#### **INVITED REVIEW**



## Complications of ureteroscopy: a complete overview

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#### Abstract

**Introduction** The aim of this paper was to give a complete overview of all published complications associated with ureteroscopy and their according management and prevention in current urological practice.

**Materials and methods** This review was registered in PROSPERO with registration number CRD42018116273. A bibliographic search of the Medline, Scopus, Embase and Web of Science databases was performed by two authors (V.D.C. and E.X.K.). According to the Population, Intervention, Comparator, Outcome (PICO) study design approach and Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) standards, a consensus between these authors was found relating to the thematic structure of this review.

**Results** Ureteral stent discomfort, ureteral wall injury and stone migration are the most frequently reported complications. The worst complications include urosepsis, multi-organ failure and death. Incidence rates on these and other complications varied extensively between the reviewed reports.

**Conclusion** Ureteroscopy seems to be associated with more complications than currently reported. The present overview may help urologists to prevent, recognize and solve complications of ureteroscopy. It may also stimulate colleagues to perform prospective studies using standardized systems for classifying complications. These are warranted to compare results among different studies, to conduct meta-analyses, to inform health care workers and to counsel patients correctly about possible risks of ureteroscopy.

Keywords Urolithiasis · Nephrolithiasis · Ureteroscopy · Retrograde intrarenal surgery · Complications · Overview

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## Introduction

Ureteroscopy is an established minimally-invasive procedure for diagnosis and treatment of upper urinary tract diseases. It is the most frequent intervention for kidney stones and one of the most commonly performed surgery in urology

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[1]. Because ureteroscopy does not require any disruption of anatomical boundaries, it is considered as a straightforwardly performable intervention with a low complication rate. Although rare, devastating complications may arise in the perioperative or postoperative course. We aimed to give a complete overview of all published complications associated with ureteroscopy and their according to management and prevention in current urological practice.

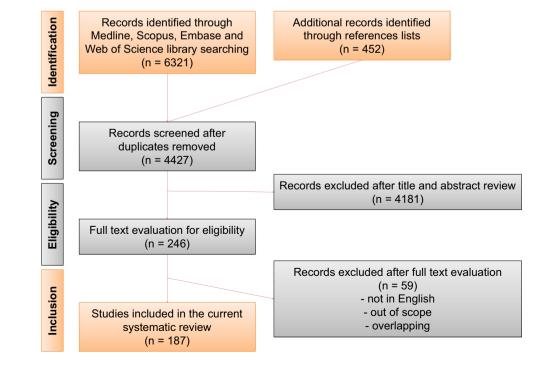
## Methods

This study was registered in PROSPERO with registration number CRD42018116273. A bibliographic search of the Medline, Scopus, Embase and Web of Science databases was performed by two authors (V.D.C. and E.X.K.) in January 2019. The search terms "complication" OR "death" AND "ureteroscopy" OR "ureterorenoscopy" OR "ureteroscopic" OR "ureterorenoscopic" OR "ureteroscope" OR "ureterorenoscope" OR "retrograde intrarenal surgery" OR "rirs" were used and the filters "humans" and "english" were applied. All original articles reporting about complications in adults were included. Additional articles identified through references lists were also included. Editorials, letters and review articles were excluded. No time period restriction was applied. Reported incidence rates were based on articles published in the twenty-first century since earlier studies were based on ancestral ureteroscopes which did not merely integrate characteristics of currently available miniaturized instruments. According to the Population, Intervention, Comparator, Outcome (PICO) study design approach and Preferred Reporting Items for Systematic Reviews and Metaanalysis (PRISMA) standards, a consensus between V.D.C. and E.X.K. was found relating to the thematic structure of this review. Figure 1 shows a flowchart summarizing the selection process. Owing to the heterogeneity of study outcomes, a narrative synthesis rather than a quantified metaanalysis of data was performed.

