit remains elevated, stop testosterone and reintroduce at a lower dose once haematocrit has normalised.	Strong
Assess prostate health by digital rectal examination and prostate-specific antigen (PSA) before the start of testosterone replacement therapy. Follow-up by PSA tests at three, six and twelve months and thereafter annually.	Strong
Assess men with cardiovascular diseases for cardiovascular symptoms before testosterone treatment is initiated and continue close clinical assessment during treatment.	Strong

This short booklet text is based on the more comprehensive EAU Guidelines (978-94-92671-01-1), available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines.

EAU GUIDELINES ON UROLOGICAL INFECTIONS

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Introduction

The European Association of Urology (EAU) Urological Infections Guidelines Panel has compiled these clinical guidelines to provide medical professionals with evidence-based information and recommendations for the prevention and treatment of urological tract infections (UTIs). These guidelines also aim to address the important public health aspects of infection control and antimicrobial stewardship.

Antimicrobial Stewardship

Stewardship programs have two main sets of actions. The first set mandates use of recommended care at the patient level conforming to guidelines. The second set describes strategies to achieve adherence to the mandated guidance. These include persuasive actions such as education and feedback together with restricting availability linked to local formularies. The important components of antimicrobial stewardship programs are:

- regular training of staff in best use of antimicrobial agents;
- adherence to local, national or international guidelines;
- regular ward visits and consultation with infectious diseases physicians and clinical microbiologists;
- audit of adherence and treatment outcomes;
- regular monitoring and feedback to prescribers of their performance and local pathogen resistance profiles.

Asymptomatic Bacteriuria

Asymptomatic bacteriuria in an individual without urinary tract symptoms is defined by a mid-stream sample of urine showing bacterial growth ≥ 10^5 cfu/mL in two consecutive samples in women and in one single sample in men.

Recommendations	Strength rating
Do not screen or treat asymptomatic bacteriuria in the following conditions:	
• women without risk factors;	Strong
• patients with well-regulated diabetes mellitus;	Strong
• post-menopausal women;	Strong
• elderly institutionalised patients;	Strong
• patients with dysfunctional and/or reconstructed lower urinary tracts;	Strong
• patients with renal transplants;	Strong
• patients prior to arthoplasty surgeries;	Strong
• patients with recurrent urinary tract infections.	Strong
Screen for and treat asymptomatic bacteriuria prior to urological procedures breaching the mucosa.	Strong
Screen for and treat asymptomatic bacteriuria in pregnant women with standard short course treatment.	Weak

Uncomplicated Cystitis

Uncomplicated cystitis is defined as acute, sporadic or recurrent cystitis limited to non-pregnant, pre-menopausal women with no known relevant anatomical and functional abnormalities within the urinary tract or comorbidities.

Recommendations for the diagnostic evaluation of uncomplicated cystitis	Strength rating
Diagnose uncomplicated cystitis in women who have no other risk factors for complicated urinary tract infections based on: • a focused history of lower urinary tract symptoms (dysuria, frequency and urgency); • the absence of vaginal discharge or irritation.	Strong
Use urine dipstick testing for diagnosis of acute uncomplicated cystitis.	Weak
Urine cultures should be done in the following situations: • suspected acute pyelonephritis; • symptoms that do not resolve or recur within four weeks after the completion of treatment; • women who present with atypical symptoms; • pregnant women.	Strong

Recommendations for antimicrobial therapy for uncomplicated cystitis	Strength rating
Prescribe fosfomycin trometamol, pivmecillinam or nitrofurantoin as first-line treatment for uncomplicated cystitis in women.	Strong
Do not use aminopenicillins or fluoroquinolones to treat uncomplicated cyctitis.	Strong

Table 1: Suggested regimens for antimicrobial therapy in uncomplicated cystitis			
Antimicrobial	**Daily dose**	**Duration of therapy**	**Comments**
First-line women			
Fosfomycin trometamol	3 g SD	1 day	Recommended only in women with uncomplicated cystitis.
Nitrofurantoin macrocrystal	50-100 mg four times a day	5 days	
Nitrofurantoin monohydrate/ macrocrystals	100 mg b.i.d	5 days	
Nitrofurantoin macrocrystal prolonged release	100 mg b.i.d	5 days	
Pivmecillinam	200 mg t.i.d	3-5 days	
Alternatives			
Cephalosporins (e.g. cefadroxil)	500 mg b.i.d	3 days	Or comparable
If the local resistance pattern for E. coli is < 20%			
Trimethoprim	200 mg b.i.d	5 days	Not in the first trimenon of pregnancy
Trimethoprim-sulphamethoxazole	160/800 mg b.i.d	3 days	Not in the last trimenon of pregnancy
Treatment in men			
Trimethoprim-sulphamethoxazole	160/800 mg b.i.d	7 days	Restricted to men, fluoroquinolones can also be prescribed in accordance with local susceptibility testing.

SD = single dose; b.i.d = twice daily; t.i.d = three times daily.

Recurrent UTIs

Recurrent UTIs (rUTIs) are recurrences of uncomplicated and/or complicated UTIs, with a frequency of at least three UTIs/year or two UTIs in the last six months.

Recommendations for the diagnostic evaluation and treatment of rUTIs	Strength rating
Diagnose recurrent UTI by urine culture.	Strong
Do not perform an extensive routine workup (e.g cystoscopy, full abdominal ultrasound) in women younger than 40 years of age with recurrent UTI and no risk factors.	Weak
Advise patients on behavioural modifications which might reduce the risk of recurrent UTI.	Weak
Use vaginal oestrogen replacement in post-menopausal women to prevent recurrent UTI.	Weak
Use immunoactive prophylaxis to reduce recurrent UTI in all age groups.	Strong
Use continuous or post-coital antimicrobial prophylaxis to prevent recurrent UTI when non-antimicrobial interventions have failed. Counsel patients regarding possible side effects.	Strong
For patients with good compliance self-administered short term antimicrobial therapy should be considered.	Strong

Uncomplicated Pyelonephritis

Uncomplicated pyelonephritis is defined as pyelonephritis limited to non-pregnant, pre-menopausal women with no known relevant urological abnormalities or comorbidities.

Recommendations for the diagnostic evaluation of uncomplicated pyelonephritis	Strength rating
Perform urinalysis (e.g. using a dipstick method), including the assessment of white and red blood cells and nitrite, for routine diagnosis.	Strong
Perform urine culture and antimicrobial susceptibility testing in patients with pyelonephritis.	Strong
Perform imaging of the urinary tract to exclude urgent urological disorders.	Strong

Recommendations for the treatment of uncomplicated pyelonephritis	Strength rating
Treat patients with uncomplicated pyelonephritis not requiring hospitalisation with short course fluoroquinolones as first-line treatment.	Strong
Treat patients with uncomplicated pyelonephritis requiring hospitalisation with an intravenous antimicrobial regimen initially.	Strong
Switch patients initially treated with parenteral therapy, who improve clinically and can tolerate oral fluids, to oral antimicrobial therapy.	Strong
Do not use nitrofurantoin, fosfomycin, and pivmecillinam to treat uncomplicated pyelonephritis.	Strong

Table 2: Suggested regimens for empirical oral antimicrobial therapy in uncomplicated pyelonephritis			
Antimicrobial	**Daily dose**	**Duration of therapy**	**Comments**
Ciprofloxacin	500-750 mg b.i.d	7 days	Fluoroquinolone resistance should be less than 10 percent.
Levofloxacin	750 mg q.d	5 days	
Trimethoprim sulphamethoxazol	160/800 mg b.i.d	14 days	If such agents are used empirically, an initial intravenous dose of a long-acting parenteral antimicrobial (e.g. ceftriaxone) should be administered.
Cefpodoxime	200 mg b.i.d	10 days	
Ceftibuten	400 mg q.d	10 days	

b.i.d = twice daily; q.d = every day.

Table 3: Suggested regimens for empirical parenteral antimicrobial therapy in uncomplicated pyelonephritis		
Antimicrobial	**Daily dose**	**Comments**
First-line treatment		
Ciprofloxacin	400 mg b.i.d	
Levofloxacin	750 mg q.d	
Cefotaxime	2 g t.i.d	Not studied as monotherapy in acute uncomplicated pyelonephritis.
Ceftriaxone	1-2 g q.d	Lower dose studied, but higher dose recommended.
Second-line treatment		
Cefepime	1-2 g b.i.d	Lower dose studied, but higher dose recommended.
Piperacillin/ tazobactam	2.5-4.5 g t.i.d	
Ceftolozane/ tazobactam	1.5 g t.i.d	
Ceftazidime/ avibactam	2.5 g t.i.d	
Gentamicin	5 mg/kg q.d	Not studied as monotherapy in acute uncomplicated pyelonephritis.
Amikacin	15 mg/kg q.d	
Alternatives		
Imipenem/ cilastatin	0.5 g t.i.d	Consider carbapenems only in patients with early culture results indicating the presence of multi-drug resistance organisms.
Meropenem	1 g t.i.d	

b.i.d = twice daily; t.i.d = three times daily; q.d = every day.

Complicated UTIs

A complicated UTI (cUTI) occurs in an individual in whom factors related to the host (e.g. underlying diabetes or immunosuppression) or specific anatomical or functional abnormalities related to the urinary tract (e.g. obstruction, incomplete voiding due to detrusor muscle dysfunction) are

believed to result in an infection that will be more difficult to eradicate than an uncomplicated infection.

Recommendations for the treatment of complicated UTIs	Strength rating
Use the combination of: • amoxicillin plus an aminoglycoside; • a second generation cephalosporin plus an aminoglycoside; • a third generation cephalosporin intravenously as empirical treatment of complicated UTI with systemic symptoms.	Strong
Only use ciprofloxacin provided that the local resistance percentages are < 10% when: • the entire treatment is given orally; • patients do not require hospitalisation; • patient has an anaphylaxis for beta-lactam antimicrobials.	Strong
Do not use ciprofloxacin and other fluoroquinolones for the empirical treatment of complicated UTI in patients from the urology department or when patients have used fluoroquinolones in the last six months.	Strong
Manage any urological abnormality and/or underlying complicating factors.	Strong

Catheter-associated UTIs

Catheter-associated UTI refers to UTIs occurring in a person whose urinary tract is currently catheterised or has been catheterised within the past 48 hours.

Recommendations for diagnostic evaluation of CA-UTI	Strength rating
Do not carry out routine urine culture in asymptomatic catheterised patients.	Strong
Do not use pyuria as an indicator for catheter-associated UTI.	Strong
Do not use the presence or absence of odorous or cloudy urine alone to differentiate catheter-associated asymptomatic bacteriuria from catheter-associated UTI.	Strong

Recommendations for disease management and prevention of CA-UTI	Strength rating
Treat symptomatic CA-UTI according to the recommendations for complicated UTIs.	Strong
Take a urine culture prior to initiating antimicrobial therapy in catheterised patients in whom the catheter has been removed.	Strong
Do not treat catheter-associated asymptomatic bacteriuria in general.	Strong
Treat catheter-associated asymptomatic bacteriuria prior to traumatic urinary tract interventions (e.g. transurethral resection of the prostate).	Strong
Replace or remove the indwelling catheter before starting antimicrobial therapy.	Strong
Do not apply topical antiseptics or antimicrobials to the catheter, urethra or meatus.	Strong
Do not use prophylactic antimicrobials to prevent catheter-associated UTIs.	Strong
The duration of catheterisation should be minimal.	Strong

Recommendations for antibiotic prophylaxis following indwelling balder catheter removal	Strength rating
Do not use antibiotic prophylaxis routinely to prevent clinical UTI after urethral catheter removal.	Weak

Urosepsis

Urosepsis is defined as life threatening organ dysfunction caused by a dysregulated host response to infection originating from the urinary tract and/or male genital organs.

Recommendations for the diagnosis and treatment of urosepsis	Strength rating
Perform the quickSOFA score to identify patients with potential sepsis.	Strong
Take a urine culture and two sets of blood cultures before starting antimicrobial treatment.	Strong
Administer parenteral high dose broad spectrum antimicrobials within the first hour after clinical assumption of sepsis.	Strong
Adapt initial empiric antimicrobial therapy on the basis of culture results.	Strong
Remove foreign bodies from and obstruction of the urinary tract.	Strong
Provide immediate adequate life-support measures.	Strong

Table 4: Suggested regimens for antimicrobial therapy for urosepsis		
Antimicrobials	**Daily dose**	**Duration of therapy**
Cefotaxime	2 g t.i.d	7-10 days Longer courses are appropriate in patients who have a slow clinical response
Ceftazidime	1-2 g t.i.d	
Ceftriaxone	1-2 g q.d	
Cefepime	2 g b.i.d	
Piperacillin/tazobactam	4.5 g t.i.d	
Ceftolozane/tazobactam	1.5 g t.i.d	
Ceftazidime/avibactam	2.5 g t.i.d	
Gentamicin*	5 mg/kg q.d	
Amikacin*	15 mg/kg q.d	
Ertapenem	1 g q.d	
Imipenem/cilastatin	0.5 g t.i.d	
Meropenem	1 g t.i.d	

** Not studied as monotherapy in urosepsis*
b.i.d = twice daily; t.i.d = three times daily; q.d = every day.

Urethritis

Inflammation of the urethra usually presents with LUTS and must be distinguished from other infections of the lower urinary tract. The following recommendations are based on a review of several European national guidelines and are aligned with the Center for Disease Control and Prevention's guidelines on sexual transmitted diseases.

Recommendations for the diagnostic evaluation and antimicrobial treatment of urethritis	Strength rating
Perform a gram stain of urethral discharge or a urethral smear to preliminarily diagnose pyogenic urethritis.	Strong

Perform a validated nucleic acid amplification tests on a mid-stream urine sample or urethral smear to diagnosis chlamydial and gonococcal infections.	Strong
Use a pathogen directed treatment based on local resistance data.	Strong

Table 5: Suggested regimens for antimicrobial therapy for urethritis

Pathogen	Antimicrobial	Dosage & Duration of therapy	Alternative regimens
Gonococcal Infection	Ceftriaxone	1 g i.m., SD	Cefixime 400 mg p.o., SD Or Azithromycin 1-1.5 g p.o., SD
	Azithromycin	1-1.5 g p.o., SD	
	Cefixime	800 mg p.o., SD	
Non-Gonococcal infection (non-identified pathogen)	Doxycycline	100 mg b.i.d, p.o., 7-10 days	Azithromycin 0.5 g p.o., day 1, 250 mg p.o., day 2-5
Chlamydia trachomatis	Azithromycin	1.0-1.5 g p.o., SD	Doxycycline 100 mg b.i.d, p.o., for 7 days
Mycoplasma genitalium	Azithromycin	0.5 g p.o., day 1, 250 mg p.o., day 2-5	Moxifloxacin 400 mg q.d., 5 days however, because of reported failures, some experts recommend 10 -14 days

Ureaplasma urealiticum	Doxycycline	100 mg b.i.d, p.o., 7 days	Azithromycin 1.0-1.5 g p.o., single dose Or clarithromycin 500 mg b.i.d, 7 days (resistance against macrolides is possible)
Trichomonas vaginalis	Metronidazole	2 g p.o., SD	Not in the last trimenon of pregnancy

SD = single dose; b.i.d = twice daily; q.d = everyday; p.o. = orally, i.m. = intramuscular.

Bacterial Prostatitis

Bacterial prostatitis is a clinical condition caused by bacterial pathogens. It is recommended that urologists use the classification suggested by the National Institute of Diabetes, Digestive and Kidney Diseases of the National Institutes of Health, in which bacterial prostatitis, with confirmed or suspected infection, is distinguished from chronic pelvic pain syndrome.

Recommendations for the diagnosis of bacterial prostatitis	**Strength rating**
Perform a gentle digital rectal examination to assess the condition of the prostate.	Weak
Take a mid-stream urine dipstick to check nitrite and leukocytes in patients with clinical suspicion of acute bacterial prostatitis.	Weak
Take a blood culture and a total blood count in case of prostatitis-related symptoms with malaise and fever.	Weak

Take a mid-stream urine culture in patients with acute prostatitis-related symptoms to guide diagnosis and plan adequate targeted antibiotic treatment.	Weak
Perform accurate microbiological evaluation for atypical pathogens such as *Chlamydia trachomatis* or Mycoplasmata in patients with chronic bacterial prostatitis (CBP).	Weak
Perform the Meares and Stamey 2- or 4-glass test in patients with CBP.	Strong
Preform transrectal ultrasound in selected cases to rule out the presence of prostatic abscess, calcification in the prostate and dilatation of the seminal vesicles.	Weak
Do not routinely perform microbiological analysis of the ejaculate alone to diagnosis CBP.	Weak

Recommendations for the disease management of bacterial prostatitis	**Strength rating**
Acute bacterial prostatitis	
Treat acute bacterial prostatitis according to the recommendations for complicated UTIs.	Strong
Chronic bacterial prostatitis (CBP)	
Prescribe a fluoroquinolone (e.g. ciprofloxacin, levofloxacin) as first-line treatment for CBP.	Strong

Prescribe a macrolide (e.g. azithromycin) or a tetracycline (e.g. doxycycline) if intracellular bacteria have been identified as the causative agent of CBP.	Strong
Prescribe metronidazole in patients with *Trichomonas vaginalis* CBP.	Strong

Table 6: Suggested regimens for antimicrobial therapy for chronic bacterial prostatitis

Antimicrobial	Daily dose	Duration of therapy	Comments
Floroquinolone	Optimal oral daily dose	4-6 weeks	
Doxycycline	100 mg b.i.d	10 days	Only for *C. trachomatis* or mycoplasma infections.
Azithromycin	500 mg 3x weekly	3 weeks	Only for *C. trachomatis* infections
Metronidazole	500 mg t.i.d.	14 days	Only for *T. vaginalis* infections

b.i.d = twice daily; t.i.d = three times daily; q.d = every day.

Acute Infective Epididymitis

Acute epididymitis is clinically characterised by pain, swelling and increased temperature of the epididymis, which may involve the testis and scrotal skin. It is generally caused by migration of pathogens from the urethra or bladder. Torsion of the spermatic cord (testicular torsion) is the most important differential diagnosis in boys and young men.

Recommendations for the diagnosis and treatment of acute infective epididymitis	Strength rating
Obtain a mid-stream urine and first voided urine for pathogen identification by culture and nucleic acid amplification test.	Strong
Initially prescribe a single antibiotic or a combination of two antibiotics active against *Chlamydia trachomatis* and Enterobacteriaceae in young sexually active men; in older men without sexual risk factors only Enterobacteriaceae have to be considered.	Strong
If gonorrhoeal infection is likely give single dose ceftriaxone 500 mg intramuscularly in addition to a course of an antibiotic active against *Chlamydia trachomatis*.	Strong
Adjust antibiotic agent when pathogen has been identified and adjust duration according to clinical response.	Weak
Follow national policies on reporting and tracing/treatment of contacts for sexually transmitted infections.	Strong

Fournier's Gangrene

Fournier's gangrene is an aggressive and frequently fatal polymicrobial soft tissue infection of the perineum, peri-anal region, and external genitalia. It is an anatomical sub-category of necrotising fasciitis with which it shares a common aetiology and management pathway.

Recommendations for the disease management of Fournier's Gangrene	Strength rating
Start treatment for Fournier's gangrene with broad-spectrum antibiotics on presentation, with subsequent refinement according to culture and clinical response.	Strong
Commence repeated surgical debridement for Fournier's gangrene within 24 hours of presentation.	Strong
Do not use adjunctive treatments for Fournier's gangrene except in the context of clinical trials.	Weak

Table 7: Suggested regimens for antimicrobial therapy for Fournier's Gangrene of mixed microbiological aetiology

Antimicrobial	Dosage
Piperacillin-tazobactam plus vancomycin	3.37 g every 6-8 h IV 15 mg/kg every 12 h
Imipenem-cilastatin	1 g every 6-8 h IV
Meropenem	1 g every 8 h IV
Ertapenem	1 g once daily
Cefotaxime plus metronidazole or clindamycin	2 g every 6 h IV 500 mg every 6 h IV 600-900 mg every 8 h IV

IV = intravenous

Detection of bacteriuria prior to urological procedures

Identifying bacteriuria prior to diagnostic and therapeutic procedures aims to reduce the risk of infectious complications by controlling any pre-operative detected bacteriuria and to optimise antimicrobial coverage in conjunction with the procedure.

Recommendation for the detection of bacteriuria prior to urological procedures	Strength rating
Use laboratory urine culture to detect bacteriuria in patients prior to undergoing urological interventions breaching the mucosa.	Weak

Peri-Procedural Antibiotic Prophylaxis

The available evidence enabled the panel to make recommendations concerning urodynamics, cystoscopy, stone procedures (extracorporeal shockwave lithotripsy, ureteroscopy and percutaneous neprolithotomy), and transurethral resection of the prostate and blabber. For nephrectomy and prostatectomy the scientific evidence was too weak to allow the panel to make recommendations either for or against antibiotic prophylaxis.

Recommendations for peri-procedural antibiotic prophylaxis	Strength rating
Do not use antibiotic prophylaxis to reduce the rate of symptomatic urinary infection following: • urodynamics; • cystoscopy; • extracorporeal shockwave lithotripsy.	Strong
Use antibiotic prophylaxis to reduce the rate of symptomatic urinary infection following ureteroscopy.	Weak
Use single dose antibiotic prophylaxis to reduce the rate of clinical urinary infection following percutaneous nephrolithotomy.	Strong

Use antibiotic prophylaxis to reduce infectious complications in men undergoing transurethral resection of the prostate.	Strong
Use antibiotic prophylaxis to reduce infectious complications in high-risk patients undergoing transurethral resection of the bladder.	Weak

Prostate biopsy

Infection is the most clinically significant harm experienced by men following prostate biopsy. Infection generally occurs by implantation of rectal commensal organisms into the prostate, urethra or bloodstream during needle insertion. Severity of infection will depend on bacterial inoculum, virulence and status of host defence.

Recommendations for non-antimicrobial intervention and antimicrobial prophylaxis prior to prostate biopsy	**Strength rating**
Use rectal cleansing with povidone-iodine in men prior to transrectal prostate biopsy.	Strong
Use antimicrobial prophylaxis in men prior to transrectal prostate biopsy.	Strong

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-01-1) available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines.

EAU GUIDELINES ON UROLITHIASIS

(Limited text update March 2018)

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Aetiology and classification

Urinary stones can be classified according to the following aspects: aetiology of stone formation, stone composition (mineralogy), stone size, stone location and X-ray characteristics of the stone. The recurrence risk is basically determined by the disease or disorder causing the stone formation.

Risk groups for stone formation

The risk status of stone formers is of particular interest because it defines the probability of recurrence or regrowth, and is imperative for pharmacological treatment (Table 1).

Table 1: High-risk stone formers

General factors
Early onset of urolithiasis (especially children and teenagers)
Familial stone formation
Brushite-containing stones ($CaHPO_4.2H_2O$)
Uric acid and urate-containing stones
Infection stones
Solitary kidney (the kidney itself does not particularly increase risk of stone formation, but prevention of stone recurrence is of more importance)

Diseases associated with stone formation
Hyperparathyroidism
Metabolic syndrome
Nephrocalcinosis
Polycystic kidney disease (PKD)
Gastrointestinal diseases (i.e., jejuno-ileal bypass, intestinal resection, Crohn's disease, malabsorptive conditions, enteric hyperoxaluria after urinary diversion) and bariatric surgery
Sarcoidosis
Spinal cord injury, neurogenic bladder
Genetically determined stone formation
Cystinuria (type A, B and AB)
Primary hyperoxaluria (PH)
Renal tubular acidosis (RTA) type I
2,8-Dihydroxyadeninuria
Xanthinuria
Lesch-Nyhan syndrome
Cystic fibrosis
Drug-induced stone formation
Anatomical abnormalities associated with stone formation
Medullary sponge kidney (tubular ectasia)
Ureteropelvic junction (UPJ) obstruction
Calyceal diverticulum, calyceal cyst
Ureteral stricture
Vesico-uretero-renal reflux
Horseshoe kidney
Ureterocele
Environmental factors
Chronic lead exposure

Diagnostic Evaluation

Diagnostic imaging

Standard evaluation of a patient includes taking a detailed medical history and physical examination. The clinical diagnosis should be supported by appropriate imaging.

Recommendation	Strength rating
With fever or solitary kidney, and when diagnosis is doubtful, immediate imaging is indicated.	Strong

Ultrasound (US) should be used as the primary diagnostic imaging tool, although pain relief, or any other emergency measures, should not be delayed by imaging assessments.

Kidney-ureter-bladder (KUB) urography should not be performed if non-contrast-enhanced computed tomography (NCCT) is considered, but KUB urography can differentiate between radiolucent and radiopaque stones and be used for comparison during follow up.

Recommendation for radiologic examinations of patients with acute flank pain/suspected ureteral stones	Strength rating
Following initial ultrasound assessment, use non-contrast-enhanced computed tomography to confirm stone diagnosis in patients with acute flank pain.	Strong

Recommendation for radiologic examination of patients with renal stones	Strength rating
Perform a contrast study if stone removal is planned and the anatomy of the renal collecting system needs to be assessed.	Strong

Diagnostics: Metabolism-related

Each emergency patient with urolithiasis needs a succinct biochemical work-up of urine and blood; no difference is made between high- and low-risk patients.

Recommendations: basic laboratory analysis - emergency stone patient	Strength rating
Urine	
Dipstick test of spot urine sample • red cells; • white cells; • nitrite; • approximate urine pH; • urine microscopy and/or culture.	Strong
Blood	
Serum blood sample • creatinine; • uric acid; • (ionised) calcium; • sodium; • potassium; • blood cell count; • C-reactive protein.	Strong
Perform a coagulation test (partial thromboplastin time and international normalised ratio) if intervention is likely or planned.	Strong

Examination of sodium, potassium, C-reactive protein (CRP), and blood coagulation time can be omitted if no intervention is planned in non-emergency stone patients. Patients at high risk for stone recurrences should undergo a more specific analytical programme (see section on Metabolic Evaluation below).

Recommendations related to stone analysis	Strength rating
Perform stone analysis in first-time stone formers using a validated procedure (X-ray diffraction or infrared spectroscopy).	Strong
Repeat stone analysis in patients: • presenting with recurrent stones despite drug therapy; • with early recurrence after complete stone clearance; • with late recurrence after a long stone-free period because stone composition may change.	Strong

Diagnosis for special groups/conditions

Pregnancy

Recommendations	Strength rating
Use ultrasound as the preferred method of imaging in pregnant women.	Strong
In pregnant women, use magnetic resonance imaging as a second-line imaging modality.	Strong
In pregnant women, use low-dose computed tomography as a last-line option.	Strong

Children

Recommendations	Strength rating
In all children, complete a metabolic evaluation based on stone analysis.	Strong
Collect stone material for analysis to classify the stone type.	Strong
Perform ultrasound (US) as first-line imaging modality in children when a stone is suspected; it should include the kidney, fluid-filled bladder and the ureter.	Strong
Perform a kidney-ureter-bladder radiography (or low-dose non-contrast-enhanced computed tomography) if US will not provide the required information.	Strong

In children, the most common non-metabolic disorders facilitating stone formation are vesicoureteral reflux, UPJ obstruction, neurogenic bladder, and other voiding difficulties.

The radiation dose for intravenous urography (IVU) is comparable to that for voiding cystourethrography, but the need for contrast medium injection is a major drawback.

Disease Management

Acute treatment of a patient with renal colic

Pain relief is the first therapeutic step in patients with an acute stone episode.

Recommendations for pain relief during and prevention of recurrent renal colic	Strength rating
Offer a non-steroidal anti-inflammatory as the first drug of choice. e.g. metamizol (dipyrone); alternatively, paracetamol or, depending on cardio-vascular risk factors, diclofenac*, indomethacin or ibuprofen**.	Strong
Offer hydromorphine, pentazocine or tramadol as a second choice.	Weak
Offer renal decompression or ureteroscopic stone removal in case of analgesic refractory colic pain.	Strong

** Affects glomerular filtration rate in patients with reduced renal function.*

*** Recommended to counteract recurrent pain after renal colic (see extended document).*

Administration of daily α-blockers seems to reduce colic episodes, although controversy remains in the published literature.

If analgesia cannot be achieved medically, drainage, using stenting or percutaneous nephrostomy, or stone removal, should be performed.

Management of sepsis and anuria in the obstructed kidney

The obstructed, infected, kidney is a urological emergency.

Recommendations	Strength rating
Urgently decompress the collecting system in case of sepsis with obstructing stones, using percutaneous drainage or ureteral stenting.	Strong
Delay definitive treatment of the stone until sepsis is resolved.	Strong

In exceptional cases, with severe sepsis and/or the formation of abscesses, an emergency nephrectomy may become necessary.

Recommendations - Further measures	Strength rating
Collect urine for antibiogram test following decompression.	Strong
Start antibiotics immediately (+ intensive care if necessary).	Strong
Re-evaluate antibiotic treatment regimen following antibiogram findings.	Strong

Medical expulsive therapy (MET)

Medical expulsive therapy should only be used in informed patients. Treatment should be discontinued if complications develop (infection, refractory pain, deterioration of kidney function).

Medical expulsive therapy, using α-blockers, seems to be efficacious treating patients with ureteric stones that are amenable to conservative management. Patients benefitting most might be those with larger (distal) stones.

There is no or insufficient evidence to support the use of Phosphodiesterase type 5 inhibitor (PDE-5i) or corticosteroids in combination with α-blockers as a standard adjunct to active stone removal.

Recommendation for medical expulsive therapy (MET)	Strength rating
Offer α-blockers as medical expulsive therapy as one of the treatment options for (distal) ureteral stones > 5 mm.	Strong

Chemolytic dissolution of stones

Oral chemolysis of stones or their fragments can be useful in uric acid stones. It is based on alkalinisation of urine by application of alkaline citrate or sodium bicarbonate. The pH should be adjusted to 7.0-7.2.

Recommendations - Oral chemolysis	Strength rating
Inform the patient how to monitor urine-pH by dipstick and to modify the dosage of alkalising medication according to urine pH, as changes in urine pH are a direct consequence of such medication.	Strong
Carefully monitor patients during/after oral chemolysis for uric acid stones.	Strong
Combine oral chemolysis with Tamsulosin in case of (larger) ureteral stones (if active intervention is not indicated).	Weak

Percutaneous irrigation chemolysis is rarely used any more.

Shockwave lithotripsy (SWL)

The success rate for SWL will depend on the efficacy of the lithotripter and on:

- size, location (ureteral, pelvic or calyceal), and composition (hardness) of the stones;
- patient's habitus;
- performance of SWL.

Contraindications of SWL

Contraindications are few, but include:

- pregnancy;
- bleeding diatheses; which should be compensated for at least 24 hours before and 48 hours after treatment;
- untreated urinary tract infections (UTIs);
- severe skeletal malformations and severe obesity, which prevent targeting of the stone;
- arterial aneurysm in the vicinity of the stone;
- anatomical obstruction distal to the stone.

Best clinical practice (best performance) in SWL

Stenting prior to SWL

Routine use of internal stents before SWL does not improve stone-free rates, nor lowers the number of auxiliary treatments. It may, however, reduce formation of steinstrasse.

Pacemaker

Patients with a pacemaker can be treated with SWL. Patients with implanted cardioverter defibrillators must be managed with special care (firing mode temporarily reprogrammed during SWL treatment). However, this might not be necessary with new-generation lithotripters.

Shock waves, energy setting and repeat treatment sessions

- The number of shock waves that can be delivered at each session depends on the type of lithotripter and shockwave power.
- Starting SWL on a lower energy setting with step-wise power ramping prevents renal injury.
- Optimal shock wave frequency is 1.0 to 1.5 Hz.
- Clinical experience has shown that repeat sessions are feasible (within one day for ureteral stones).

Procedural control

Recommendations - Procedural control	**Strength rating**
Ensure correct use of the coupling agent as this is crucial for effective shock wave transportation.	Strong
Maintain careful fluoroscopic and/or ultrasonographic monitoring during shock wave lithotripsy.	Strong
Use proper analgesia as it improves treatment results by limiting pain and excessive respiratory excursions.	Strong

Antibiotic prophylaxis

No standard prophylaxis prior to SWL is recommended.

Recommendation	**Strength rating**
In the case of infected stones or bacteriuria, prescribe antibiotics prior to shockwave lithotripsy.	Strong

Ureterorenoscopy (URS) *(retrograde and antegrade, RIRS)*

Apart from general problems, for example, with general anaesthesia or untreated UTIs, URS can be performed in all patients without any specific contraindications.

If ureteral access is not possible, insertion of a JJ stent followed by URS after several days is an alternative. During URS, placement of a safety wire is recommended, even though some groups have demonstrated that URS can be performed without it.

Ureteral access sheaths allow easy, multiple, access to the upper urinary tract; however, its insertion may lead to ureteral damage.

Recommendations	Strength rating
Use holmium: yttrium-aluminium-garnet (Ho:YAG) laser lithotripsy for (flexible) ureterorenoscopy.	Strong
Perform stone extraction only under direct endoscopic visualisation of the stone.	Strong
Do not insert a stent in uncomplicated cases.	Strong
Pre-stenting facilitates ureterorenoscopy (URS) and improves outcomes of URS (in particular for renal stones).	Strong
Offer MET for patients suffering from stent-related symptoms and after Ho:YAG laser lithotripsy for the passage of fragments.	Strong

Percutaneous nephrolithotomy (PNL)

Patients with bleeding diathesis or receiving anticoagulant therapy must be monitored carefully pre- and post-operatively. Anticoagulant therapy must be discontinued before PNL contraindications, which include:

- untreated UTI;
- tumour in the presumptive access tract area;

- potential malignant kidney tumour;
- pregnancy.

Best clinical practice

Both prone and supine positions are equally safe. Percutaneous nephrolithotomy performed with small instruments tended to be associated with significantly lower blood loss, but the duration of procedure tended to be significantly longer.

Recommendations	Strength rating
Perform pre-procedural imaging, including contrast medium where possible or retrograde study when starting the procedure, to assess stone comprehensiveness and anatomy of the collecting system to ensure safe access to the renal stone.	Strong
In uncomplicated cases, perform a tubeless (without nephrostomy tube) or totally tubeless (without nephrostomy tube and ureteral stent) percutaneous nephrolithotomy procedure.	Strong

Stone Removal

Recommendations	Strength rating
Obtain a urine culture or perform urinary microscopy before any treatment is planned.	Strong
Exclude or treat urinary tract infection prior to stone removal.	Strong
Offer peri-operative antibiotic prophylaxis to all patients undergoing endourological treatment.	Strong
Offer active surveillance to patients at high risk for thrombotic complications in the presence of an asymptomatic calyceal stone.	Weak
Decide on temporary discontinuation, or bridging of antithrombotic therapy in high-risk patients, in consultation with the internist.	Strong
Retrograde (flexible) ureterorenoscopy Is the preferred intervention if stone removal is essential and antithrombotic therapy cannot be discontinued, since it is associated with less morbidity.	Strong

Radiolucent uric acid stones can be dissolved by oral chemolysis.

Ureteral stones

Observation of ureteral stones is feasible in informed patients who develop no complications (infection, refractory pain, deterioration of kidney function).

Recommendations	Strength rating
In patients with newly diagnosed small* ureteral stones, if active stone removal is not indicated, observe patient initially along with periodic evaluation.	Strong
Offer α-blockers as medical expulsive therapy as one of the treatment options for (distal)ureteral stones ≥ 5 mm.	Strong
Inform patients that ureterorenoscopy (URS) has a better chance of achieving stone-free status with a single procedure.	Strong
Inform patients that URS has higher complication rates when compared to shock wave lithotripsy.	Strong
In cases of severe obesity use URS as first-line therapy for ureteral (and renal) stones.	Strong

**see stratification data (J Urol, 2007. 178: 2418).*

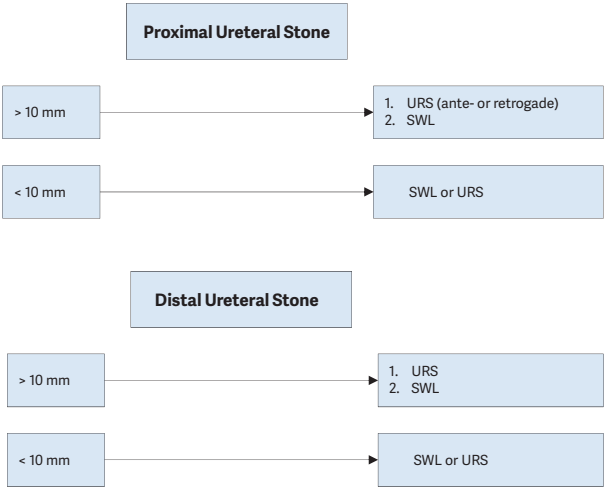
Indication for active stone removal and selection of procedure

Ureter:

- stones with a low likelihood of spontaneous passage;
- persistent pain despite adequate pain medication;
- persistent obstruction;
- renal insufficiency (renal failure, bilateral obstruction, single kidney).

The suspected stone composition might influence the choice of treatment modality.

Figure 1: Treatment algorithm for ureteral stones (If active stone removal is indicated) (Strength rating: Strong)



SWL = shock wave lithotripsy; URS = ureterorenoscopy.

Recommendation	Strength rating
Use percutaneous antegrade removal of ureteral stones as an alternative when shockwave lithotripsy is not indicated or has failed, and when the upper urinary tract is not amenable to retrograde ureterorenoscopy.	Strong

Renal stones

It is still debatable whether renal stones should be treated, or whether annual follow-up is sufficient for asymptomatic calyceal stones that have remained stable for six months.

Recommendations	Strength rating
Follow-up periodically in cases where renal stones are not treated (initially after six months and then yearly, evaluating symptoms and stone status [either by ultrasound, kidney-ureter-bladder radiography or computed tomography]).	Strong
Offer active treatment for renal stones in case of stone growth, *de novo* obstruction, associated infection, and acute and/or chronic pain.	Weak
Assess comorbidity, stone composition and patient preference when making treatment decisions.	Weak
Offer shock wave lithotripsy (SWL) and endourology (percutaneous nephrolithotomy [PNL], retrograde renal surgery [RIRS]) as treatment options for stones < 2 cm within the renal pelvis and upper or middle calices.	Strong
Perform PNL as first-line treatment of larger stones > 2 cm.	Strong
In case PNL is not an option, treat larger stones (> 2 cm) with flexible ureterorenoscopy or SWL. However, in such instances there is a higher risk that a follow-up procedure and placement of a ureteral stent may be needed.	Strong

For the lower pole, perform PNL or RIRS, even for stones > 1 cm, as the efficacy of SWL is limited (depending on favourable and unfavourable factors for SWL).	Strong

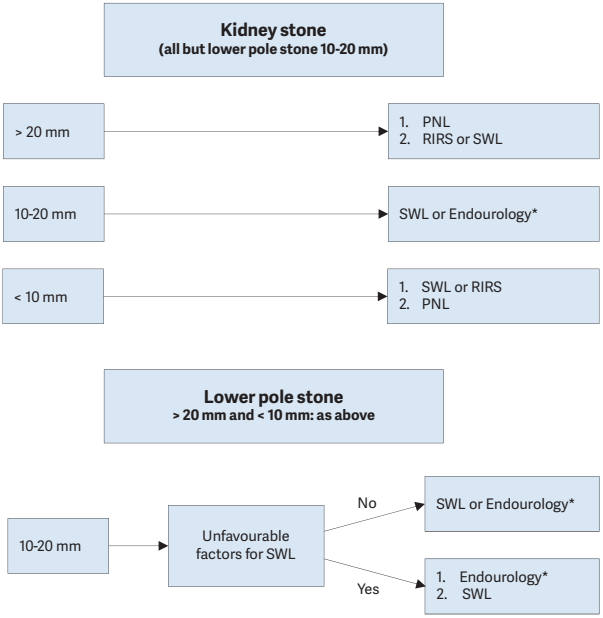
Indication for active stone removal and selection of procedure

Kidney:

- stone growth;
- stones in high-risk patients for stone formation;
- obstruction caused by stones;
- infection;
- symptomatic stones (e.g. pain, haematuria);
- stones > 15 mm;
- stones < 15 mm if observation is not the option of choice;
- patient preference;
- comorbidity;
- social situation of the patient (e.g., profession or travelling);
- choice of treatment.

The suspected stone composition might influence the choice of treatment modality.

Figure 2: Treatment algorithm for renal stones (if active treatment is indicated). (Strength rating: Strong)



** The term 'Endourology' encompasses all PNL and URS interventions.*

PNL = percutaneous nephrolithotomy; RIRS = retrograde renal surgery; SWL = shockwave lithotripsy; URS = ureterorenoscopy.

Recommendation	Strength rating
Use flexible ureterorenoscopy in cases where percutaneous nephrolithotomy or shockwave lithotripsy are not an option (even for stones > 2 cm). However, in this case there is a higher risk that a follow-up procedure and placement of a ureteral stent may be needed. In complex stone cases, use open or laparoscopic approaches as possible alternatives.	Strong

Open and laparoscopic surgery

Recommendations	Strength rating
Offer laparoscopic or open surgical stone removal in rare cases in which shockwave lithotripsy (SWL), (flexible) ureterorenoscopy and percutaneous nephrolithotomy fail, or are unlikely to be successful.	Strong
Perform surgery laparoscopically before proceeding to open surgery.	Strong
For ureterolithotomy, perform laparoscopy for large impacted stones when endoscopic lithotripsy or SWL has failed, or is contraindicated.	Strong

Steinstrasse

The major factor in steinstrasse formation is stone size. Medical expulsion therapy increases the stone expulsion rate of steinstrasse. When spontaneous passage is unlikely, further treatment of steinstrasse is indicated.

Recommendations	Strength rating
Treat steinstrasse associated with urinary tract infection/fever preferably with percutaneous nephrostomy.	Weak
Treat steinstrasse when large stone fragments are present with shockwave lithotripsy or ureterorenoscopy.	Weak

Management of patients with residual stones

Following initial treatment with SWL, URS or PNL residual fragments may remain and require additional intervention. The indications for active removal of residual stones and selection of the procedure are based on the same criteria as for primary stone treatment. For well-disintegrated stone material in the lower calix, inversion therapy with simultaneous mechanical percussion manoeuvre under enforced diuresis may facilitate stone clearance.

Recommendation in case of residual fragments	Strength rating
Perform imaging after shockwave lithotripsy, ureterorenoscopy or percutaneous nephrostomy to determine presence of residual fragments.	Strong

Management of urinary stones and related problems during pregnancy

Recommendation	Strength rating
Treat all uncomplicated cases of urolithiasis in pregnancy conservatively (except those that have clinical indications for intervention).	Strong

If intervention becomes necessary, placement of a ureteral stent or a percutaneous nephrostomy tube are readily available primary options. Ureteroscopy is a reasonable alternative to avoid long-term stenting/drainage. There is a higher tendency for stent encrustation during pregnancy.

Management of stones in patients with urinary diversion

Patients with urinary diversion are at high risk for stone formation in the renal collecting system and ureter or in the conduit or continent reservoir.