## Results

## **Classification sytems of complications**

The modified Clavien classification system (MCCS) and the modified Satava classification system have been proposed for ureteroscopy (Tables 1, 2) [2-5]. The MCCS for ureteroscopy was introduced in 2012 by Mandal et al. to report and grade the severity of perioperative complications occurring during stone removal with a ureteroscope. Perioperative complications (up to three months after surgery) are stratified into five grades. The authors proposed to stratify grade 1 and 2 complications as "minor" and MCCS grades 3, 4 and 5 as major complications [2, 3]. Major complications require surgical, endoscopic or radiological intervention or are life-threatening complications. In the Satava classification, complications are stratified into three grades. Grade 1 complications have no consequences for the patient, grade 2 complications require endoscopic surgery, and grade 3 complications require open or laparoscopic surgery [4, 5].



### Fig. 1 PRISMA flow diagram

#### Table 1 Modified Clavien classification system [3]

Grade	Complication				
I	Any deviation from normal postoperative course without the need for pharmacologic treatment or surgical, endoscopic, or radiologic intervention. The allowed therapeutic regimens include drugs such as antiemetics, antipyretics, analgesics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside				
II	Complications requiring pharmacologic treatment with drugs other than those allowed for grade I complication. The use of blood transfusions and total parenteral nutrition is also included				
III	Complications requiring surgical, endoscopic, or radiologic intervention				
IIIa	Intervention required without general anesthesia				
IIIb	Intervention required with general anesthesia				
IV	Life-threatening complications, including central nervous system complications, requiring intensive care unit stay				
IVa	Single organ dysfunction, including requiring dialysis				
IVb	Multiorgan dysfunction				
V	Death of the patient				

 Table 2 Modified Satava classification system [4, 5]

Grade	Complication
1	Incidents without consequences
2	Incidents treated with endoscopic surgery
2a	Incidents treated intraoperatively with endoscopic surgery
2b	Incidents requiring endoscopic re-treatment
3	Incidents requiring open or laparoscopic surgery

In this review, complications are classified in intraoperative, early postoperative (within 3 weeks following ureteroscopy) and late postoperative complications (more than 3 weeks after surgery). They are further subdivided in major (surgical, endoscopic or radiological intervention required or life-threatening complications) and minor complications. Management of complications and preventive measures are summarized in Table 3.

#### Intraoperative complications

#### **Major complications**

**Ureteral avulsion** Ureteral avulsion is one of most devastating complications of ureteroscopy (supplementary figure). It is relatively rare, with a reported incidence between 0.04 and 0.9% [2, 6–16]. While it may be assumable that avulsion occurs more commonly in the proximal ureter due to its thinner muscular wall, a relationship with stone location within the ureter has not yet been found [13].

The most commonly involved mechanism of ureteral avulsion is when excessive force is applied during retrieval of a stone that would be too large to be passed through the ureteral lumen [2, 6-14]. This commonly occurs when stones are entrapped within a basket without having been reduced to small fragments. Ureteral avulsion has also been reported

after endopyelotomy procedures, where the ureteropelvic junction becomes particularly vulnerable [17]. There are case reports of ureteral avulsion in which an access sheath was used. However, it remains unclear if the access sheath itself played a role in the development of the avulsion [18].

A less known mechanism of ureteral injury is the twopoint or "scabbard" ureteral avulsion in which the ureteroscope is wedged in the intramural ureter. It involves a proximal and distal discontinuity of the ureter, with a resultant scabbard, since the ureter is withdrawn like a sheath on the ureteroscope [18–20]. The authors attribute this complication to the tapered design of a ureteroscope, in which the larger proximal shaft becomes wedged in the intramural ureter. This may also occur in case of accordioning of the distal bending rubber component of a flexible ureteroscope, resulting in a retained ureteroscope [21].

Ureteral avulsion may also occur during the removal trial of a ureteroscope with a broken and locked deflection mechanism (supplementary figures). Such damage to the deflection mechanism may occur when a flexible ureteroscope is pulled through a stenotic infundibulum in maximal deflection [22, 23]. In case of locked flexible ureteroscope, it is recommended to manually straighten the ureteroscope by passing a coaxial dilator alongside the ureteroscope [22]. In case of failure, one may try to remove the ureteroscope without damaging the urinary tract by cutting the handle of the flexible ureteroscope or by cutting the distal part through a percutaneous access.

A ureteral avulsion can either be repaired immediately at the time of recognition or in a staged session after discussing the treatment options with the patient. In case of delayed repair, an appropriate urinary drainage should be guaranteed through a nephrostomy tube. Definitive surgical options include several types of ureteral reimplantation (e.g. psoas hitch or a Boari flap procedure) depending on the level of avulsion, ileal interposition or renal autotransplantation [24].