Recommendation	Strength rating
Perform percutaneous lithotomy to remove large renal stones in patients with urinary diversion, as well as for ureteral stones that cannot be accessed via a retrograde approach or that are not amenable to shockwave lithotripsy.	Strong

Management of stones in patients with neurogenic bladder

Patients with neurogenic bladder are more prone to development of urinary calculi.

In myelomeningocoele patients, latex allergy is common so that appropriate measures need to be taken regardless of the treatment.

Management of stones in transplanted kidneys

Transplanted patients are at additional risk due to their dependency on a solitary kidney, immunosuppression therapy and possible metabolic impairments. Conservative treatment for small asymptomatic stones is only possible under close surveillance and in absolutely compliant patients.

Stones causing urinary stasis/obstruction require immediate intervention or drainage of the transplanted kidney.

Recommendations	Strength rating
Perform ultrasound or non-contrast-enhanced computed tomography to rule out calculi in patients with transplanted kidneys, unexplained fever, or unexplained failure to thrive (particularly in children).	Strong
Offer patients with transplanted kidneys, any of the contemporary management options, including shockwave therapy, flexible ureterorenoscopy, and percutaneous nephrolithotomy.	Weak

Special problems in stone removal

Calyceal diverticulum stones	• Shockwave lithotripsy (SWL), percutaneous nephrolithotomy (PNL) (if possible) or retrograde renal surgery (RIRS). • Can also be removed using laparoscopic retroperitoneal surgery. • Patients may become asymptomatic due to stone disintegration (SWL), whilst well-disintegrated stone material remains in the original position due to a narrow calyceal neck.
Horseshoe kidneys	• Can be treated in line with the options described above. • Passage of fragments after SWL might be poor. • Acceptable stone-free rates (SFRs) can be achieved with flexible ureterorenoscopy (URS).

Stones in pelvic kidneys	• SWL, RIRS, PNL or laparoscopic surgery. • In obese patients, the options are RIRS, PNL or open surgery.
Patients with obstruction of the ureteropelvic junction	• When outflow abnormality requires correction, stones can be removed by PNL together with percutaneous endopyelotomy or open/laparoscopic reconstructive surgery. • Ureterorenoscopy together with endopyelotomy with holmium-yttrium-aluminium-garnet laser. • Incision with an Acucise® balloon catheter might be considered, provided the stones can be prevented from falling into the pyeloureteral incision. • Open surgery with correction of the UPJ obstruction (pyloplasty) and stone removal is a feasible option.

Management of urolithiasis in children

In children, the indication for SWL and for PNL is similar to those in adults. Compared to adults, children pass fragments more rapidly after SWL. For endourological procedures, the smaller organs in children must be considered when selecting instruments for PNL or URS.

Children with renal stones of a diameter up to 20 mm (~300 mm^2) are ideal candidates for SWL.

Recommendations	Strength rating
Offer children with ureteral stones shockwave lithotripsy (SWL) as first-line but consider uretero-renoscopy if SWL is not possible and in case of larger distal ureteric stones.	Strong
Offer children with renal stones with a diameter of up to 20 mm (~300 mm^2) SWL.	Strong
Offer children with renal pelvic or calyceal stones with a diameter > 20 mm(~300 mm^2) percutaneous nephrolithotomy.	Strong

Metabolic evaluation and recurrence prevention

After stone passage, every patient should be assigned to a low- or high-risk group for stone formation. For correct classification, two analyses are mandatory:

- reliable stone analysis by infrared spectroscopy or X-ray diffraction;
- basic analysis.

Only high-risk stone formers require specific metabolic evaluation. Stone type is the deciding factor for further diagnostic tests. For both groups, general preventive measures apply:

General preventive measures	
Fluid intake (drinking advice)	Fluid amount: 2.5-3.0 L/day Circadian drinking Neutral pH beverages Diuresis: 2.0-2.5 L/day Specific weight of urine: < 1010 L/day

Nutritional advice for a balanced diet	Rich in vegetables and fibre Normal calcium content: 1-1.2 g/day Limited NaCl content: 4-5 g/day Limited animal protein content: 0.8-1.0 g/kg/day Avoid excessive consumption of vitamin supplements
Lifestyle advice to normalise general risk factors	Body mass index (BMI): retain a normal BMI level Adequate physical activity Balancing of excessive fluid loss

Caution: The protein need is age-group dependent; therefore, protein restriction in childhood should be handled carefully.

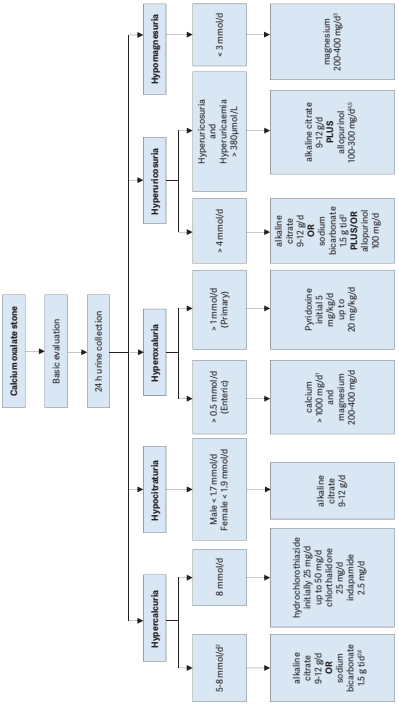
Calcium oxalate stones

Hyperparathyroidism is excluded by blood analysis.

Recommendations for pharmacological treatment of patients with specific abnormalities in urine composition (based on 24-hour urine samples)		
Urinary risk factor	**Suggested treatment**	**Strength rating**
Hypercalcuria	Thiazide + potassium citrate	Strong
Hyperoxaluria	Oxalate restriction	Weak
Enteric hyperoxaluria	Potassium citrate	Weak
	Calcium supplement	Weak
	Diet reduced in fat and oxalate	Weak
Hypocitraturia	Potassium citrate	Strong
Hypocitraturia	Sodium bicarbonate if intolerant to potassium citrate	Strong

Hyperuricosuria	Allopurinol	Strong
	Febuxostat	Strong
High sodium excretion	Restricted intake of salt	Strong
Small urine volume	Increased fluid intake	Strong
Urea level indicating a high intake of animal protein	Avoid excessive intake of animal protein	Strong

Figure 3: Diagnostic and therapeutic algorithm for calcium oxalate stones



[1] Be aware of excess calcium excretion.

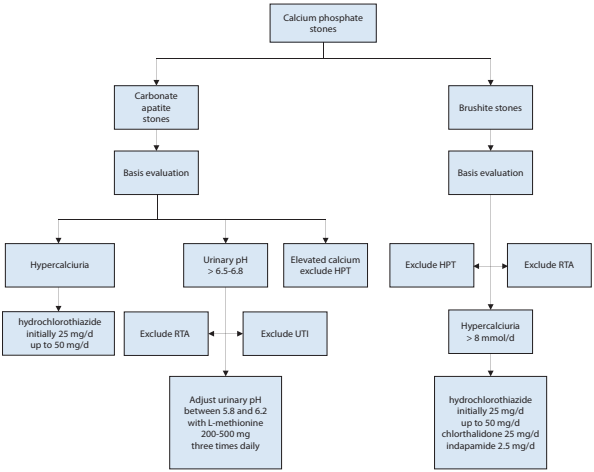
[2] tid = three times/day (24h).

[3] No magnesium therapy for patients with renal insufficiency.

[4] There is no evidence that combination therapy (thiazide + citrate) or (thiazide + allopurinol) is superior to thiazide therapy alone.

[5] Febuxostat 80 mg/day.

Figure 4: Diagnostic and therapeutic algorithm for calcium phosphate stones



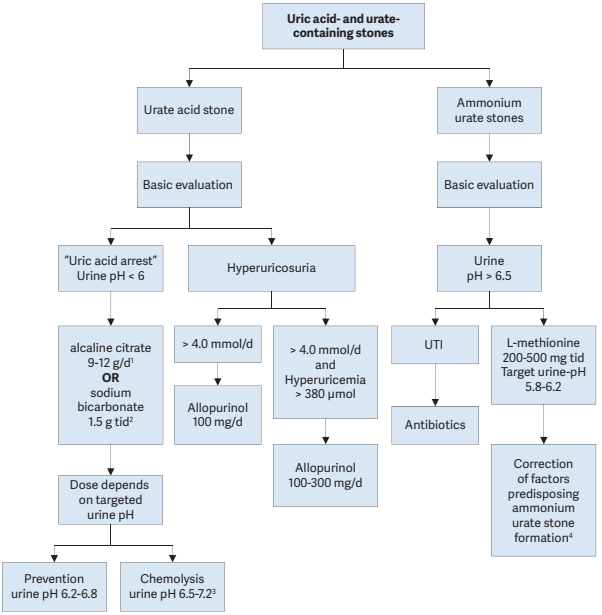
HPT = hyperparathyroidism; RTA = renal tubular acidosis; UTI = urinary tract infection.

Recommendations	Strength rating
Prescribe thiazide in case of hypercalciuria.	Strong
Advise patients to acidify their urine in case of high urine pH.	Weak

Hyperparathyroidism

Elevated levels of ionized calcium in serum (or total calcium and albumin) require assessment of intact parathyroid hormone to confirm or exclude suspected hyperparathyroidism (HPT). Primary HPT can only be cured by surgery.

Figure 5: Diagnostic and therapeutic algorithm for uric acid and urate-containing stones



UTI = urinary tract infection.

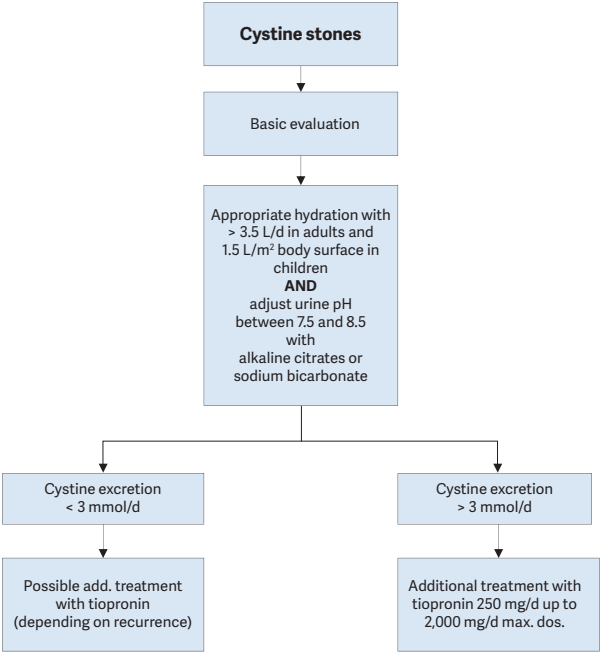
[1] d: day.

[2] tid: three times a day.

[3] A higher pH may lead to calcium phosphate stone formation.

[4] In patients with high uric acid excretion, allopurinol may be helpful.

Figure 6: Metabolic management of cystine stones.



Struvite/infection stones

Recommendations for therapeutic measures of infection stones	Strength rating
Surgically remove the stone material as completely as possible.	Strong
Prescribe antibiotics in case of persistent bacteriuria.	Strong
Prescribe ammonium chloride, 1 g, two or three times daily to ensure urinary acidification.	Weak
Prescribe methionine, 200-500 mg, one to three times daily, as an alternative, to ensure urinary acidification.	Weak

2,8-Dihydroyadenine stones and xanthine stones

Both stone types are rare. In principle, diagnosis and specific prevention is similar to that of uric acid stones.

Drug stones

Drug stones are induced by pharmacological treatment. Two types exist:

- stones formed by crystallised compounds of the drug;
- stones formed due to unfavourable changes in urine composition under drug therapy.

Treatment includes general preventive measures and the avoidance of the respective drugs.

Investigating a patient with stones of unknown composition

Investigation	Rationale for investigation
Medical history	• Stone history (former stone events, family history) • Dietary habits • Medication chart
Diagnostic imaging	• Ultrasound in the case of a suspected stone • Unenhanced helical computed tomography • Determination of Hounsfield units provides information on the possible stone composition
Blood analysis	• Creatinine • Calcium (ionised calcium or total calcium + albumin) • Uric acid
Urinalysis	• Urine pH profile (measurement after each voiding, minimum four times daily) • Dipstick test: leukocytes, erythrocytes, nitrite, protein, urine pH, specific weight • Urine culture • Microscopy of urinary sediment (morning urine) • Cyanide nitroprusside test (cysteine exclusion)

Further examinations depend on the results of the investigations listed above.

This short booklet text is based on the more comprehensive EAU Guidelines (978-94-92671-01-1) available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines/.

EAU GUIDELINES ON PAEDIATRIC UROLOGY

(Limited text update March 2018)

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Introduction

Due to the scope of the extended Guidelines on Paediatric Urology, no attempt has been made to include all topics, but rather to provide a selection based on practical considerations.

PHIMOSIS

Background

At the end of the first year of life, retraction of the foreskin behind the glandular sulcus is possible in 50% of boys. The phimosis is either primary (physiological), with no sign of scarring, or secondary (pathological), resulting from scarring due to conditions such as balanitis xeroticaobliterans.

Phimosis must be distinguished from normal agglutination of the foreskin to the glans, which is a physiological phenomenon. If the tip remains narrow and glandular adhesions are separated, then the space is filled with urine during voiding, causing the foreskin to balloon outward.

Treatment

Conservative treatment

Administration of a corticoid ointment or cream is an option for primary phimosis with a success rate of > 90%, but with a

recurrence rate of 17%. Agglutination of the foreskin does not respond to steroid treatment.

Circumcision: indication and contraindication

Childhood circumcision should not be recommended without a medical reason. An absolute indication for circumcision is secondary phimosis. Contraindications for circumcision are acute local infection and congenital anomalies of the penis, particularly hypospadias or buried penis, as the foreskin may be required for a reconstructive procedure.

Plastic circumcision (dorsal incision, partial circumcision) carries the potential for recurrence of phimosis. Associated frenulum breve is corrected by frenulotomy. Meatoplasty is added if necessary.

Paraphimosis

It is characterised by retracted foreskin with the constrictive ring localised at the level of the sulcus. A dorsal incision of the constrictive ring may be required, or circumcision is carried out immediately or in a second session.

UNDESCENDED TESTES

Background

Cryptorchidism or undescended testis is one of the most common congenital malformations of male neonates. In newborn cases with non-palpable or undescended testes on both sides and any sign of disorders of sex development (DSD) like concomitant hypospadias, urgent endocrinological and genetic evaluation is required.

Classification

The term cryptorchidism is most often used synonymously for undescended testes. The most useful classification of undescended testes is into palpable and non-palpable testes, and clinical management is decided by the location and

presence of the testes. Approximately 80% of all undescended testes are palpable.

Palpable testes include true undescended testes and ectopic testes. Non-palpable testes include intra-abdominal, inguinal, absent, and sometimes also some ectopic testes.

Most importantly, the diagnosis of a palpable or non-palpable testis needs to be confirmed once the child is under general anaesthesia, as the first step of any surgical procedure for undescended testes. See figure 1.

Diagnostic Evaluation

History taking and physical examination are key points in evaluating boys with undescended testes. Localisation studies using different imaging modalities are usually without any additional benefit.

Management

Treatment should be started at the age of six months. After that age, undescended testes rarely descend. Any kind of treatment leading to a scrotally positioned testis should be finished by twelve months, or eighteen months at the latest, because histological examination of undescended testes at that age has already revealed a progressive loss of germ and Leydig cells. The early timing of treatment is also driven by the final adult results on spermatogenesis and hormone production, as well as on the risk of tumour development. See figure 2.

Medical therapy for testicular descent

Unfortunately, most of the studies on hormonal treatment have been of poor quality, with heterogeneous and mixed patient populations, testis location, schedules and dosages of hormonal administration. Additionally, long-term data are almost completely lacking.

Hormonal therapy using human chorionic gonadotropin or gonadotrophin-releasing hormone (GnRH) is based on the hormonal dependence of testicular descent, but has a maximum success rate of only 20%. In general, success rates depend on testicular location. The higher the testis is located prior to therapy, the lower the success rate. The Panel consensus is that endocrine treatment to achieve testicular descent is not recommended.

Medical therapy for fertility potential

Hormonal treatment may improve fertility indices and therefore serve as an additional tool to orchidopexy. It is still unknown whether this effect on testicular histology persists into adulthood but it has been shown that men who were treated in childhood with buserelin had better semen analyses compared with men who had childhood orchidopexy alone or placebo treatment.

Identification of specific subgroups of boys with undescended testes who would benefit from such an approach using hormones is difficult. The Panel consensus recommends endocrine treatment with GnRH analogues for boys with bilateral undescended testes to preserve the fertility potential.

Surgical Treatment

If a testis has not concluded its descent at the age of six months (corrected for gestational age), and since spontaneous testicular descent is unlikely to occur after that age, surgery should be performed within the subsequent year, at age eighteen months, at the latest.

Palpable testes

Surgery for palpable testes includes orchidofunicolysis and orchidopexy, either via an inguinal or scrotal approach.

Non-palpable testes

For non-palpable testes, surgery must clearly determine whether a testis is present or not. If a testis is found, the decision has to be made to remove it or bring it down to the scrotum.

An important step in surgery is a thorough re-examination once the boy is under general anaesthesia, since a previously non-palpable testis might be identifiable and subsequently change the surgical approach to standard inguinal orchidopexy, as described above. Otherwise, the easiest and most accurate way to locate an intra-abdominal testis is diagnostic laparoscopy. Subsequent removal or orchidolysis and orchidopexy can be carried out using the same approach to achieve the therapeutic aims.

In case of a vanishing testis, the procedure is finished once blind-ending spermatic vessels are clearly identified. If the vessels enter the inguinal canal, one may find an atrophic testis upon inguinal exploration or a healthy testis that needs to undergo standard orchidopexy. A peeping testis can be placed down in the scrotum laparoscopically or via an inguinal incision. Placement of an intra-abdominal testis can sometimes be a surgical challenge. Usually, testes lying > 2 cm above the internal inguinal ring may not reach the scrotum without division of the testicular vessels. Under such circumstances, a Fowler–Stephens orchidopexy might be an option.

Undescended testes and fertility

The association of undescended testes with compromised fertility is extensively discussed in the literature and seems to be a result of multiple factors, including germ cell loss, impaired germ cell maturation, Leydig cell diminution, and testicular fibrosis.

Although boys with one undescended testis have a lower fertility rate, they have the same paternity rate as those with bilateral descended testes. Boys with bilateral undescended testes suffer both lower fertility and paternity rates.

Regarding preservation of fertility potential, early surgical correction of undescended testes is highly recommended before twelve months of age, and by eighteen months at the latest.

Undescended testes and malignancy

Boys who are treated for an undescended testis have an increased risk of developing testicular malignancy. Screening and self-examination during and after puberty is therefore recommended.

Pre-pubertal orchidopexy may reduce the risk of testicular cancer and early surgical intervention is indicated in boys with undescended testes.

Recommendations	Strength rating
The Panel do not recommend medical or surgical treatment for retractile testes but recommend close follow-up on a yearly basis until puberty.	Strong
Perform surgical orchidolysis and orchidopexy before the age of twelve months, and by eighteen months at the latest.	Strong
Evaluate male neonates with bilateral non-palpable testes for possible disorders of sex development.	Strong
Perform a diagnostic laparoscopy to locate an intra-abdominal testicle.	Strong

Hormonal therapy in unilateral undescended testes is of no benefit for future paternity.	Weak
Offer endocrine treatment in case of bilateral undescended testes.	Weak
Inform the patient/caregivers about the increased risk of a later malignancy with an undescended testis in a post-pubertal boy or older and discuss removal in case of a contralateral normal testis in a scrotal position.	Weak

Figure 1: Classification of undescended testes

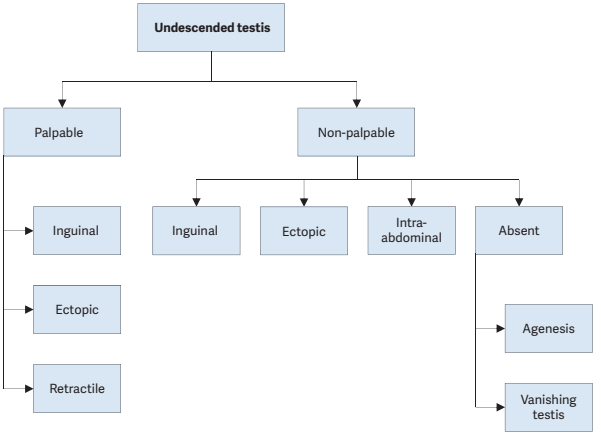
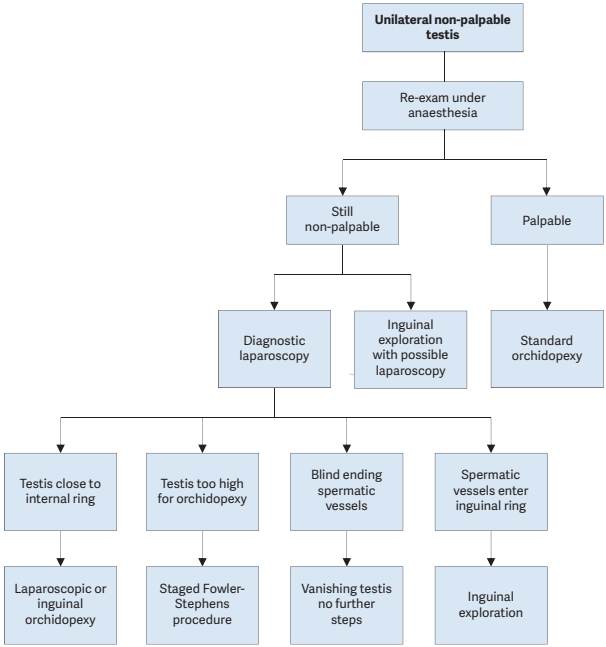


Figure 2: Algorithm for the management of unilateral non-palpable undescended testis



HYDROCELE

Background

Non-communicating hydroceles are found secondary to minor trauma, testicular torsion, epididymitis, or varicocele operation, or may appear as a recurrence after primary repair of a communicating hydrocele.

A communicating hydrocele vacillates in size, usually relative to activity. It is diagnosed by medical history and physical investigation, the swelling is translucent, and transillumination of the scrotum confirms the diagnosis. If there are any doubts about intra-scrotal mass, ultrasound (US) should be performed. Contralateral disease should be excluded.

Surgical Treatment

Surgical treatment of hydrocele is not indicated within the first 12-24 months because of the tendency for spontaneous resolution.

However, early surgery is indicated if there is suspicion of a concomitant inguinal hernia or underlying testicular pathology. There is no evidence that this type of hydrocele risks testicular damage.

The surgical procedure consists of ligation of the patent processus vaginalis via an inguinal incision, leaving the distal stump open, whereas in hydrocele of the cord, the cystic mass is excised or unroofed. Sclerosing agents should not be used because of the risk of chemical peritonitis in the communicating processus vaginalis peritonei.

The scrotal approach (Lord or Jaboulay technique) is used in the treatment of a secondary non-communicating hydrocele.

Recommendations	Strength rating
Observe hydrocele for twelve months prior to considering surgical treatment ~~in the majority of infants~~.	Strong
Perform early surgery if there is suspicion of a concomitant inguinal hernia or underlying testicular pathology.	Strong

Perform a scrotal ultrasound in case of doubt about the character of an intra-scrotal mass.	Strong
Do not use sclerosing agents because of the risk for chemical peritonitis.	Strong

HYPOSPADIAS

Background

Hypospadias are usually classified according to the anatomical location of the proximally displaced urethral orifice:

- distal - anterior hypospadias (glanular, coronal or distal penile);
- intermediate - middle (penile);
- proximal - posterior (penoscrotal, scrotal, perineal).

The pathology may be much more severe after skin release.

Diagnostic Evaluation

Patients with hypospadias should be diagnosed at birth. The diagnostic evaluation also includes an assessment of associated anomalies, which include cryptorchidism and open processus vaginalis or inguinal hernia. Severe hypospadias with unilaterally or bilaterally impalpable testis, or with ambiguous genitalia, require a complete genetic and endocrine work-up immediately after birth to exclude DSD, especially congenital adrenal hyperplasia.

Trickling urine and ballooning of the urethra require exclusion of meatal stenosis.

The length of the hypospadiac penis may be distorted by penile curvature, penoscrotal transposition, or may be smaller due to hypogonadism.

Differentiation between functionally necessary and aesthetically feasible operative procedures is important for

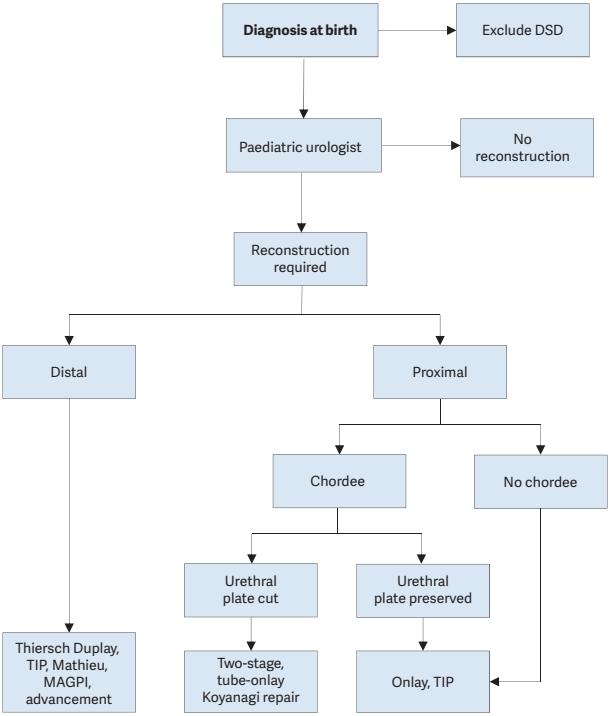
therapeutic decision-making. As all surgical procedures carry the risk of complications; thorough pre-operative counselling of the caregivers is crucial. The therapeutic objectives are to correct the penile curvature, to form a neourethra of an adequate size, to bring the neomeatus to the tip of the glans, if possible, and to achieve an overall acceptable cosmetic appearance. This goal is achieved by using different surgical techniques according to the individual findings.

Surgical Treatment

For repeat hypospadias repairs, no definitive guidelines can be given.

Excellent long-term functional and cosmetic results can be achieved after repair of anterior penile hypospadias. The complication rate in proximal hypospadias repair is higher. Figure 3 provides an algorithm for the management of hypospadias.

Figure 3: Algorithm for the management of hypospadias



DSD = disorders of sex development; GAP = glans approximation procedure; TIP = tubularised incised plate urethroplasty; MAGPI = meatal advancement and glanuloplasty incorporated.

MICROPENIS

Micropenis is defined as a small but otherwise normally formed penis with a stretched length of less than 2.5 cm ± standard deviation (SD) below the mean (Table 1).

Table 1: Length of the penis in boys
(according to Feldmann and Smith)

Age	Mean ± SD (cm)
Newborns	3.5 ± 0.4
0-5 months	3.9 ± 0.8
6-12 months	4.3 ± 0.8
1-2 years	4.7 ± 0.8
2-3 years	5.1 ± 0.9
3-4 years	5.5 ± 0.9
4-5 years	5.7 ± 0.9
5-6 years	6.0 ± 0.9
6-7 years	6.1 ± 0.9
7-8 years	6.2 ± 1.0
8-9 years	6.3 ± 1.0
9-10 years	6.3 ± 1.0
10-11 years	6.4 ± 1.1
Adults	13.3 ± 1.6

VARICOCELE IN CHILDREN AND ADOLESCENTS

Background

Varicocele is unusual in boys under ten years of age, but becomes more frequent at the beginning of puberty. Fertility problems will arise in about 20% of adolescents with varicocele. The adverse influence of varicocele increases with time.

Testicular catch-up growth and improvement in sperm parameters after varicocelectomy has been reported in adolescents. Varicocele is mostly asymptomatic, rarely causing pain at this age. It may be noticed by the patient or caregivers, or discovered by the paediatrician at a routine visit. Diagnosis and classification depends upon the clinical finding and US investigation.

Surgical Treatment

Surgical intervention is based on ligation or occlusion of the internal spermatic veins. Microsurgical lymphatic-sparing repairs (microscopic or laparoscopic) are associated with the lowest recurrence and complication rates. There is no evidence that treatment of varicocele at paediatric age will offer a better andrological outcome than an operation performed later.

Conservative treatment and follow-up

During adolescence, testicular size should be checked annually. After adolescence, repeated sperm analysis is recommended. Figure 4 shows an algorithm for the diagnosis of varicocele in children and adolescents, and Figure 5 shows an algorithm for its treatment.

Figure 4: Algorithm for the diagnosis of varicocele in children and adolescents

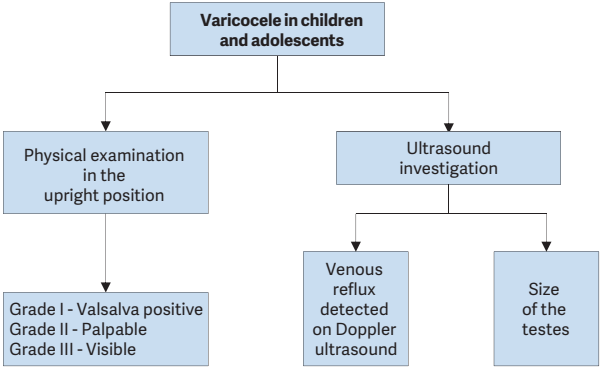
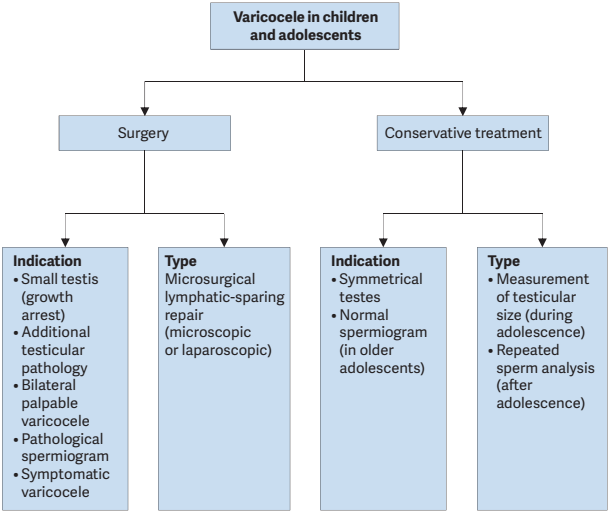


Figure 5: Algorithm for the management of varicocele in children and adolescents



URINARY TRACT INFECTIONS IN CHILDREN

Background

Urinary tract infections (UTIs) represent the most common bacterial infection in children. In neonates, the symptoms differ in many aspects from those in infants and children. The prevalence is higher; there is a male predominance; infections not caused by *Escherichia coli* are more frequent, and there is a higher risk of urosepsis.

- *Site:* Lower urinary tract (cystitis) versus upper urinary tract (pyelonephritis);

- *Episode:* first UTI versus unresolved infection, persistent infection and re-infection;
- *Severity:* simple UTI versus severe UTI;
- *Symptoms:* asymptomatic bacteriuria versus symptomatic UTI;
- *Complicating factors:* uncomplicated versus complicated UTI.

Diagnostic Evaluation

Diagnosis includes a medical history, searching for clinical signs and symptoms and a complete physical examination.

Urine sampling, analysis and culture

Urine sampling has to be performed before any antimicrobial agent is administered. The technique for obtaining urine is important to confirm or exclude UTI. Sampling in neonates, infants and non-toilet-trained children:

- **Plastic bag:** (high incidence of false positive results [85-99%]). Only helpful to exclude a UTI if the dipstick is negative for leukocyte esterase and the culture results are negative, otherwise the UTI has to be confirmed by a more specific method.
- **Clean-catch urine collection:** has a false-positive rate of 5% and false-negative rate of 12% and the contamination rate is higher compared to supra-pubic bladder aspiration (SPA).
- **Bladder catheterisation:** In female infants and in neonates, this technique may be an alternative to SPA, however with a higher contamination rate.
- **Supra-pubic bladder aspiration:** This is the most sensitive method to obtain an uncontaminated urine sample in non-toilet trained children.
- **Midstream urine** in toilet-trained, children who can void on command, could be an acceptable technique for obtaining urine after cleaning the urethral meatus and perineum.

Urinalysis:

- **Dipsticks:** are ready to use and helpful when the result is positive, because it is highly specific.
- **Microscopy:** can be used after centrifugation as well as in uncentrifuged urine and has been demonstrated to be sensitive for UTI. This is rarely done in an outpatient setting.
- **Flow imaging analysis technology:** is being increasingly used to classify particles in uncentrifuged urine specimens and correlates well with manual methods.
- **Urine culture:** is generally not necessary after negative results for dipstick, microscopic or automated urinalysis. If the dipstick result is positive, confirmation by urine culture is strongly recommended.

Pyuria without bacteriuria (sterile pyuria) may be due to incomplete antibiotic treatment, urolithiasis, or foreign bodies in the urinary tract, and infections caused by *Mycobacterium tuberculosis or Chlamydia trachomatis*.

Table 2: Criteria for UTI in children

Urine specimen from suprapubic bladder puncture	Urine specimen from bladder catheterisation	Urine specimen from midstream void
Any number of cfu/mL (at least 10 identical colonies)	≥ 10^3 - 10^5 cfu/mL	≥ 10^4 cfu/mL with symptoms ≥ 10^5 cfu/mL without symptoms

Imaging

Ultrasound (US): of the kidneys and bladder as soon as possible is advised in infants with febrile UTI to exclude obstruction of the upper and lower urinary tract and post-void residual urine should be measured in toilet-trained children to exclude voiding abnormalities as a cause of UTI.

Radionuclide scanning: changes in dimercaptosuccinic acid (DMSA) clearance during acute UTI (up to four to six weeks) indicating pyelonephritis and renal scars can be detected after three to six months. This correlates well with the presence of dilating reflux and the risk of further pyelonephritis episodes, breakthrough infections and future renal scarring.
Voiding cystourethrography (VCUG): is best practice to exclude or confirm vesicoureteral reflux, due to the risk of renal scarring, VCUG is recommended after the first episode of febrile UTI in boys and girls depending on sex, age and clinical presentation (see Figure 6). Another option is doing DMSA first, followed by VCUG if there is renal cortical uptake deficiency after UTI.

Bladder and bowel dysfunction (BBD) are risk factors for which each child with UTI should be screened for upon presentation. If there are signs of BBD at infection-free intervals, further diagnosis and effective treatment are strongly recommended.

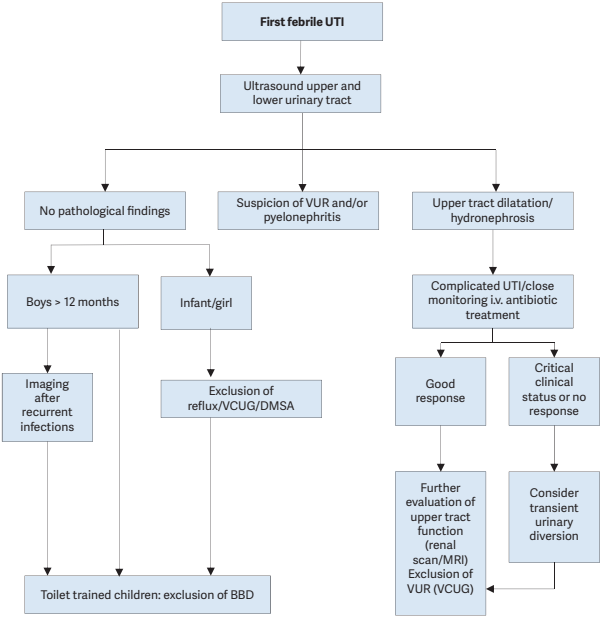
Status of circumcision should be checked in boys and treatment of the phimosis considered in those with pyelonephritis.

Management

Administration route: the choice between oral and parenteral therapy should be based on patient age; clinical suspicion of urosepsis; illness severity; refusal of fluids, food and/or oral medication; vomiting; diarrhoea; non-compliance; and complicated pyelonephritis (e.g. urinary obstruction). Febrile UTI in early infancy should be treated by i.v. fluids and antibiotics and under close monitoring within the hospital.
Duration of therapy: outcomes of short courses (one to three days) are inferior to those of seven to fourteen days. In late infancy, oral therapy with a third-generation cephalosporin (e.g. cefixime or ceftibuten) is equivalent to the usual two to

four days intravenous therapy followed by oral treatment in uncomplicated UTI's. In complicated UTI parenteral treatment with broad-spectrum antibiotics is preferred.

Figure 6: Algorithm for the management of a first febrile UTI



BBD = Bladder Bowel Dysfunction; DMSA = technetium^{99}-labelled dimercaptosuccinic acid; MRI = magnetic resonance imaging; UTI = urinary tract infection; VCUG = voiding cystourethrography; VUR = vesicoureteral reflux; i.v. = intravenous.

Monitoring of UTI

Urine usually becomes sterile after 24 hours, and leukocyturia disappears within three to four days. Normalisation of body temperature can be expected within 24-48 hours after the start of therapy in 90% of cases. In patients with prolonged fever and failing recovery, treatment-resistant uropathogens or the presence of congenital uropathy or acute urinary obstruction should be considered. Immediate US examination is recommended.

Procalcitonin (among other laboratory inflammatory parameters such as C-reactive protein and leukocyte count) is a reliable serum marker for early prediction of renal parenchymal inflammation. In patients with febrile UTI, serum electrolytes and blood cell counts should be obtained.

Recommendations	Strength rating
Take a medical history, assess clinical signs and symptoms and perform a physical examination to diagnose children suspected of having a urinary tract infection (UTI).	Strong
Exclude bladder and bowel dysfunction (BBD) in any child with febrile and/or recurrent UTI and do not delay diagnosis and treatment of BBD.	Strong
The most effective way to collect an uncontaminated urine sample in an infant is through suprapubic bladder aspiration, bladder catheterisation is an alternative with a higher contamination rate.	Strong

Do not use plastic bags for urine sampling in non-toilet-trained children since it has a high risk of false-positive results. Clean catch urine is an acceptable technique for toilet-trained children.	Strong
Urinalysis by dipstick yields rapid results, but it should be used with caution. Microscopic investigation is the standard method of assessing pyuria after centrifugation. Using flow imaging analysis, the numbers of white blood cells, squamous epithelial cells and red cells correlate well with manual methods.	Weak
The choice between oral and parenteral therapy should be based on patient age; clinical suspicion of urosepsis; illness severity; refusal of fluids, food and/or oral medication; vomiting; diarrhoea; non-compliance; complicated pyelonephritis.	Strong
Treat UTIs with four to seven day courses of oral or parenteral therapy.	Strong
Offer long-term antibacterial prophylaxis in case of high susceptibility to UTI and risk of acquired renal damage and lower urinary tract symptoms.	Weak
Treat complicated UTI, with broad-spectrum antibiotics (parenteral).	Weak
In infants with febrile UTI, use renal and bladder ultrasound to exclude obstruction of the upper and lower urinary tract.	Strong

In all infants, exclude vesicoureteral reflux (VUR) after the first episode of febrile UTI, using voiding cystourethography (VCUG) or a dimercaptosuccinic acid (DMSA) scan first (in case of a positive DMSA-scan, follow-up with VCUG). In boys more than one year of age, exclude VUR after the second febrile UTI.	Strong

MONOSYMPTOMATIC NOCTURNAL ENURESIS - BEDWETTING

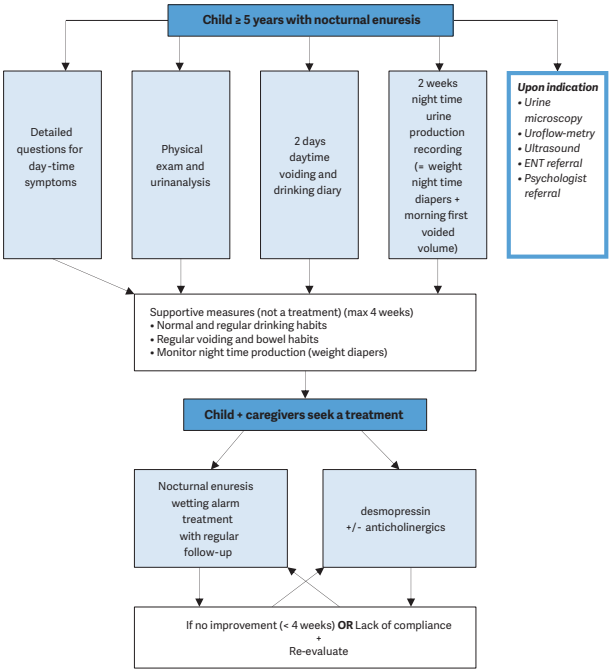
Background

Monosymptomatic nocturnal enuresis is incontinence during the night. Any wetting during sleep above the age of five years is considered nocturnal enuresis. It is important to note that there is a single symptom only. Due to an imbalance between night-time urine output and night-time bladder capacity, the bladder can easily become full at night, and the child will either wake-up to empty the bladder or will void during sleep.

Diagnostic Evaluation

A voiding diary, registering the day-time bladder function and the night-time urine output will help guide the treatment. Measuring the day-time bladder capacity gives an estimate of bladder capacity to compare with normal values for age. Figure 7 presents an algorithm for the diagnosis and treatment of monosymptomatic nocturnal enuresis.

Figure 7: Algorithm for the assessment and management of nocturnal enuresis



ENT = ear, nose, throat

VESICOURETERIC REFLUX IN CHILDREN

Background

Vesicoureteric reflux presents with a wide range of severities, and the majority of reflux patients will not develop renal scars and probably will not need any intervention. The main goal in management is the preservation of kidney function.

Diagnostic evaluation

The diagnostic work-up should evaluate the overall health and development of the child. A basic diagnostic work-up includes a detailed medical history (including family history, and screening for lower urinary tract dysfunction [LUTD]), physical examination including blood pressure measurement, urinalysis (assessing proteinuria), urine culture, and serum creatinine in patients with bilateral renal parenchymal abnormalities.

Prenatally diagnosed hydronephrosis

Ultrasound of the kidney and bladder is the first standard evaluation tool for children with prenatally diagnosed hydronephrosis.

It should be delayed until the end of first week after birth because of early oliguria in the neonate. It is essential to evaluate the bladder, as well as the kidneys.

Recommendations	Strength rating
Inform parents of children with vesicoureteric reflux (VUR) that siblings and offspring have a high prevalence of VUR.	Strong
Use renal ultrasound (US) for screening of sibling(s).	Strong
Use voiding cystourethrography if there is evidence of renal scarring on US or a history of urinary tract infection.	Weak

Do not screen older toilet-trained children since there is no added value in screening for VUR.	Weak

Conservative therapy

The objective of conservative therapy is prevention of febrile UTI. It is based on the understanding that:

- VUR resolves spontaneously, mostly in young patients with low-grade reflux. However, spontaneous resolution is low in bilateral high-grade reflux.
- VUR does not damage the kidney when patients are free of infection and have a normal lower urinary tract function.
- There is no evidence that small scars can cause hypertension, renal insufficiency or problems during pregnancy and in the long-term.
- The conservative approach includes watchful waiting, intermittent or continuous antibiotic prophylaxis, and bladder rehabilitation in those with LUTD.
- Circumcision in early infancy may be considered as part of the conservative approach, because it is effective in reducing the risk of infection in normal children.