Complication (incidence %)         Management         Pervention           Ureteral stem discomfort (1.1–8%)         Analgesiss         Obviate rout           Ureteral stem discomfort (1.1–8%)         Analgesis         Oviate rout           Ureteral stem discomfort (1.1–8%)         Analgesis         Oviate rout           Ureteral stem discomfort (1.1–8%)         Remove stome         Oviate rout           Ureteral vall injury (mucosal erosion, false passage and perfo- ration) (0.13–6.2.1%)         Ureteral steming after ureteropyolography         Use small-s provine and provine and residual fragments (0.1–59%)         Remove stome         Oviate rout           Proximal stome migration and residual fragments (0.1–59%)         Remove stome         Ureteral steming after ureteropyolography         Use small-s prove stome           Difficult ureteral access of ureteroscope (1–37%)         Remove stome         Ureteral steming dilation up to the size of the uretero- store and distoring or remove steming         Use small-sterateral distore up to the size of the uretero- store and distore a ureteral steming after intercering in operatore         Back dudit           Vesicoureteral reflux (0.07–20%)         Kaposition or remove steming         Back dudit         Back dudit           Vesicoureteral reflux (0.07–20%)         Ureteral steming after indeperption the intervention in case of the intraoperative bleeding (0.1–19.9%)         Conservative management         Anoid digree vesope in greetion           <	Table 3         Summary of the management and prevention of complications in ureteroscopy	ations in ureteroscopy	
Analgesics         ge and perfo-       Ureteral stenting after ureteropyelography         (0.1–59%)       Remove stone         (0.1–59%)       Remove stone         (0.1–59%)       Remove stone         (0.1–59%)       Remove stone         Place ureteral stent       Only perform minimal dilation up to the size of the uretero-scope in prestented patients         Reposition or remove stent       Conservative management         Submucosal collagen injection       Use low-pressure irrigation         Use low-pressure irrigation       Use low-pressure irrigation         Place a ureteral stent and postpone the intervention in case of prolonged poor vision       Antipyretics         Antipyretics       Culture-based antibiotic therapy         Analgesics       Ureteral stenting	Complication (incidence %)	Management	Prevention
<pre>ge and perfo- Ureteral stenting after ureteropyelography (0.1–59%) Remove stone (0.1–59%) Remove stone Place ureteral stent Only perform minimal dilation up to the size of the uretero- scope in prestneted patients Reposition or remove stent Conservative management Submucosal collagen injection Use low-pressure irrigation Use low-pressure irrigation Place a ureteral stent and postpone the intervention in case of prolonged poor vision Antipyretics Culture-based antibiotic therapy Antigesics Ureteral stenting </pre>	Ureteral stent discomfort (1.1–88%)	Analgesics	Obviate routine stenting after uncomplicated ureteroscopic stone removal
<ul> <li>(0.1-59%) Remove stone</li> <li>Place ureteral stent</li> <li>Only perform minimal dilation up to the size of the uretero- scope in prestented patients</li> <li>Reposition or remove stent</li> <li>Conservative management</li> <li>Submucosal collagen injection</li> <li>Use low-pressure irrigation</li> <li>Use low-pressure irrigation</li> <li>Place a ureteral stent and postpone the intervention in case of prolonged poor vision</li> <li>Antipyretics</li> <li>Culture-based antibiotic therapy</li> <li>Analgesics</li> <li>Ureteral stenting</li> </ul>	Ureteral wall injury (mucosal erosion, false passage and perforation) (0.13–62.1%)	Ureteral stenting after ureteropyelography	Use small-sized instruments adapted to the patient's anatomy Place a ureteral stent in case of ureteral narrowing Only use baskets under direct vision Fragment or dust ureteral stones from the center towards the periohery.
Place ureteral stent Only perform minimal dilation up to the size of the uretero- scope in prestented patients Reposition or remove stent Conservative management Submucosal collagen injection Use low-pressure irrigation Place a ureteral stent and postpone the intervention in case of prolonged poor vision Antipyretics Antipyretics Culture-based antibiotic therapy Analgesics Ureteral stenting	Proximal stone migration and residual fragments (0.1–59%)	Remove stone	Use low-pressure irrigation Apply laser lithotripsy (long pulses and low energy) instead of pneumatic lithotripsy Use anti-retropulsion devices Inspect the whole pelvicalyceal system and the urinary tract after lithotripsy
Reposition or remove stent Reposition or remove stent Conservative management Submucosal collagen injection Use low-pressure irrigation Place a ureteral stent and postpone the intervention in case of prolonged poor vision Prolonged poor vision A A A A A A A A A A A A A	Difficult ureteral access of ureteroscope $(1-37\%)$	Place ureteral stent Only perform minimal dilation up to the size of the uretero- scope in prestented patients	Use small-sized ureteroscope Backload ureteroscope over working guidewire alongside safety guidewire
Conservative management Submucosal collagen injection Use low-pressure irrigation Place a ureteral stent and postpone the intervention in case of prolonged poor vision A A A A A Antipyretics Culture-based antibiotic therapy Analgesics Ureteral stenting C	Ureteral stent migration $(0.1-26.3\%)$	Reposition or remove stent	Chose a sufficiently long stent Place the proximal curl in the pelvis instead of the upper calyx Ensure to have appropriate distal curl in the bladder
Use low-pressure irrigation Place a ureteral stent and postpone the intervention in case of prolonged poor vision A A A A Antipyretics Culture-based antibiotic therapy A Analgesics Cureteral stenting C	Vesicoureteral reflux (0.07–20%)	Conservative management Submucosal collagen injection	Avoid dilatation of the ureterovesical junction
Antipyretics Culture-based antibiotic therapy Analgesics Ureteral stenting	Minor intraoperative bleeding (0.1–19.9%)	Use low-pressure irrigation Place a ureteral stent and postpone the intervention in case of prolonged poor vision	Avoid iatrogenic ureteral wall trauma using small caliber ureteroscopes and instruments Eroscopes and instruments Keep intrapelvic pressure as low as possible Avoid applying energy (laser, ultrasonic, electrohydraulic) on the mucosa Vaporize urothelial carcinoma of the upper tract with "non- contact technique" with a low energy, low frequency and long pulse duration for Ho:YAG laser or use a Tm:YAG laser Avoid active aspiration in the upper urinary tract Stop anticoagulants and antiplatelet agents if possible
Analgesics Ureteral stenting	Fever and urinary tract infection (0.2–15%)	Antipyretics Culture-based antibiotic therapy	Prevent predisposing factors like urinoma, subcapsular hema- toma or perforation
	Pain and renal colic (1.1–10.2%)	Analgesics Ureteral stenting	Avoid ureteral dilation Consider not placing a ureteral access sheath systematically Consider placing a ureteral stent
Bleeding following endoureterotomy or endopyelotomy (up to Tamponade bleeding with ureteral dilating balloon       Perform a control of the bleeding with ureteral dilating balloon         10%)       Urgent embolization or endovascular or open repair, depend- Air bubbles ing on the damaged vessels       Carefully characterial of the bleeding characterial of the blee	Bleeding following endoureterotomy or endopyelotomy (up to 10%)	Tamponade bleeding with ureteral dilating balloon Urgent embolization or endovascular or open repair, depend- ing on the damaged vessels	Perform a contrast-enhanced CT pre-operatively Air bubbles help in orientation Carefully chose the site of incision
Preterm labor (4.3–8.7%) Diagnose and treat underlying cause Approach th	Preterm labor (4.3–8.7%)	Diagnose and treat underlying cause	Approach the pregnant patient multidisciplinary