Surgical Treatment

Surgical treatment comprises endoscopic injection of bulking agents or ureteral re-implantation.

Subureteric injection of bulking agents: Due to the availability of biodegradable substances, endoscopic subureteric injection of bulking agents has become an alternative to long-term antibiotic prophylaxis and surgical intervention.

Open surgical techniques: Overall, all surgical procedures offer very high and similar success rates for correcting VUR.

Laparoscopy: A laparoscopic approach cannot be recommended as a routine procedure. It can be offered as an alternative to the caregivers in centres where there is enough experience.

Recommendations	Strength rating
Initially treat all patients diagnosed within the first year of life with continuous antibiotic prophylaxis, regardless of the grade of reflux or presence of renal scars.	Weak
Offer immediate, parenteral antibiotic treatment for febrile breakthrough infections.	Strong
Offer definitive surgical or endoscopic correction to patients with frequent breakthrough infections.	Weak
Offer open surgical correction to patients with persistent high-grade reflux and endoscopic correction for lower grades of reflux.	Strong
Initially manage all children presenting at age one to five years conservatively.	Strong
Offer surgical repair to children above the age of one presenting with high-grade reflux and abnormal renal parenchyma.	Weak
Offer close surveillance without antibiotic prophylaxis to children presenting with lower grades of reflux and without symptoms.	Strong

Ensure that a detailed investigation for the presence of lower urinary tract dysfunction (LUTD) is done in all and especially in children after toilet-training. If LUTD is found, the initial treatment should always be for LUTD.	Strong
Offer surgical correction, if parents prefer definitive therapy to conservative management.	Strong
Select the most appropriate management option based on: • the presence of renal scars; • clinical course; • the grade of reflux; • ipsilateral renal function; • bilaterality; • bladder function; • associated anomalies of the urinary tract; • age and gender; • compliance; • parental preference. Refer to Table 3 for risk factors and follow-up.	Weak
In high-risk patients who already have renal impairment, a more aggressive, multi-disciplinary approach is needed.	Strong

This short booklet text is based on the more comprehensive EAU/ESPU Paediatric Urology Guidelines (ISBN 978-94-92671-01-1), available at their website, http://www.uroweb.org/guidelines.

Table 3: Management and follow-up according to different risk groups

Risk Groups	Presentation	Initial treatment
High	Symptomatic male or female patients after toilet-training with high-grade reflux (grades IV-V), abnormal kidneys and LUTD	Initial treatment is always for LUTD with CAP; intervention may be considered in cases of BT infections or persistent reflux
High	Symptomatic male or female patients after toilet-training with high-grade reflux (grade IV-V), abnormal kidneys and no LUTD	Intervention should be considered
Moderate	Symptomatic male or female patients before toilet-training, with high-grade reflux and abnormal kidneys	CAP is the initial treatment. Intervention may be considered in cases of BT infections or persistent reflux
Moderate	Asymptomatic patients (PNH or sibling) with high-grade reflux and abnormal kidneys	Initial treatment is always for LUTD with CAP. Intervention may be considered in cases of BT infections or persistent reflux
Moderate	Symptomatic male or female patients after toilet-training, with high-grade reflux and normal kidneys with LUTD	Initial treatment is always for LUTD with CAP. Intervention may be considered in cases of BT infections or persistent reflux

Comment	Follow-up
Greater possibility of earlier intervention	More aggressive follow-up for UTI and LUTD; full re-evaluation after 6 months
Open surgery has better results than endoscopic surgery	Post-operative VCUG on indication only; follow-up of kidney status until after puberty
Spontaneous resolution is higher in males	Follow-up for UTI/ hydronephrosis; full re-evaluation after 12-24 months
	Follow-up for UTI/ hydronephrosis; full re-evaluation after 12-24 months
In case of persistent LUTD, despite urotherapy, intervention should be considered. The choice of intervention is controversial	Follow-up for UTI and LUTD, kidney status; full re-evaluation after successful urotherapy

Moderate	Symptomatic male or female patients after toilet-training with low-grade reflux, abnormal kidneys with or without LUTD	Choice of treatment is controversial. Endoscopic treatment may be an option. LUTD treatment should be given if needed
Moderate	All symptomatic patients with normal kidneys, with low-grade reflux, with LUTD	Initial treatment is always for LUTD with or without CAP
Low	All symptomatic patients with normal kidneys, with low-grade reflux, with no LUTD	No treatment or CAP
Low	All asymptomatic patients with normal kidneys with low-grade reflux	No treatment or CAP in infants

CAP = continuous antibiotic prophylaxis; LUTD = lower urinary tract dysfunction; PNH = prenatal diagnosed hydronephrosis; UTI = urinary tract infection; VCUG = voiding cystourethrography.

	Follow-up for UTI, LUTD, and kidney status until after puberty
	Follow-up for UTI and LUTD
If no treatment is given, caregivers should be informed about risk of infection	Follow-up for UTI
If no treatment is given, caregivers should be informed about risk of infection	Follow-up for UTI

EAU GUIDELINES ON UROLOGICAL TRAUMA

(Limited text update March 2018)

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Introduction

Genito-urinary trauma is seen in both sexes and in all age groups, but is more common in males. Traumatic injuries are classified according to the basic mechanism into **penetrating** and **blunt**.

Penetrating trauma is further classified according to the velocity of the projectile:
1. High-velocity projectiles (e.g. rifle bullets - 800-1000 m/sec).
2. Medium-velocity (e.g. handgun bullets - 200-300 m/sec).
3. Low-velocity items (e.g. knife stab).

High-velocity weapons inflict greater damage as the bullets transmit large amounts of energy to the tissues, resulting in damage to a much larger area then the projectile tract itself. In lower velocity injuries, the damage is usually confined to the tract of the projectile.

Blast injury is a complex cause of trauma, it commonly includes both blunt and penetrating trauma, and may also be accompanied by burn injuries.

Initial evaluation and management

The first priority is stabilisation of the patient and treatment of associated life-threatening injuries. A direct history is obtained from the patient (if conscious) or from witnesses/emergency personnel (if patient is unconscious and/or seriously injured).

In penetrating injuries, assess size of the weapon in stabbings, and the type and calibre of the weapon used in gunshot wounds. The medical history should be as detailed as possible. It is important to recognise the high risk of hepatitis B and C infection in trauma patients and take appropriate precautions. In any penetrating trauma, tetanus vaccination should be considered according to the patient's vaccination history and nature of the wound.

Renal Trauma

Renal injuries are associated with young age and male gender, the incidence is approximately 4.9 per 100,000 of the population. The most commonly used classification system is that of the American Association for the Surgery of Trauma. This validated system has clinical relevance and helps to predict the need for intervention. It also predicts morbidity after blunt or penetrating injury and mortality after blunt injury.

Diagnostic evaluation

Recommendations	Strength rating
Assess haemodynamic stability upon admission.	Strong
Record past renal surgery, and known pre-existing renal abnormalities (ureteropelvic junction obstruction, large cysts, lithiasis).	Strong
Test for haematuria in a patient with suspected renal injury.	Strong

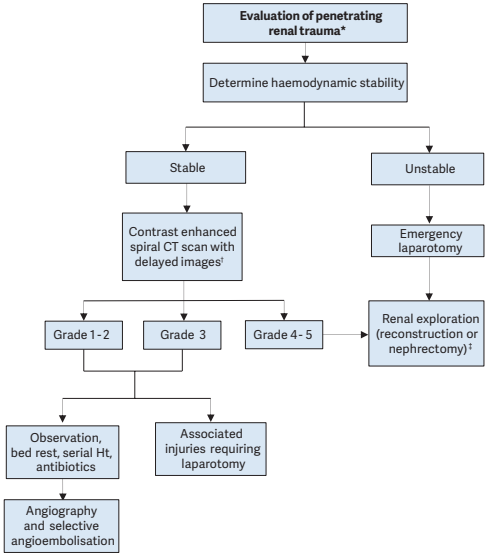
Perform a contrast enhanced CT scan in blunt trauma patients with; • visible haematuria; • non-visible haematuria with haemodynamic instability; • a history of rapid deceleration injury and/or significant associated injuries; • penetrating abdominal or lower thoracic injury.	Strong
Perform CT delayed phase images in case of haemodynamic stability.	Strong

Management

Recommendations	Strength rating
Manage stable patients with blunt renal trauma conservatively with close monitoring of vital signs.	Strong
Manage isolated grade 1-3 stab and low-velocity gunshot wounds in stable patients, expectantly.	Strong
Use angioembolisation for active renal bleeding if there are no other indications for immediate laparotomy.	Strong
Proceed with renal exploration in the presence of: • persistent haemodynamic instability; • expanding or pulsatile peri-renal haematoma; • grade 5 vascular injury; • exploration for associated injuries.	Strong
Attempt renal reconstruction if haemorrhage is controlled and there is sufficient viable renal parenchyma.	Weak

Figure 1: Evaluation of blunt renal trauma in adults

Figure 2: Evaluation of penetrating renal trauma in adults



** Suspected renal trauma results from reported mechanism of injury and physical examination.*

† Renal imaging: CT scans are the gold standard for evaluating blunt and penetrating renal injuries in stable patients. In settings where CT is not available, the urologist should rely on other imaging modalities (IVP, angiography, radiographic scintigraphy, MRI).

‡ Renal exploration: Although renal salvage is a primary goal for the urologist, decisions concerning the viability of the organ and the type of reconstruction are made during the operation.

CT = computed tomography; Ht = haematocrit; IVP = intravenous pyelography.

Post-operative care, follow-up and complications

Recommendations	Strength rating
Repeat imaging in case of fever, worsening flank pain, or falling haematocrit.	Strong
Follow-up approximately three months after major renal injury with: • physical examination; • urinalysis; • individualised radiological investigation including nuclear scintigraphy; • serial blood pressure measurements; • renal function tests.	Weak

Iatrogenic renal injuries

- Iatrogenic renal injuries are procedure-dependent (1.8-15%).
- Significant injury requiring intervention is rare; the most common injuries are vascular.
- Renal allografts are more susceptible.
- Injuries occurring during surgery should be rectified immediately.
- Symptoms suggestive of a significant injury require investigation.

The recommendations for iatrogenic renal injuries are the same as those for follow-up.

Ureteral Trauma

Ureteral injuries are quite rare - most are iatrogenic. They are often missed intra-operatively, usually involve the lower ureter, and may result in severe sequelae. Risk factors include advanced malignancy, prior surgery or irradiation - i.e. conditions which alter the normal anatomy. Pre-operative prophylactic stents do not prevent ureteral injury, but may

assist in its detection. External ureteral trauma usually accompanies severe abdominal and pelvic injuries. Gunshot wounds account for the majority of penetrating ureteral trauma, while motor vehicle accidents account for most blunt injuries.

Diagnostic evaluation

- A high index of suspicion of ureteral injury should be maintained as the majority of cases are diagnosed late, predisposing the patient to pain, infection, and renal function impairment.
- Haematuria is an unreliable indicator.
- Extravasation of contrast material in computed tomography (CT) is the hallmark sign of ureteral trauma.
- In unclear cases, a retrograde or antegrade urography is required for confirmation.

Management

Recommendations	Strength rating
Visually identify the ureters to prevent ureteral trauma during abdominal and pelvic surgery.	Strong
Beware of concomitant ureteral injury in all abdominal penetrating trauma, and in deceleration-type blunt trauma.	Strong
Use pre-operative prophylactic stents in high-risk cases.	Strong

The type of repair procedure depends on the site of the injury (Table 2), and should follow the principles outlined in Table 3.

Table 2: Ureteral reconstruction options by site of injury	
Site of injury	**Reconstruction options**
Upper ureter	Uretero-ureterostomy Transuretero-ureterostomy Uretero-calycostomy
Mid ureter	Uretero-ureterostomy Transuretero-ureterostomy Ureteral re-implantation and a Boari flap
Lower ureter	Ureteral re-implantation Ureteral re-implantation with a psoas hitch
Complete	Ileal interposition graft Autotransplantation

Table 3: Principles of surgical repair of ureteral injury
Debridement of necrotic tissue
Spatulation of ureteral ends
Watertight mucosa-to-mucosa anastomosis with absorbable sutures
Internal stenting
External drain
Isolation of injury with peritoneum or omentum

Bladder Trauma

Bladder injuries can be due to external (blunt or penetrating) or iatrogenic trauma. Iatrogenic trauma is caused by external laceration or internal perforation (mainly during transurethral resection of the bladder). Blunt bladder injuries are strongly associated with pelvic fractures. Bladder injuries are classified as extraperitoneal, intraperitoneal or combined.

Diagnostic evaluation

Clinical signs and symptoms

External trauma

- Cardinal sign: visible haematuria.
- Others: abdominal tenderness, inability to void, bruises over the suprapubic region, and abdominal distension (in case of urinary ascites).
- Penetrating bladder injury: entrance and exit wounds in lower abdomen or perineum.
- Bloody urethrorrhagia: suspect concomitant urethral injury.

Iatrogenic trauma

- External perforation: extravasation of urine, visible laceration, clear fluid in the surgical field, appearance of the bladder catheter, and blood and/or gas (in case of laparoscopy) in the urine bag.
- Internal perforation: fatty tissue or bowel between detrusor muscle fibres, inability to distend the bladder, low return of irrigation fluid and/or abdominal distension.
- Post-operative symptoms of unrecognised bladder perforation: haematuria, lower abdominal pain, abdominal distension, ileus, peritonitis, sepsis, urine leakage from the wound, decreased urinary output, and increased serum creatinine.

Imaging – Cystography and Cystoscopy

Recommendations	Strength rating
Perform cystography in case of suspected iatrogenic bladder injury in the post-operative setting.	Strong
Perform cystography in the presence of visible haematuria and pelvic fracture.	Strong

Perform cystography with active retrograde filling of the bladder with dilute contrast.	Strong
Use cystoscopy to rule out bladder injury after suburethral sling procedure by the retropubic route.	Strong
Do not perform cystography to assess bladder wall healing after repair of a simple injury in a healthy patient.	Weak
Perform cystography to assess bladder wall healing after repair of a complex injury or in case of risk factors for wound healing.	Strong

Management

- Surgical repair (two-layer vesicorraphy)
- Conservative management (urinary catheter)

Recommendations	Strength rating
Manage a blunt extraperitoneal bladder injury operatively in cases of bladder neck involvement and/or associated injuries that require surgical intervention.	Strong
Manage uncomplicated blunt extraperitoneal bladder injury conservatively.	Weak
Manage intraperitoneal injuries caused by blunt trauma by surgical exploration and repair.	Strong
Manage small uncomplicated iatrogenic intraperitoneal bladder injuries conservatively.	Weak

Urethral Trauma

- Injuries to the anterior urethra (AU) are caused by trauma during sexual intercourse (associated with penile fracture), penetrating trauma, placement of penile constriction bands, and from iatrogenic trauma e.g. endoscopic instruments, catheterisation.
- Injuries to the posterior urethra (PU) occur with pelvic fractures, mostly as a result of motor vehicle accidents.
- The male PU is injured in 4-19% of pelvic fractures, and the female urethra in 0-6% of all pelvic fractures.
- The combination of straddle fractures with diastasis of the sacroiliac joint has the highest risk of urethral injury.
- Injuries can vary from simple stretching to partial rupture to complete disruptions.
- Urethral injuries in women are rare.

Diagnostic evaluation

- Blood at the external urethral meatus is the most common clinical sign, and indicates the need for further diagnostic work up.
- Although non-specific, haematuria on a first voided specimen may indicate urethral injury. The amount of urethral bleeding correlates poorly with the severity of injury.
- Pain on urination or inability to void may indicate disruption.
- Blood at the vaginal introitus is present in more than 80% of female patients with pelvic fractures and co-existing urethral injuries.
- Rectal examination may reveal a “high riding” prostate. However, this is an unreliable finding. Blood on the examination finger is suggestive of a rectal injury associated with pelvic fracture.
- Urethral bleeding or urinary extravasation can cause penile and scrotal swelling and haematoma.

- Retrograde urethrography is the gold standard for evaluating urethral injury and urethral catheterisation should be avoided until the urethra is imaged.
- In an unstable patient, however, an attempt can be made to pass a urethral catheter (gently, by someone with urological experience). If this is not possible, a suprapubic catheter is inserted and a retrograde urethrogram is performed later.
- In females, urethroscopy may be an important adjunct for the identification and staging of urethral injuries.

Management

Urethral trauma

Recommendations	Strength rating
Evaluate urethral injuries with flexible cystoscopy and/or retrograde urethrography.	Strong
Treat blunt anterior urethral injuries by suprapubic diversion.	Strong
Treat partial posterior urethral ruptures by urethral or suprapubic catheterisation.	Strong
Perform early endoscopic re-alignment when feasible.	Weak
Manage complete posterior urethral disruption with suprapubic diversion and deferred (at least three months) urethroplasty.	Strong

Iatrogenic urethral trauma

Recommendations	Strength rating
Provide appropriate training to reduce the risk of traumatic catheterisation.	Strong
Keep duration of catheterisation to a minimum.	Strong

Genital Trauma

Of all genito-urinary injuries, one-third to two-thirds involve the external genitalia and are much more common in males due to anatomical differences, increased frequency of road traffic accidents, physical sports, violent crime, and war-fighting. Eighty percent is blunt trauma, 20% is due to penetrating injuries.

Diagnostic evaluation

- Urinalysis should be performed.
- Visible- and/or non-visible haematuria requires a retrograde urethrogram in males, whilst cystoscopy should be considered in females.
- In women with genital injuries and blood at the vaginal introitus, further gynaecologic investigation to exclude vaginal injury is required.
- In cases of suspected sexual abuse gynaecologic and forensic support and advice is necessary. The emotional situation and privacy of the patient must be respected.

Blunt penile trauma

Usually results from trauma to the erect penis during sexual intercourse or masturbation.

Penile fracture

- Sudden cracking or popping sound, pain and immediate detumescence.
- Local swelling of the penile shaft is seen and this may extend to the lower abdominal wall.
- The rupture of the tunica may be palpable.
- Thorough history and examination confirms diagnosis.
- Imaging ultrasound (US) or magnetic resonance imaging (MRI) may be useful.

Management

- Subcutaneous haematoma, without associated rupture of the cavernosal tunica albuginea does not require surgical intervention. Non-steroidal analgesics and ice-packs are recommended.
- In penile fracture, early surgical intervention with closure of the tunica albuginea is recommended.
- Intra-operative flexible cystoscopy is useful to diagnose urethral injury and to further localise tunical damage.
- Conservative management of penile fracture is not recommended.

Penetrating penile trauma

- Rarely seen in isolation.
- Due to gunshot/knife injury, animal or human bites, assault and industrial or self-inflicted mutilation.
- Non-operative management is recommended in small superficial injuries with intact Buck's fascia.
- More significant injuries require surgical exploration and debridement of necrotic tissue.
- In extended injuries of the penis, primary alignment of the disrupted tissues may allow for acceptable healing because of the robust penile blood supply.
- In avulsion of the penis, resuscitate the patient and attempt re-implantation of the penis (if not too badly damaged) - ideally microsurgically.

Blunt scrotal trauma

- May result in testicular dislocation, haematocoele, testicular rupture and/or scrotal haematoma.
- Dislocation of the testicle is rare. Treat by manual replacement and secondary orchidopexy. If manual repositioning cannot be performed, immediate orchidopexy is indicated.
- If haematocele is smaller than three times the size of the contralateral testis – conservative management.

- If large haematocele - explore.
- If testicular rupture suspected, explore, evacuate clot and any necrotic testicular tubules and close the tunica albuginea.

Penetrating scrotal trauma

- Surgical exploration with conservative debridement of nonviable tissue.
- Primary reconstruction of testis and scrotum can be performed in most cases.
- In complete disruption of the spermatic cord, re-alignment without vaso-vasostomy may be considered.
- In extensive destruction of the tunica albuginea, mobilisation of a free tunica vaginalis flap can be performed for testicular closure.
- If reconstruction cannot be achieved, orchiectomy is indicated.
- In improvised explosive device blast injury, the extensive loss of genital tissue often requires complex and staged reconstructive surgical procedures.

Genital trauma in females

- In blunt trauma to the external genitalia, imaging studies of the pelvis with US, CT, or MRI should be performed.
- Vulvar haematomas usually do not require surgical intervention, but in massive vulvar haematoma or haemodynamically unstable patients, surgical intervention, lavage and drainage is indicated.
- In vulvar laceration, suturing after conservative debridement is indicated with concomitant primary repair of any associated vaginal injuries.

Polytrauma, Damage Control and Mass Casualty Events

Urological trauma is often associated with significant and higher priority injuries in the polytraumatised patient. Damage

control principles govern the management of the severely injured patient and urologists need to understand their role in the context of polytrauma.

Damage control is a three-phase approach - rapid control of haemorrhage and wound contamination, resuscitation in the intensive care unit, and delayed definitive surgery.

Procedures should be directed at the rapid control of bleeding, debridement of dead and devitalised tissue, and minimising urinary extravasation by simple diversionary measures.

A mass casualty event is one in which the number of injured people is significantly higher than the number of healthcare providers available. Examples include the collapse of buildings or bridges, earthquakes, floods, tsunamis, train collisions, aircraft catastrophes, civilian terrorism.