Complication (incidence %)		
	Management	Prevention
Instrument malfunction or breakage (0.1–5.3%) R	Remove and replace the instrument	Proper instrument selection and examination before use Adapted instruments to patient's anatomy Handle instruments with care during use, sterilization and stor- age Remove and replace the equipment immediately in case of mal- function or breakage of a lithotripsy probe, laser fiber, basket, forcens or interferonce
Urosepsis (0.1–4.3%) E In S C	Early recognition Immediate resuscitation Source control with appropriate drainage of the urinary tract Culture-based antibiotic therapy	Treat urinary tract infections prior to ureteroscopy Give preoperative antibiotic prophylaxis Send stones for culture
Ureteral stricture (0.1–3%) S B Ureteral stricture (0.1–3%) R R	Stricture dilation, incision or resection Buccal ureteroplasty Ureteral reimplantation Renal autotransplantation	Avoid direct mechanical trauma or perforation of the ureteral wall (e.g. guidewire, lithotripter, ureteroscope), foreign body (e.g. guidewire introducer), thermal injury (e.g. laser), ischemia (e.g. impacted stone) or infection (e.g. schistosomia- sis)
Ureteral obstruction or Steinstrasse (0.3–2.5%) U	Ureteral stenting or nephrostomy Ureteroscopy	Avoid mucosal edema or aggregation of stone fragments or blot clots in the ureter
Urinoma, perirenal abscess and subcapsular, perirenal and Eretroperitoneal hematoma (0.4–2.2%) R	Drainage Selective embolization Repair of the ruptured pelvicalyceal system	Avoid perforation of upper urinary tract Use atraumatic guidewires Use low-pressure irrigation Limit operative time
Ureteral avulsion (0.04–0.9%) IJ	Immediate repair (depending of the level: ureteral reimplanta- tion, ileal interposition or renal autotransplantation) Nephrostomy placement and delayed repair	Retrieve only small stone fragments under direct ureteroscopic vision Know maneuvers to treat stone basket entrapment Always be aware of the position of the ureteroscope within the confines of the collecting system Never apply force during ureteroscopy Adapt instruments to the anatomy of the upper urinary tract
Death (21 cases) N	N/A	Diagnose and treat urosepsis, multiple organ failure, arrhyth- mia, cardiac death and lung thromboembolism as early as possible
Cerebrovascular accident and transient ischemic attack (case In reports)	Image and treat patients with stroke-like symptoms urgently	Assess cardiovascular risk factors pre-operatively
Deep venous thrombosis (case reports)	Anticoagulation and compression stockings	Pharmacological or mechanical prophylaxis with low molecu- lar weight heparin or anti-embolism stockings in high-risk patients
Renal pseudoaneurysm, arteriovenous fistula, uretero-iliac E fistula (case reports)	Embolization or surgical intervention	Perform endopyelotomy, lithotripsy and ureteral access sheath placement with the rules of art
Forgotten ureteral stent (case reports) R	Remove or replace stent	Digital local or web-based stent registries