Triage sorts patients into four groups:

1. Patients with life-threatening injuries that require immediate intervention, presenting with airway compromise, breathing failure and/or circulatory compromise from ongoing external haemorrhage.
2. Patients with severe but non-life-threatening injuries, in whom treatment can be acceptably delayed: major fractures, vascular injuries of the limbs and large soft tissue wounds.
3. 'Walking wounded' with minimal injuries.
4. Patients who are so severely injured that treatment would require allocation of resources and time that would deny other, more salvageable patients, timely care. These patients are given minimal or no treatment, and re-evaluated when resources become available. There is no absolute definition for this group because triage is

individualised according to the number and severity of casualties related to the available resources.

Principles for urological consultations to follow during a mass casualty scenario:

- Rule out under-triage by the surgeon in charge, and perform a rapid primary survey of every patient.
- Avoid unnecessary imaging procedures such as CT scans and retrograde urethrography. These procedures should be performed later, after mass casualty protocols have been suspended.
- Treat unstable patients who are to have surgery using damage control principles.
- Stable patients with suspected renal injuries should be transferred to the surgical ward without imaging procedures. Re-evaluate if there is any change in their haemodynamic status, or when possible as dictated by the constraints of the mass casualty event. Patients managed in this delayed fashion should be treated according to traditional trauma management protocols.
- 'Minimal acceptable' procedures should be performed in order to transfer patients to the surgical wards, e.g. suprapubic drainage of the bladder when bladder or urethral injuries are suspected, clamping and ligation of bleeding vessels from wounds to the external genitalia, etc.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-02-8) available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines.

EAU GUIDELINES ON CHRONIC PELVIC PAIN

(Limited text update March 2018)

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Introduction

The EAU Guideline for Chronic Pelvic Pain plays an important role in the process of consolidation and improvement of care for patients with abdominal and pelvic pain. From both literature and daily practice it has become clear that abdominal and pelvic pain are areas still under development. The EAU Guideline aims to expand the awareness of caregivers in the field of abdominal and pelvic pain and to assist those who treat patients with abdominal and pelvic pain in their daily practice. The guideline is a useful instrument not only for urologists, but also for gynaecologists, surgeons, physiotherapists, psychologists and pain doctors.

This pocket version aims to synthesise the important clinical messages described in the full text and is presented as a series of 'strength rated recommendations', which follow the standard for levels of evidence used by the EAU (see Introduction chapter of the EAU Guidelines book and online at the EAU website http://www.uroweb.org/guideline/).

Table 1: Classification of chronic pelvic pain syndromes

Axis I Region		Axis II System	Axis III End-organ as pain syndrome as identified from Hx, Ex and Ix	
Chronic pelvic pain	Specific disease associated pelvic pain OR Pelvic pain syndrome	Urological	Prostate	
			Bladder	
			Scrotal Testicular Epididymal	
			Penile Urethral	
			Post-vasectomy	
		Gynaecological	Vulvar Vestibular Clitoral	
			Endometriosis associated	
			CPPS with cyclical exacerbations	
			Dysmenorrhoea	
		Gastrointestinal	Irritable bowel	
			Chronic anal	
			Intermittent chronic anal	
		Peripheral nerves	Pudendal pain syndrome	
		Sexological	Dyspareunia	
			Pelvic pain with sexual dysfunction	
		Psychological	Any pelvic organ	
		Musculo-skeletal	Pelvic floor muscle Abdominal muscle Spinal	
			Coccyx	

	Axis IV Referral character-istics	Axis V Temporal characteristics	Axis VI Character	Axis VII Associated symptoms	Axis VIII Psychological symptoms
	Suprapubic Inguinal Urethral Penile/clitoral Perineal Rectal Back Buttocks Thighs	ONSET Acute Chronic ONGOING Sporadic Cyclical Continuous TIME Filling Emptying Immediate post Late post TRIGGER Provoked Spontaneous	Aching Burning Stabbing Electric	UROLOGICAL Frequency Nocturia Hesitance Dysfunctional flow Urgency Incontinence GYNAECOLOGICAL Menstrual Menopause GASTROINTESTINAL Constipation Diarrhoea Bloatedness Urgency Incontinence NEUROLOGICAL Dysaesthesia Hyperaesthesia Allodynia Hyperalegesie SEXOLOGICAL Satisfaction Female dyspareunia Sexual avoidance Erectile dysfunction Medication MUSCLE Function impairment Fasciculation CUTANEOUS Trophic changes Sensory changes	ANXIETY About pain or putative cause of pain Catastrophic thinking about pain DEPRESSION Attributed to pain or impact of pain Attributed to other causes Unattributed PTSD SYMPTOMS Re-experiencing Avoidance

Chronic pelvic pain syndromes

Classification

Much debate over the classification of chronic pelvic pain (CPP) has occurred, is ongoing and will continue in the future. Classification involves three aspects of defining a condition: phenotyping, terminology and taxonomy.

Definition of CPP

Chronic pelvic pain is chronic or persistent pain perceived* in structures related to the pelvis of either men or women. It is often associated with negative cognitive, behavioural, sexual and emotional consequences as well as with symptoms suggestive of lower urinary tract, sexual, bowel, pelvic floor or gynaecological dysfunction.

*(*Perceived indicates that the patient and clinician, to the best of their ability from the history, examination and investigations (where appropriate) have localised the pain as being perceived in the specified anatomical pelvic area.)*

Definition of CPPS

Chronic pelvic pain syndrome (CPPS) is the occurrence of CPP when there is no proven infection or other obvious local pathology that may account for the pain. It is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract, sexual, bowel or gynaecological dysfunction. CPPS is a subdivision of CPP.

Table 2: Chronic Pelvic Pain Syndromes

Urological Pain Syndromes	
Prostate pain syndrome (PPS)	Prostate pain syndrome is the occurrence of persistent or recurrent episodic pain (which is con-vincingly reproduced by prostate palpation). There is no proven infection or other obvious local pathology. Prostate pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract and sexual dysfunction. The term "chronic prostatitis" continues to be equated with that of PPS. In the authors' and others' opinion, this is an inappropriate term, although it is recognised that it has a long history of use. The National Institutes of Health (NIH) consensus includes infection (types I and II), which the authors feel should not be considered under PPS, but as specific disease-associated pelvic pain. The term prostadynia has also been used in the past but is no longer recommended by the panel. Please note that some of the authors of the International Association for the Study of Pain document disagree with this term and suggest that CPPS of the male is used instead of PPS, which has been agreed by the majority.

Bladder pain syndrome (BPS)	Bladder pain syndrome is the occurrence of persistent or recurrent pain perceived in the urinary bladder region, accompanied by at least one other symptom, such as pain worsening with bladder filling and day-time and/or night-time urinary frequency. There is no proven infection or other obvious local pathology. Bladder pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract and sexual dysfunction. Bladder pain syndrome is believed to represent a heterogeneous spectrum of disorders. There may be specific types of inflammation as a feature in subsets of patients. Localisation of the pain can be difficult by examination, and consequently, another localising symptom is required. Cystoscopy with hydrodistension and biopsy may be indicated to define phenotypes. Recently, the International Society for the Study of BPS has suggested a standardised scheme of subclassifications to acknowledge differences and make it easier to compare various studies. Other terms that have been used include "interstitial cystitis" (IC), "painful bladder syndrome" (PBS), and "PBS/IC" or "BPS/IC". These terms are no longer recommended.
Scrotal pain syndrome	Scrotal pain syndrome is the occurrence of persistent or recurrent episodic pain localised within the organs of the scrotum, and may be associated with symptoms suggestive of lower urinary tract or sexual dysfunction. There is no proven infection or other obvious local pathology. Scrotal pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences. Scrotal pain syndrome is a generic term and is used when the site of the pain is not clearly testicular or epididymal. The pain is not in the skin of the scrotum as such, but perceived within its contents, in a similar way to idiopathic chest pain.

Testicular pain syndrome	Testicular pain syndrome is the occurrence of persistent or recurrent episodic pain perceived in the testes, and may be associated with symptoms suggestive of lower urinary tract or sexual dysfunction. There is no proven infection or other obvious local pathology. Testicular pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences. Previous terms have included orchitis, orchialgia and orchiodynia. These terms are no longer recommended.
Epididymal pain syndrome	Epididymal pain syndrome is the occurrence of persistent or recurrent episodic pain perceived in the epididymis, and may be associated with symptoms suggestive of lower urinary tract or sexual dysfunction. There is no proven infection or other obvious local pathology. Epididymal pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences.
Penile pain syndrome	Penile pain syndrome is the occurrence of pain within the penis that is not primarily in the urethra, in the absence of proven infection or other obvious local pathology. Penile pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract and sexual dysfunction.
Urethral pain syndrome	Urethral pain syndrome is the occurrence of chronic or recurrent episodic pain perceived in the urethra, in the absence of proven infection or other obvious local pathology. Urethral pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract, sexual, bowel or gynaecological dysfunction. Urethral pain syndrome may occur in men and women.

Post-vasectomy scrotal pain syndrome	Post-vasectomy scrotal pain syndrome is a scrotal pain syndrome that follows vasectomy. Post-vasectomy scrotal pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract and sexual dysfunction. Post-vasectomy pain may be as frequent as 1% following vasectomy, possibly more frequent. The mechanisms are poorly understood and for that reason it is considered a special form of scrotal pain syndrome.
Gynaecological Pain Syndromes: external genitalia	
Vulvar pain syndrome	Vulvar pain syndrome is the occurrence of persistent or recurrent episodic vulvar pain. There is no proven infection or other local obvious pathology. It is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract, sexual, bowel or gynaecological dysfunction. Although pain perceived in the vulva was included under sexual disorders in the The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-R) for classifying psychiatric disorders, there is no scientific basis for this classification, and pain perceived in the vulva is best understood as a pain problem that usually has psychological consequences. There is no evidence for its classification as a psychia-tric disorder. The International Society for the Study of Vulvovaginal Disease (ISSVD) has used the term vulvodynia, where we use the term vulvar pain syndrome. According to the ISSVD, vulvodynia is vulvar pain that is not accounted for by any physical findings. The ISSVD has defined vulvodynia as "vulvar discomfort, most often described as burning pain, occurring in the absence of relevant visible findings or a specific, clinically identifiable, neurologic disorder". If physical findings are present, the patient is said to have vulvar pain due to a specified cause. The ISSVD has subdivided vulvodynia based on pain location and temporal characteristics of the pain (e.g. provoked or unprovoked). The following definitions are based on that approach.

Generalised vulvar pain syndrome	Generalised vulvar pain syndrome refers to a vulvar pain syndrome in which the pain/burning cannot be consistently and precisely localised by point-pressure mapping via probing with a cotton-tipped applicator or similar instrument. Rather, the pain is diffuse and affects all parts of the vulva. The vulvar vestibule (the part that lies between the labia minora into which the urethral meatus and vaginal introitus open) may be involved but the discomfort is not limited to the vestibule. This pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences. Previous terms have included "dysesthetic vulvodynia" and "essential vulvodynia", but are no longer recommended.
Localised vulvar pain syndrome	Localised vulvar pain syndrome refers to pain that can be consistently and precisely localised by point-pressure mapping to one or more portions of the vulva. Clinically, the pain usually occurs as a result of provocation (touch, pressure or friction). Localised vulvar pain syndrome can be sub-divided into vestibular pain syndrome and clitoral pain syndrome.
Vestibular pain syndrome	Vestibular pain syndrome refers to pain that can be localised by point-pressure mapping to the vestibule or is well perceived in the area of the vestibule.
Clitoral pain syndrome	Clitoral pain syndrome refers to pain that can be localised by point-pressure mapping to the clitoris or is well-perceived in the area of the clitoris.

Gynaecological Pain Syndromes: internal pelvic pain syndromes	
Endometriosis-associated pain syndrome	Endometriosis-associated pain syndrome is chronic or recurrent pelvic pain in patients with laparoscopically confirmed endometriosis, and the term is used when the symptoms persist despite adequate endometriosis treatment. It is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract, sexual, bowel or gynaecological dysfunction. Many patients have pain above and beyond the endometriotic lesions; this term is used to cover that group of patients. Endometriosis may be an incidental finding, is not always painful, and the degree of disease seen laparoscopically does not correlate with severity of symptoms. As with other patients, they often have more than one end-organ involved. It has been suggested that this phenotype should be removed from the classification because the endometriosis may be irrelevant.
Chronic pelvic pain syndrome with cyclical exacerbations	Chronic pelvic pain syndrome with cyclical exacerbations covers the non-gynaecological organ pain that frequently shows cyclical exacerbations (e.g., Irritable bowel syndrome (IBS) or BPS) as well as pain similar to that associated with endometriosis/adenomyosis but where no pathology is identified. This condition is different from dysmenorrhoea, in which pain is only present with menstruation.
Dysmenorrhoea	Dysmenorrhoea is pain with menstruation that is not associated with well-defined pathology. Dysmenorrhoea needs to be considered as a chronic pain syndrome if it is persistent and associated with negative cognitive, behavioural, sexual or emotional consequences.

Gastrointestinal Pelvic Pain Syndromes	
Irritable bowel syndrome	Irritable bowel syndrome is the occurrence of chronic or recurrent episodic pain perceived in the bowel, in the absence of proven infection or other obvious local pathology. Bowel dysfunction is frequent. Irritable bowel syndrome is often associated with worry and pre-occupation about bowel function, and negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract or gynaecological dysfunction. The above classification is based upon the Rome III Criteria: three months of continuous or recurring symptoms of abdominal pain or irritation that may be relieved with a bowel movement, may be coupled with a change in frequency, or may be related to a change in stool consistency. Two or more of the following are present at least 25% of the time: change in stool frequency (more than three bowel movements per day or less than three per week); noticeable difference in stool form (hard, loose, watery or poorly formed stools); passage of mucus in stools; bloating or feeling of abdominal distension; or altered stool passage (e.g., sensation of incomplete evacuation, straining, or urgency). Extra-intestinal symptoms include: nausea, fatigue, full sensation after even a small meal and vomiting.
Chronic anal pain syndrome	Chronic anal pain syndrome is the occurrence of chronic or recurrent episodic pain perceived in the anus, in the absence of proven infection or other obvious local pathology. Chronic anal pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract, sexual, bowel or gynaecological dysfunction.
Intermittent chronic anal pain syndrome	Intermittent chronic anal pain syndrome refers to severe, brief, episodic pain that seems to arise in the rectum or anal canal and occurs at irregular intervals. This is unrelated to the need to or the process of defecation. It may be considered a subgroup of the chronic anal pain syndromes. It was previously known as “proctalgia fugax” but this term is no longer recommended.

Musculoskeletal System	
Pelvic floor muscle pain syndrome	Pelvic floor muscle pain syndrome is the occurrence of persistent or recurrent episodic pelvic floor pain. There is no proven well-defined local pathology. It is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract, sexual, bowel or gynaecological dysfunction. This syndrome may be associated with over-activity of or trigger points within the pelvic floor muscles. Trigger points may also be found in several muscles, such as the abdominal, thigh and paraspinal muscles and even those not directly related to the pelvis.
Coccyx pain syndrome	Coccyx pain syndrome is the occurrence of chronic or recurrent episodic pain perceived in the region of the coccyx, in the absence of proven infection or other obvious local pathology. Coccyx pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract, sexual, bowel or gynaecological dysfunction. The term "coccydynia" was used but is no longer recommended.

Epidemiology, Aetiology and Pathophysiology
Chronic visceral pain, pelvic pain and abdominal aspects of pelvic pain

Recommendations	Strength rating
All of those involved in the management of Chronic Pelvic Pain (CPP) should have knowledge of peripheral and central pain mechanisms.	Strong
The early assessment of patients with CPP should involve investigations aimed at specific disease-associated pelvic pain.	Strong
The early assessment of patients with CPP should involve assessment of functional, emotional, behavioural, sexual and other quality of life issues, such as effect on work and socialisation.	Strong
Manage Chronic Pelvic Pain Syndrome patients in a multispecialty and multidisciplinary environment with consideration of all their symptoms.	Strong

Diagnostic Evaluation
History and physical examination
History is very important for the evaluation of patients with CPP. Pain syndromes are symptomatic diagnoses which are derived from a history of pain perceived in the region of the pelvis, and absence of other pathology, for a minimum of three out of the past six months. This implies that specific disease-associated pelvic pain caused by bacterial infection, cancer, primary anatomical or functional disease of the pelvic organs, and neurogenic disease must be ruled out. The history should be comprehensive covering functional as well as pain related symptoms. The clinical examination often serves to

confirm or refute the initial impressions gained from a good history. The examination should be aimed at specific questions where the outcome of the examination may change management. As well as a local examination, a general musculoskeletal and neurological examination should be considered an integral part of the assessment and be undertaken, if appropriate.

Figure 1: Diagnosing chronic pelvic pain

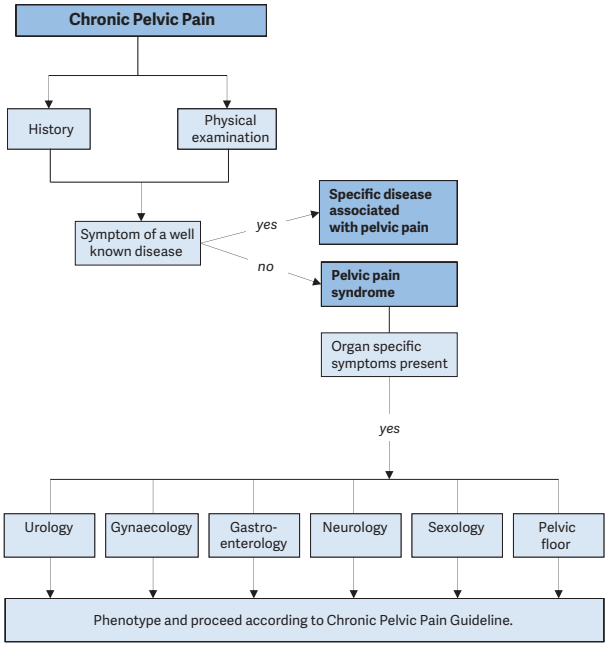

Figure 2: Phenotyping of pelvic pain

Phenotyping	Assessment
Urology	Urinary flow, micturition diary, cystoscopy, ultrasound, uroflowmetry
Psychology	Anxiety about pain, depression and loss of function, history of negative sexual experiences
Organ specific	Ask for gynaecological, gastro-intestinal, ano-rectal, sexological complaints Gynaecological examination, rectal examination
Infection	Semen culture and urine culture, vaginal swab, stool culture
Neurological	Ask for neurological complaints (sensory loss, dysaesthesia). Neurological testing during physical examination: sensory problems, sacral reflexes and muscular function.
Tender muscle	Palpation of the pelvic floor muscles, the abdominal muscles and the gluteal muscles
Sexological	Erectile function, ejaculatory function, post-orgasmic pain

Recommendations for diagnostic evaluation

Recommendations for the diagnostic evaluation of Prostate Pain Syndrome	Strength rating
Adapt diagnostic procedures to the patient. Exclude specific diseases with similar symptoms.	Strong
Use a validated symptom and quality of life scoring instrument, such as the National Institutes of Health Chronic Prostatitis Symptom Index, for initial assessment and follow-up.	Strong
Assess prostate pain syndrome associated negative cognitive, behavioural, sexual, or emotional consequences, as well as symptoms of lower urinary tract and sexual dysfunctions.	Strong

Recommendations for the diagnostic evaluation of Bladder Pain Syndrome	Strength rating
Perform general anaesthetic rigid cystoscopy in patients with bladder pain to subtype and rule out confusable disease.	Strong
Diagnose patients with symptoms according to the EAU definition, after primary exclusion of specific diseases, with bladder pain syndrome (BPS) by subtype and phenotype.	Strong
Assess BPS associated non-bladder diseases systematically.	Strong
Assess BPS associated negative cognitive, behavioural, sexual, or emotional consequences.	Strong
Use a validated symptom and quality of life scoring instrument for initial assessment and follow-up.	Strong

Recommendations for the diagnostic evaluation of gynaecological aspects of CPP	Strength rating
Take a full gynaecological history and evaluate to rule out a treatable cause (e.g. endometriosis) in all women with chronic pelvic pain.	Strong
Refer to a gynaecologist if clinical suspicion of a gynaecological cause for pain following complete urological evaluation. Laparoscopy should be undertaken in accordance with gynaecological guidelines.	Strong

Recommendation for the diagnostic evaluation of Anorectal Pain Syndrome	Strength rating
Anorectal function tests are recommended in patients with anorectal pain.	Strong

Recommendations for the diagnostic evaluation of Pudendal Neuralgia	Strength rating
Rule out confusable diseases, such as neoplastic disease, infection, trauma and spinal pathology.	Strong
If a peripheral nerve pain syndrome is suspected, refer early to an expert in the field, working within a multi-disciplinary team environment.	Weak
Imaging and neurophysiology help diagnosis but image and nerve locator guided local anaesthetic injection is preferable.	Weak

Recommendation for the diagnostic evaluation of sexological aspects in CPP	Strength rating
Screen patients presenting with symptoms suggestive for chronic pelvic pain syndrome for abuse, without suggesting a causal relation with the pain.	Weak

Recommendations for the diagnostic evaluation of psychological aspects of CPP	Strength rating
Assess patient psychological distress in relation to their pain.	Strong
Ask patients what they think is the cause of their pain to allow the opportunity to inform and reassure.	Strong

Recommendations for the diagnostic evaluation of pelvic floor function	Strength rating
Use ICS classification for pelvic floor muscle function and dysfunction.	Strong
Actively look for the presence of myofascial trigger points in patients with chronic pelvic pain syndrome.	Weak

Management

The philosophy for the management of CPP is based on a bio-psychosocial model. This is a holistic approach with the patients' active involvement. Single interventions rarely work in isolation and need to be considered within a broader personalised management strategy. The management strategy may well have elements of self-management. Pharmacological and non-pharmacological interventions should be considered with a clear understanding of the potential outcomes and end points. These may include: psychology, physiotherapy, drugs and more invasive interventions. Providing information that is personalised and responsive to the patient's problems, conveying belief and concern, is a powerful way to allay anxiety. Additional written information or direction to reliable sources is useful; practitioners tend to rely on locally produced material or pharmaceutical products of variable quality while endorsing the need for independent materials for patients.

Recommendations for the management of Prostate Pain Syndrome	Strength rating
Offer multimodal and phenotypically directed treatment options for Prostate Pain Syndrome (PPS).	Weak
Use antimicrobial therapy (quinolones or tetracyclines) over a minimum of six weeks in treatment-naïve patients with a duration of PPS less than one year.	Strong
Use α-blockers for patients with a duration of PPS less than one year.	Strong
Offer high-dose oral pentosane polysulphate in PPS.	Weak
Offer acupuncture for use in PPS.	Strong
Offer non-steroidal anti-inflammatory drugs in PPS, but long-term side-effects have to be considered.	Weak

Recommendations for the management of Bladder Pain Syndrome	Strength rating
Offer subtype and phenotype-oriented therapy for the treatment of Bladder Pain Syndrome (BPS).	Strong
Always consider offering multimodal behavioural, physical and psychological techniques alongside oral or invasive treatments of BPS.	Strong
Administer amitriptyline for treatment of BPS.	Strong
Offer oral pentosane polysulphate for the treatment of BPS.	Strong

Offer oral pentosane polysulphate plus subcutaneous heparin in low responders to pentosane polysulphate alone.	Weak
Administer intravesical lidocaine plus sodium bicarbonate prior to more invasive methods.	Weak
Administer intravesical pentosane polysulphate before more invasive treatment alone or combined with oral pentosane polysulphate.	Strong
Administer submucosal injection of Botulinum toxin type A (BTX-A) plus hydrodistension if intravesical instillation therapies have failed.	Strong
Only undertake ablative organ surgery as the last resort and only by experienced and BPS-knowledgeable surgeons.	Strong
Offer intravesical hyaluronic acid before more invasive measures.	Weak
Offer intravesical chondroitin sulphate before more invasive measures.	Weak
Offer transurethral resection (or coagulation or laser) of bladder lesions, but in BPS type 3 C only.	Strong
Offer neuromodulation before more invasive interventions.	Weak
Offer dietary advice.	Weak
Offer intravesical heparin before more invasive measures alone or in combination treatment.	Weak
Offer intravesical bladder wall and trigonal injection of BTX-A if intravesical instillation therapies have failed.	Strong

Do not recommend corticosteroids for long-term treatment.	Strong
Do not use bladder distension as a treatment of BPS.	Weak

Recommendations for the management of Scrotal Pain Syndrome	**Strength rating**
Inform about the risk of post-vasectomy pain when counselling patients planned for vasectomy.	Strong
Do open instead of laparoscopic inguinal hernia repair, to reduce the risk of scrotal pain.	Strong
In patients with testicular pain improving after spermatic block, offer microsurgical denervation of the spermatic cord.	Weak

Recommendations for the management of gynaecological aspects of CPP	**Strength rating**
Involve a gynaecologist to provide therapeutic options such as hormonal therapy or surgery in well-defined disease states.	Strong
Provide a multidisciplinary approach to pain management in persistent disease states.	Strong

Recommendations for functional anorectal pain	**Strength rating**
Undertake biofeedback treatment in patients with chronic anal pain.	Strong

Offer Botulinum toxin type A and electro-galvanic stimulation in chronic anal pain syndrome.	Strong
Offer percutaneous tibial nerve stimulation in chronic anal pain syndrome.	Weak
Offer sacral neuromodulation in chronic anal pain syndrome.	Weak
Offer inhaled salbutamol in intermittent chronic anal pain syndrome.	Weak

Recommendation for the management of pudendal neuralgia	**Strength rating**
Neuropathic pain guidelines are well-established. Use standard approaches to management of neuropathic pain.	Strong

Recommendations for the management of sexological aspects in CPP	**Strength rating**
Offer behavioural strategies to the patient and his/her partner to reduce sexual dysfunctions.	Weak
Offer pelvic floor muscle therapy as part of the treatment plan to improve quality of life and sexual function.	Weak

Recommendation for the management of psychological aspects in CPP	**Strength rating**
For CPP with significant psychological distress, refer patient for CPP-focused psychological treatment.	Strong

Recommendations for the management of pelvic floor dysfunction	Strength rating
Apply myofascial treatment as first line treatment.	Weak
Offer biofeedback as therapy adjuvant to muscle exercises, in patients with anal pain due to an overactive pelvic floor.	Strong

Recommendations for the management of chronic/non-acute urogenital pain by opioids	Strength rating
Prescribe opioid treatment, following multidisciplinary assessment and only after other reasonable treatments have been tried and failed.	Strong
The decision to instigate long-term opioid therapy should be made by an appropriately trained specialist in consultation with the patient and their family doctor.	Strong
Where there is a history or suspicion of drug abuse, involve a psychiatrist or psychologist with an interest in pain management and drug addiction.	Strong

This short booklet is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-01-1), available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines/.

EAU GUIDELINES ON RENAL TRANSPLANTATION

(Text update March 2018)

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Introduction

The European Association of Urology (EAU) Renal Transplantation Guidelines aim to provide a comprehensive overview of the medical and technical aspects relating to renal transplantation.

Organ retrieval and transplantation surgery

Living-donor nephrectomy

Recommendations	Strength rating
Offer pure or hand-assisted laparoscopic/ retroperitoneoscopic surgery as the preferential technique for living-donor nephrectomy.	Strong
Perform open living-donor nephrectomy in centres where endoscopic techniques are not implemented.	Strong
Perform laparo-endoscopic single site surgery, robotic and natural orifice trans-luminal endoscopic surgery-assisted living-donor nephrectomy in highly-specialised centres only.	Strong

Organ preservation

Recommendations for kidney storage solutions	Strength rating
Use either University of Wisconsin or histidine tryptophane ketoglutarate preservation solutions for cold storage.	Strong
Use Celsior or Soltran solution for cold storage if University of Wisconsin or histidine tryptophane ketoglutarate solutions are not available.	Strong

Recommendations for kidney preservation: static and dynamic preservation	Strength rating
Use cold and warm ischemia time as predictors of delayed graft function.	Strong
Use hypothermic machine-perfusion in type III kidneys from donors after cardiac death, kidneys with prolonged simple cold storage and expanded criteria donor kidneys.	Strong
Hypothermic machine-perfusion may be used in standard criteria deceased donor kidneys.	Strong
Use low pressure values in hypothermic machine perfusion preservation.	Strong
Hypothermic machine-perfusion must be continuous and controlled by pressure and not flow.	Strong
Do not discard grafts due to only increased vascular resistance and high perfusate injury marker concentrations during hypothermic machine perfusion preservation.	Weak

Donor kidney biopsies

Recommendations	Strength rating
Do not base decisions on the acceptance of a donor organ on histological findings alone, since this might lead to an unnecessary high rate of discarded grafts. Interpret histology in context with clinical parameters of donor and recipient including perfusion parameters where available.	Strong
Use paraffin histology for histomorphology as it is superior to frozen sections, however, its diagnostic value has to be balanced against a potential delay of transplantation.	Strong
Submit 14 or 16 G needle core biopsies, wedge biopsies or skin punch biopsies for histopathology.	Weak
Procurement biopsies should be read by a renal pathologist or a general pathologist with specific training in kidney pathology.	Strong

Living and deceased donor implantation surgery

Recommendations	Strength rating
Immediate pre-op haemodialysis	
Use dialysis or conservative measures to manage fluid and electrolyte imbalance prior to transplant surgery taking into consideration the likelihood of immediate graft function.	Weak

Operating on patients taking anti-platelet and anti-coagulation agents	
Consider continuing anti-platelet therapy in patients on the transplant waiting list.	Weak
Discuss patients who take anti-platelet and anti-coagulation agents prior to transplant surgery with relevant cardiologist / haematologist /nephrologist.	Weak
Prevention of venous thrombosis including deep vein thrombosis during and after renal transplant	
Do not routinely give post-operative prophylactic unfractionated or low-molecular-weight heparin to low-risk living donor transplant recipients.	Weak
Peri-operative antibiotics in renal transplant	
Use single-dose, rather than multi-dose, peri-operative prophylactic antibiotics in routine renal transplant recipients.	Strong
Specific fluid regimes during renal transplantation	
Optimise pre-, peri- and post-operative hydration to improve renal graft function.	Strong
Use balanced crystalloid solutions for intra-operative intravenous fluid therapy.	Weak
Use target directed intra-operative hydration to decrease delayed graft function rates and optimise early graft function.	Strong
Dopaminergic drugs in renal transplantation	
Do not routinely use low-dose dopaminergic agents in the early post-operative period.	Weak

Surgical approaches for first, second, third and further transplants

Single kidney transplant – living and deceased donors

Recommendations	Strength rating
Assess the utility (including inspection) of the kidney for transplantation before commencement of immunosuppression and induction of anaesthesia for deceased donor kidney transplantation.	Strong
Choose either iliac fossa for placement of a first or second single kidney transplant.	Weak
Ligate peri-iliac vessel lymphatics (lymphostasis) to reduce post-operative lymphocele.	Weak
Assess the length of the donor renal vein and if it is short consider one of a variety of surgical techniques to optimise the venous anastomosis.	Weak
Use the external or common iliac arteries for an end-to-side arterial anastomosis to donor renal artery.	Weak
Use an end-to-end anastomosis to the internal iliac artery as an alternative to external or common iliac arteries.	Weak
Check the intima of the donor and recipient arteries prior to commencing the arterial anastomosis to ensure that there is no intimal rupture/flap. If this is found it must be repaired prior to/as part of the arterial anastomosis.	Strong

Pre-operatively plan the surgical approach in third or further transplants, to ensure that appropriate arterial inflow and venous outflow exists with adequate space to implant the new kidney.	Strong

Emerging surgical technologies

Robot-assisted kidney transplant (RAKT) surgery is being evaluated in prospective non-randomised trials (using IDEAL consortium principles). Whilst potential advantages may exist (decreased post-operative pain, length of hospital stay, incision length and lymphocele rate), evidence is too premature to recommend RAKT.

Dual kidney transplants

Dual kidney transplant is performed when the quality of a single deceased donor kidney is thought to be insufficient for appropriate long-term graft function and that the outcome with both kidneys would be better. A variety of surgical techniques have been described to implant a pair of donor kidneys these include: unilateral extra-peritoneal or intra-peritoneal and bilateral extra-peritoneal or intra-peritoneal that can be via a midline or two lateral incisions. No randomised controlled trials exist to recommend one technique for all patients or situations.

Ureteric implantation in normal urinary tract

Ureteric anastomotic techniques described for renal transplant recipients with no underlying urological abnormality include: extra (Lich-Gregoir) or intra (Ledbetter-Politano) vesical uretero-neo-cystotomy and uretero-ureterostomy using native ureter.

Recommendations	Strength rating
Perform Lich-Gregoir-like extra-vesical ureteric anastomosis technique to minimise urinary tract complications in renal transplant recipients with normal urological anatomy.	Strong
Pyelo/uretero-ureteral anastomosis is an alternative especially for a very short or poorly vascularised transplant ureter.	Strong

Transplantation/ureteric implantation in abnormal urogenital tract

The following points should be considered when performing kidney transplantation in the abnormal urogenital tract:

- In patients with an ileal conduit, a kidney transplant may be placed upside down to align the ureter to the conduit and avoid a redundant ureter.
- The technique used to implant transplant ureter(s) into an ileal conduit is the same as the method used with native ureter(s) (Bricker; Wallace).
- In bladder augmentation or continent pouches, ureters should be implanted with a tunnel technique or extra-vesically (Lich-Gregoir). The latter is favoured in most patients.
- In patients with a Mitrofanoff catheterisable stoma or continent ileo-caecal pouch with catheterisable stoma, consideration should be given to the positioning of the catheterisable stoma (umbilical or iliac fossa - usually right-side) with clear communication with the transplant surgeons so that the position of any future transplant kidney is not compromised. If an intraperitoneal placement of a future kidney transplant is likely, then placement of a Mitrofanoff exiting in the iliac fossa is preferable at the umbilicus. If a future kidney transplant is likely in the right

iliac fossa then placement of a Mitrofanoff exiting at the umbilicus or left iliac fossa may be preferable.

Donor complications

Living-donor nephrectomy, like any other intervention, is potentially associated with complications and mortality. However, the fact that the operation is performed on a healthy individual amplifies the relevance of any complications. Intra-operative complications occur in 2.2% (the most common being bleeding in 1.5% and injury to other organs in 0.8%) and post-operative complications occur in 7% (infectious complications in 2.6% and bleeding in 1%). Potential complications should be included in the process of informed consent. Long term complications are mostly related to the single-kidney condition. Health related quality of life, including mental condition, remains on average better than the general population after donation.

Recommendations	Strength rating
Restrict living donor nephrectomy to specialised centres.	Strong
Offer long-term follow-up to all living kidney donors.	Strong

Recipient complications

Surgical complications during and after kidney transplantation may expose the recipient to an increased risk of morbidity and mortality. The incidence and management of such complications is therefore of primary importance. The most common surgical complications in renal transplantation are summarised below.

Haemorrhage

The incidence of haematomas is reported to be between 0.2-25%. Small and asymptomatic hematomas do not usually

require any intervention. In case of larger hematomas, clinical signs and symptoms due to external pressure with graft dysfunction and/or thrombotic graft vessels complications can be present. These cases may be treated by percutaneous drainage under computed tomography or ultrasound guidance or may require surgical treatment.

Arterial thrombosis

Transplant renal artery thrombosis is a rare complication (prevalence 0.5-3.5%).

Recommendations	Strength rating
Perform ultrasound-colour-doppler in case of suspected graft thrombosis.	Strong
Perform surgical exploration in case of ultrasound finding of poor graft perfusion.	Strong
Perform a surgical thrombectomy in case of a salvageable graft if arterial thrombosis is confirmed intra-operatively.	Weak
Perform an allograft nephrectomy in case of a non-viable graft.	Strong

Venous thrombosis

Transplant renal vein thrombosis is an early complication (prevalence 0.5-4%) and one of the most important causes of graft loss during the first post-operative month.

Recommendations	Strength rating
Perform ultrasound-colour-doppler in case of suspected graft thrombosis.	Strong
Perform surgical exploration in case of ultrasound finding of poor graft perfusion.	Weak

If venous thrombosis is confirmed intra-operatively, perform a surgical thrombectomy in case of a salvageable graft or an allograft nephrectomy in case of a non-viable graft.	Weak
Do not routinely use pharmacologic prophylaxis to prevent transplant renal vein thrombosis.	Strong

Transplant renal artery stenosis

The incidence of transplant renal artery stenosis is 1-25%. Risk factors include small calibre and atherosclerosis of the donor artery, trauma to donor artery at procurement, absence of arterial patch, suturing technique (interrupted versus continuous), and damage to the iliac artery during transplantation.

Recommendations	**Strength rating**
Perform ultrasound-colour-doppler to diagnose an arterial stenosis, in case of undetermined results on ultrasound consider a magnetic resonance or computed tomography angiogram.	Strong
Perform percutaneous transluminal angioplasty/stent, if feasible, as first-line treatment for an arterial stenosis.	Strong
Offer surgical treatment in case of recent transplant, multiple, long and narrow stenosis, or after failure of angioplasty.	Strong

Arteriovenous fistulae and pseudo-aneurysms after renal biopsy

Percutaneous biopsy may result in arteriovenous fistulae and/or intrarenal pseudo-aneurysms in 1-18% of cases.

Recommendations	Strength rating
Perform a ultrasound-colour-doppler if a arteriovenous fistulae or pseudo-aneurysm is suspected.	Strong
Perform angiographic embolisation as first-line treatment in symptomatic cases of arteriovenous fistulae or pseudo-aneurysm.	Strong

Lymphocele

Lymphocele is a relatively common complication (prevalence 1-26%). There is a significant aetiological association with diabetes, m-TOR inhibitors (i.e sirolimus) therapy, and acute rejection.

Recommendations	Strength rating
Perform percutaneous drainage placement as the first treatment for large and symptomatic lymphocele.	Strong
Perform fenestration when percutaneous treatments fail.	Strong

Urinary leak

Urinary leakage occurs in 0-9.3% of cases.

Recommendations	Strength rating
Manage urine leak by JJ-stent and bladder catheter and/or percutaneous nephrostomy tube.	Strong
Perform surgical repair in cases of failure of conservative management.	Strong

Ureteral stenosis

Ureteral stenosis is a common complication in recipients, with an incidence of 0.6-10.5%. Early stenosis (within three months

of surgery) is usually caused by surgical technique or compromised ureteral blood supply during surgery. Late stenosis (after six months) is provoked by infection, fibrosis, progressive vascular disease and/or rejection.

Recommendations	Strength rating
In case of ureteral stricture, place a nephrostomy tube for both kidney decompression and stricture diagnosis via an antegrade pyelogram.	Strong
Manage strictures < 3 cm in length either with surgical reconstruction or endoscopically (percutaneous balloon dilation or antegrade flexible ureteroscopy and holmium laser incision).	Strong
Treat late stricture recurrence and/or stricture > 3 cm in length with surgical reconstruction in appropriate recipients.	Strong

Haematuria

The incidence of haematuria ranges from 1-34%. The Lich-Gregoire technique provides the lowest incidence of haematuria. Bladder irrigation is the first line of treatment. Some cases require cystoscopy with evacuation of clots and/or fulguration of bleeding sites.

Reflux and acute pyelonephritis

The frequency of vesicoureteral reflux is between 1-86%. Acute graft pyelonephritis occurs in 13% of graft recipients. Patients with lower tract urinary infections and cytomegalovirus (CMV) infection present a higher risk of acute graft pyelonephritis.

Recommendations	Strength rating
Use an endoscopic approach as first-line treatment for symptomatic reflux.	Weak

Kidney stones

Urolithiasis occurs in 0.2-1.7% of recipients.

Recommendations	Strength rating
Evaluate the causes of urolithiasis in the recipient.	Strong
Treat ureteral obstruction due to a stone with a percutaneous nephrostomy tube or JJ-stent placement.	Strong
Perform shockwave lithotripsy or antegrade/retrograde ureteroscopy for stones < 15 mm.	Strong
Perform percutaneous nephrolithotomy for stones > 20 mm.	Weak

Wound infection

Wound infections occur in about 4% of cases. Subcutaneous sutures, pre-dialysis transplantation, sealing or ligation of lymphatic trunks, prophylactic fenestration, reducing corticosteroid load, and avoiding sirolimus/everolimus therapy can decrease wound complication rates.

Incisional hernia

Incisional hernia occurs in approximately 4% of open kidney transplantations. Mesh infection is a risk factor for incisional hernia recurrence. Open and laparoscopic repair approaches are safe and effective.

Matching of donors and recipients

Histocompatibility antigens show remarkable polymorphism and human leukocyte antigen (HLA) matching is still very important in kidney transplantation as transplant outcome correlates with the number of HLA mismatches.

Recommendations	Strength rating
Determine the ABO blood group and the human leukocyte antigen A, B, C and DR phenotypes for all candidates awaiting kidney transplantation.	Strong
Test both the donor and recipient for human leukocyte antigen DQ. Human leukocyte antigen DP testing may be performed for sensitised patients.	Strong
Perform thorough testing for HLA antibodies before transplantation.	Strong
Perform adequate cross-match tests to avoid hyper-acute rejection, before each kidney and combined kidney/pancreas transplantation.	Strong

Immunosuppression after kidney transplantation

The principle underlying successful immunosuppression is 'the balance of survival'. Practitioners must prescribe a dosage of drug high enough to suppress rejection without endangering the recipient's health.

The currently recommended standard initial immunosuppression regime provides excellent efficacy with good tolerability. It is given to most patients and consists of:

- calcineurin inhibitors (preferably tacrolimus, alternatively cyclosporine);

- mycophenolate (MMF or enteric-coated mycophenolate sodium;
- steroids (prednisolone or methylprednisolone);
- induction therapy (preferably basiliximab in low and standard risk patients and anti-thymocyte globulin (ATG) in high risk patients).

Recommendations	Strength rating
General immunosuppression after kidney transplantation	
Perform initial rejection prophylaxis with a combination therapy of a calcineurin inhibitor (preferably tacrolimus), mycophenolate, steroids and an induction agent (either basiliximab or anti-thymocyte globulin).	Strong
Calcineurin inhibitors	
Use calcineurin inhibitors for rejection prophylaxis as they represent current best practice pending publication of long-term results using newer agents.	Strong
Use tacrolimus as first-line calcineurin inhibitor due to its higher efficacy.	Strong
Monitor blood-levels of both cyclosporine and tacrolimus to allow appropriate dose adjustment of calcineurin inhibitors.	Strong
Mycophenolates ~~(MPA)~~	
Administer mycophenolate as part of the initial immunosuppressive regimen.	Strong
Azathioprine	
Azathioprine may be used in a low-risk population as an immunosuppressive drug, especially for those intolerant to mycophenolate formulations.	Weak

Steroids	
Initial steroid therapy should be part of immunosuppression in the peri-operative and early post-transplant period.	Strong
Consider steroid withdrawal in standard immunological risk patients on combination therapy with calcineurin inhibitors and mycophenolic acid after the early post-transplant period.	Weak
Inhibitors of the mammalian target of rapamycin (m-TOR)	
The m-TOR inhibitors may be used to prevent rejection in patients who are intolerant to standard therapy.	Weak
Significantly reduce calcineurin inhibitor dosage in a combination regimen with m-TOR inhibitors to prevent aggravated nephrotoxicity.	Strong
Do not convert patients with proteinuria and poor renal function to m-TOR inhibitors.	Strong
Monitor blood-levels of both sirolimus and everolimus to allow for appropriate dose adjustment.	Strong
Induction with Interleukin-2 receptor antibodies	
Use interleukin-2 receptor antibodies for induction in patients with normal immunological risk in order to reduce incidence of acute rejection.	Weak
T-cell depleting induction therapy	
T-cell depleting antibodies may be used for induction therapy in immunologically high risk patients.	Weak

Belatacept	
Belatacept may be used for immuno-suppressive therapy in immunologically low risk patients, who have a positive Epstein-Barr virus serology.	Weak

Immunological complications

Immunological rejection is a common cause of early and late transplant dysfunction. There is great variation in the timing and severity of rejection episodes and how they respond to treatment. Two main types of immunological reactions are distinguished: T-cell mediated rejections (TCMR) and antibody-mediated rejections (ABMR). Antibody-mediated rejection and TCMR may be diagnosed together, called mixed acute rejection. Antibody-mediated rejection may occur as hyperacute rejection, acute rejection or chronic rejection. Chronic ABMR is considered as one of the leading causes of late graft loss.

Recommendations	**Strength rating**
Monitor transplant recipients for signs of acute rejection, particularly during the first six months post-transplant.	Strong
Take regular blood samples in addition to regular monitoring of urine output and ultrasound examinations in order to detect graft dysfunction during hospitalisation.	Strong
Immediately rule out other potential causes of graft dysfunction in cases of suspected acute rejection. An ultrasound of the kidney transplant should be performed.	Strong
Perform a renal biopsy, graded according to the most recent Banff criteria, in patients with suspected acute rejection episodes.	Strong

Only if contraindications to renal biopsy are present, can 'blind' steroid bolus therapy be given.	Strong
Test patients who suffer acute rejection as soon as possible for anti-HLA antibodies against the graft.	Strong
Re-assess the immunosuppressive therapy of all patients with rejection, including patient adherence to the medication, which is of particular importance in late rejections.	Strong

Hyper-acute rejection

Hyper-acute rejection is the most dramatic and destructive immunological attack on the graft. It results from circulating, complement-fixing IgG antibodies, specifically reactive against incompatible donor antigen, which engages with and destroys the vascular endothelium within minutes or hours after vascularisation.

Recommendations	**Strength rating**
Prevent hyper-acute rejection by adequate ABO blood group and HLA matching of donor and recipients.	Strong

Treatment of T-cell mediated acute rejection

Recommendations	**Strength rating**
Use steroid bolus therapy as first-line treatment for T-cell mediated rejection in addition to ensuring adequate baseline immunosuppression.	Strong

In severe or steroid-resistant rejection, use intensified immunosuppression, high-dose steroid treatment, and eventually T-cell depleting agents.	Strong

Treatment of antibody mediated rejection

Recommendations	Strength rating
Treatment of antibody mediated rejection should include antibody elimination.	Strong

Follow-up after transplantation

Long-term graft function is of critical importance for the success of a transplant. Therefore, regular long-term follow-up by experienced transplant physicians is essential in order to detect complications or graft dysfunction early and reassure adherence to the immunosuppressive regimen.

Recommendations	Strength rating
Provide lifelong regular post-transplant follow-up by an experienced and trained transplant specialist at least every six to twelve months.	Strong
Advise patients on appropriate lifestyle changes, potential complications, and the importance of adherence to their immunosuppressive regimen.	Strong

Regularly monitor (approximately every four to eight weeks) serum creatinine, estimated glomerular filtration rate, blood pressure, urinary protein excretion, immunosuppression and complications after renal transplantation. Changes in these parameters over time should trigger further diagnostic work-up including renal biopsy, a search for infectious causes and anti-HLA antibodies.	Strong
Perform an ultrasound of the graft, in case of graft dysfunction, to rule out obstruction and renal artery stenosis.	Strong
In patients with interstitial fibrosis and tubular atrophy undergoing calcineurin inhibitor therapy and/or with histological signs suggestive for calcineurin inhibitor toxicity (e.g. arteriolar hyalinosis, striped fibrosis) consider calcineurin inhibitor reduction or withdrawal.	Strong
Initiate appropriate medical treatment, e.g. tight control of hypertension, diabetes, proteinuria, cardiac risk factors, infections, and other complications according to current guidelines.	Strong

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-01-1) available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines.

EAU GUIDELINES ON THROMBOPROPHYLAXIS IN UROLOGICAL SURGERY

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Introduction

Utilising recent studies and newly summarised evidence, the EAU Guidelines on Thromboprophylaxis provide practical evidence-based guidance regarding post-surgery thromboprophylaxis and peri-operative management of antithrombotic agents in urology.

The Thromboprophylaxis Panel used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach for assessment of quality of evidence and grading of recommendations. GRADE offers four levels of evidence quality, reflecting the degree of certainty or confidence in the evidence: high, moderate, low, and very low. The strength of a recommendation reflects the extent to which we can be confident that desirable effects of an intervention outweigh undesirable effects. GRADE classifies recommendations as strong or weak.

Thromboprophylaxis post-surgery

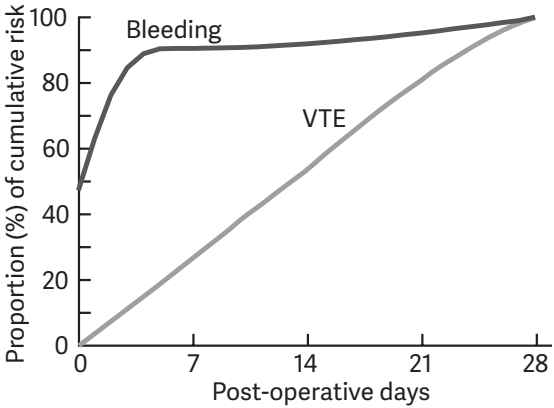
This guideline provides procedure and patient risk-specific guidance weighing the benefit of reduced venous thromboembolism (VTE) against the harm of increased bleeding. The Panel provides recommendations for numerous urologic procedures, with variation across patient risk strata (Table 1). When creating recommendations, the Panel

first calculated the net benefit (absolute reduction in VTE risk – absolute increase in bleeding risk) and then considered quality of evidence for both pharmacological and mechanical prophylaxis (Figure 1).

Table 1: Venous thromboembolism (VTE) according to patient risk factors

	Risk factors
Low risk	No risk factors
Medium risk	Any one of the following: age 75 years or more; body mass index 35 or more; VTE in 1st degree relative (parent, full sibling, or child).
High risk	Prior VTE Patients with any combination of two or more risk factors

Figure 1: Proportion of cumulative risk (%) of venous thromboembolism (VTE) and major bleeding by week since surgery during the first four post-operative weeks



	Proportion of 28-day cumulative bleeding risk
Operation day	47.4%
Post-operative day 1	63.3%
Post-operative day 2	76.6%
Post-operative day 3	84.9%
Post-operative day 4	89.2%
Post-operative day 28	100.0%

The bleeding pattern depicted applies to most bleeds for most surgeries. However, some urological surgeries, such as transurethral resection of the the prostate (TURP), are associated with later bleeding. This is typically minor and occurs around ten days post-surgery.

General statements for all procedure-specific recommendations

The following apply to all recommendations for pharmacological prophylaxis:

- All recommendations are based on a starting time of the morning after surgery.
- The optimal duration of pharmacological prophylaxis for all recommendations is approximately four weeks post-surgery.
- There are number of acceptable alternatives for pharmacologic prophylaxis (Table 2).
- All recommendations for mechanical prophylaxis are until ambulation.

Table 2: Alternative regimens for pharmacological prophylaxis

Pharmacological agent	Dosage*
Low molecular weight heparins:	
Dalteparin	5,000 IU injection once a day
Enoxaparin	40 mg injection once a day
Tinzaparin	3,500/4,500 IU injection once a day
Unfractionated heparin	5,000 IU injection two or three times a day
Fondaparinux†	2.5 mg injection once a day
Direct acting oral anticoagulants†:	
Dabigatran	220 mg tablet once a day
Apixaban	2.5 mg tablet once a day
Edoxaban	30 mg tablet once a day
Rivaroxaban	10 mg tablet once a day

** Dosages may not apply in renal impairment.*

† Fondaparinux and direct acting oral anticoagulants have not been sufficiently studied in urology to warrant on-label use for post-surgery thromboprophylaxis.

Recommendations for prophylaxis in specific procedures according to patient risk

Ambulatory day surgery

R1. In all patients undergoing minor ambulatory day surgery (for example, circumcision, hydrocelectomy and vasectomy), the Panel recommends against use of pharmacological prophylaxis ***(strong, moderate-quality evidence)***, and against use of mechanical prophylaxis ***(strong, moderate-quality evidence)***.

Open radical cystectomy

R2. In all patients undergoing open radical cystectomy, the Panel recommends use of pharmacological prophylaxis ***(strong, moderate or high-quality evidence depending on risk stratum)***, and suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

Robotic radical cystectomy

R3. In all patients undergoing robotic radical cystectomy, the Panel suggests use of pharmacological prophylaxis ***(weak, low-quality evidence)***, and suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

Laparoscopic radical prostatectomy

R4. For patients undergoing laparoscopic radical prostatectomy without pelvic lymph node dissection (PLND), for those at low risk of VTE, the Panel recommends against use of pharmacological prophylaxis ***(strong, moderate-quality evidence)*** and suggests against use of mechanical prophylaxis ***(weak, low-quality evidence)***; for those at moderate and high risk, the Panel suggests against use of pharmacological prophylaxis ***(weak, moderate- or high-quality evidence)*** and suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

R5. For patients undergoing laparoscopic radical prostatectomy with standard PLND, for those at low risk of VTE, the Panel recommends against use of pharmacological prophylaxis ***(strong, moderate-quality evidence)***; for those at medium risk, the Panel suggests against use of pharmacological prophylaxis ***(weak, moderate-quality evidence)***; for those at high risk, the Panel recommends use of pharmacological prophylaxis ***(strong, high-quality evidence)***; and for all patients, the Panel suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

R6. For patients undergoing laparoscopic radical prostatectomy with extended PLND, for those at low risk of VTE, the Panel suggests against use of pharmacological prophylaxis ***(weak, moderate-quality evidence)***; for those at medium risk, the Panel suggests use of pharmacological prophylaxis ***(weak, high-quality evidence)***; for those at high risk, the Panel recommends use of pharmacological prophylaxis ***(strong, high-quality evidence)***; and for all patients, the Panel suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

Open radical prostatectomy

R7. For patients undergoing open radical prostatectomy without PLND or with standard PLND, for those at low risk of VTE, the use of pharmacological prophylaxis is suggested ***(weak, moderate-quality evidence)***; for those at medium and high risk, use of pharmacological prophylaxis is recommended ***(strong, moderate- or high-quality evidence)***; and for all patients, the Panel suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

R8. For all patients undergoing open radical prostatectomy with extended PLND, the Panel recommends use of pharmacological prophylaxis ***(strong, moderate or high-quality evidence)***, and suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

Robotic radical prostatectomy

R9. For patients undergoing robotic radical prostatectomy without PLND, for those at low risk of VTE, the Panel recommends against use of pharmacological prophylaxis ***(strong, moderate-quality evidence)*** and suggests against use of mechanical prophylaxis ***(weak, low-quality evidence)***; for those at medium and high risk, the Panel suggests against use of pharmacological prophylaxis ***(weak, moderate-quality evidence)*** and suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

R10. For patients undergoing robotic radical prostatectomy with standard PLND, for those at low risk of VTE, the Panel recommends against use of pharmacologic prophylaxis ***(strong, moderate-quality evidence)***; for those at medium risk, the Panel suggests against use of pharmacologic prophylaxis ***(weak, moderate-quality evidence)***; for those at high risk, the Panel suggests use of pharmacologic prophylaxis ***(weak, moderate-quality evidence)***; and for all patients, the Panel suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

R11. For patients undergoing robotic radical prostatectomy with extended PLND, for those at low risk of VTE, the Panel suggests against use of pharmacologic prophylaxis ***(weak, moderate-quality evidence)***; for those at medium risk, the Panel suggests use of pharmacologic prophylaxis ***(weak, moderate-quality evidence)***; for those at high risk, the Panel recommends use of pharmacologic prophylaxis ***(strong, moderate-quality evidence)***; and for all patients, the Panel suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

Nephrectomy

R12. For patients undergoing laparoscopic partial nephrectomy, for those at low and medium risk of VTE, the Panel suggests against use of pharmacologic prophylaxis ***(weak, low-quality evidence)***; for those at high risk, the Panel recommends use of pharmacologic prophylaxis ***(strong, moderate-quality evidence)***; and for all patients, the Panel suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

R13. For all patients undergoing open partial nephrectomy, the Panel suggests use of pharmacologic prophylaxis ***(weak, very low quality evidence)***, and suggests use of mechanical prophylaxis ***(weak, very low quality evidence)***.

R14. For patients undergoing robotic partial nephrectomy, for those at low risk of VTE, the Panel suggests against use of pharmacologic prophylaxis ***(weak, moderate-quality evidence)***; for those at medium risk, the Panel suggests use of pharmacologic prophylaxis ***(weak, moderate-quality evidence)***; for those at high risk, the Panel recommends use of pharmacologic prophylaxis ***(strong, high-quality evidence)***; and for all patients, the Panel suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

R15. For patients undergoing laparoscopic radical nephrectomy, for those at low or medium risk of VTE, the Panel suggests against use of pharmacologic prophylaxis ***(weak, very low quality evidence)***; for those at high risk, the Panel suggests use of pharmacologic prophylaxis ***(weak, very low quality evidence)***; and for all patients, the Panel suggests use of mechanical prophylaxis ***(weak, very low quality evidence)***.

R16. For patients undergoing open radical nephrectomy, the Panel suggests use of pharmacologic prophylaxis ***(weak, very low quality evidence)***, and suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

R17. For all patients undergoing radical nephrectomy with thrombectomy, the Panel suggests use of pharmacologic prophylaxis ***(weak, very low quality evidence)***, and suggests use of mechanical prophylaxis ***(weak, very low quality evidence)***.

R18. For all patients undergoing open nephroureterectomy, the Panel suggests use of pharmacologic prophylaxis ***(weak, very low quality evidence)***, and suggests use of mechanical prophylaxis ***(weak, very low quality evidence)***.

R19. For all patients undergoing primary nerve sparing retroperitoneal lymph node dissection, the Panel suggests use of pharmacologic prophylaxis ***(weak, very low quality evidence)***, and suggests use of mechanical prophylaxis ***(weak, very low quality evidence)***.

Non-cancer urological procedures

R20. For all patients undergoing transurethral resection of the prostate (TURP) or equivalent procedures, the Panel suggests against use of pharmacologic prophylaxis ***(weak, very low quality evidence)***; for those at low or medium risk of VTE, the Panel suggests against use of mechanical prophylaxis ***(weak, low-quality evidence)***; and for those at high risk, the Panel suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

R21. For patients undergoing laparoscopic donor nephrectomy or open donor nephrectomy, for those at low risk of VTE, the Panel suggests against use of pharmacologic prophylaxis ***(weak, very low or low -quality evidence)***, and suggests against use of mechanical prophylaxis ***(weak, very low or low -quality evidence)***; for medium-risk patients, the Panel suggests against use of pharmacologic prophylaxis ***(weak, very low or low -quality evidence)***, and suggests use of mechanical prophylaxis ***(weak, very low or low -quality evidence)***; and for high-risk patients, the Panel suggests use of pharmacologic prophylaxis ***(weak, very low or low -quality evidence)***, and suggests use of mechanical prophylaxis ***(weak, very low or low -quality evidence)***.

R22. For all patients undergoing open prolapse surgery or reconstructive pelvic surgery, the Panel suggests against the use of pharmacologic prophylaxis ***(weak, very low quality evidence)***; for those at low or medium risk of VTE, the Panel suggests against use of mechanical prophylaxis ***(weak, very low or low -quality evidence)***; while for those at high risk, the Panel suggests use of mechanical prophylaxis ***(weak, very low or low -quality evidence)***.

R23. For all patients undergoing percutaneous nephrolithotomy, the Panel suggests against use of pharmacologic prophylaxis ***(weak, very low quality evidence)***; for those at low or medium risk of VTE, the Panel suggests against use of mechanical prophylaxis ***(weak, very low quality evidence)***; while for those at high risk, the Panel suggests use of mechanical prophylaxis ***(weak, very low quality evidence)***.

Peri-operative management of antithrombotic agents in urology

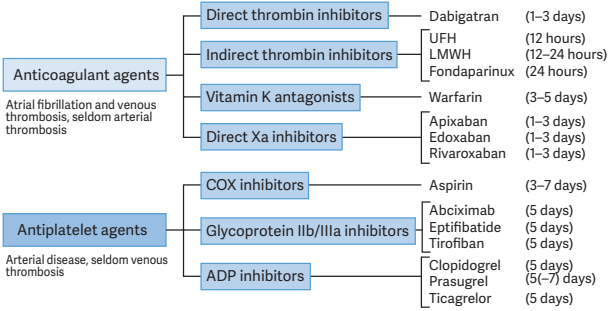
In principle, there are four options to manage use of antithrombotic agents (Figure 2) during the peri-operative period:

1) to defer surgery until antithrombotic agents are not needed;
2) stop antithrombotic agents prior to surgery and restart sometime after surgery;
3) continue through the surgical procedure;
4) administer alternative antithrombotic agents that may still reduce the risk of thrombosis but with less risk of bleeding than agents patients are currently using ("bridging").

Recent evidence has demonstrated that bridging increases bleeding without preventing thrombosis. The Panel therefore makes one of two recommendations for patients receiving antithrombotic agents regularly and contemplating surgery:

1) discontinue antithrombotic therapy for the period around surgery;
2) in those with a temporary very high risk of thrombosis, delay surgery until that risk decreases. If it is not possible to delay, continuing antithrombotic therapy or bridging through surgery may be advisable.

Figure 2: The most widely used antithrombotic agents in patients undergoing urologic surgery
Required period of stopping drug before surgery (if desired) provided in parentheses.



Recommendations for peri-operative management

Five days is an appropriate time to stop antiplatelet agents before surgery, while the optimal time to stop varies across anticoagulants (for details, see Figure 2).

R24. In all patients receiving antiplatelet agents (aspirin, clopidogrel, prasugrel, ticagrelor), except those with very high risk of thrombosis (see recommendations 26 and 27), the Panel recommends stopping antiplatelet agents before surgery and not initiating any alternative antithrombotic therapy ***(strong, high-quality evidence)***.

R25. In patients in whom antiplatelet agents have been stopped before surgery, the Panel recommends restarting when bleeding is no longer a serious risk - typically four days post-surgery - rather than withholding for longer periods ***(strong, moderate-quality evidence)***.

R26. In patients with very high risk of thrombosis receiving antiplatelet agents (those with drug-eluting stent placement within six months, those with bare metal stent placement within six weeks, those with transient ischemic attack (TIA) or stroke within 30 days) in whom surgery can be delayed, the Panel recommends delaying surgery ***(strong, high-quality evidence)***.

R27. In patients with very high risk of thrombosis receiving antiplatelet agents (those with drug-eluting stent placement within six months, those with bare metal stent placement within six weeks, those with TIA or stroke within 30 days) in whom surgery cannot be delayed, the Panel suggests continuing the drugs through surgery ***(weak, low-quality evidence)***.

R28. In all patients receiving anticoagulant agents (unfractionated heparin, low molecular weight heparin [LMWH], warfarin, fondaparinux, dabigatran, apixaban, rivaroxaban, edoxaban), except those with very high risk of thrombosis (see recommendation 26), the Panel recommends stopping drugs before surgery (see Figure 2) and not initiating any alternative antithrombotic therapy ***(strong, high-quality evidence)***.
Note: Patients with creatinine clearance <30 ml/min should not receive dabigatran, apixaban, rivaroxaban or edoxaban.

R29. In patients in whom anticoagulants have been stopped before surgery, the Panel recommends restarting when bleeding is no longer a serious risk - typically four days post-surgery - rather than withholding for longer periods ***(strong, moderate-quality evidence)***.

R30. In patients with a new VTE, it is recommended that surgery is delayed for at least one month, and if possible three months, to permit discontinuation of anticoagulation pre-operatively, rather than operating within one month of thrombosis ***(strong, high-quality evidence)***.

R31. In patients receiving any anticoagulant with a severe thrombophilia, such as antithrombin deficiency and antiphospholipid antibody syndrome, the Panel suggests anticoagulation with either heparin or LMWH through surgery, rather than stopping anticoagulation before and after surgery ***(weak, low-quality evidence)***.

R32. In patients with high-risk mechanical prosthetic heart valves, such as cage-ball valves, receiving warfarin, the Panel recommends bridging with LMWH prior and subsequent to surgery, rather than discontinuing anticoagulation peri-operatively ***(strong, high-quality evidence)***. Anticoagulation in these patients involves stopping the warfarin five days prior, commencing LMWH four days prior, omitting LMWH on the day of surgery, and recommencing LMWH and warfarin after surgery.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN: 978-94-92671-01-1), available to all members of the European Association of Urology at their website: http://www.uroweb.org/guidelines/.

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