Table 3 (continued)

Intravascular ureteral stent migration (case reports) Extraction by endovascular or open access	
Post-obstructive diuresis (case reports) Ureteral stenting	Use fluoroscopy during stent placement Check post-operative kidney function Exclude post-operative hydronephrosis

Table 3 (continued)

Grade	Complication
0 (low)	No lesion found or only mucosal petechiae
1 (low)	Ureteral mucosal erosion without smooth muscle injury
2 (high)	Ureteral wall injury, including mucosa and smooth muscle, with adventitial preservation (periureteral fat not seen)
3 (high)	Ureteral wall injury, including mucosa and smooth muscle, with adventitial perforation (periureteral fat seen)
4 (high)	Total ureteral avulsion

To avoid this calamitous complication, retrieval of small stone fragments with a basket should always be performed under direct ureteroscopic vision. When a basket is impacted in the ureter, one should try to release the stones by opening the basket and pushing it gently against the ureteral wall. Tipless stone baskets disengage more easily after a stone is captured. A basket should be at least 4 mm larger than the targeted stone [25]. In case of a failing release, a laser fiber should be inserted parallel to the basket in the working channel to perform laser lithotripsy and reduction of the size of the stone fragments. Another option is to cut the wires of the basket or to dismantle the handle of the basket. To prevent ureteroscope breakage with a locked deflection mechanism, the urologist should always be aware of the position of the ureteroscope within the confines of the collecting system using fluoroscopy. Force should never be applied during ureteroscopy and instruments should always be adapted to the anatomy of the upper urinary tract and not vice versa.

**Ureteral wall injury** The lumen of a ureter is lined by urothelium that is underlined by the lamina propria, which contains blood vessels and lymphatics. These layers are surrounded by longitudinal and circular muscle layers that are responsible for ureteral peristalsis. The ureteral sheath or adventitia surrounds these muscular layers and contains the vascular plexus responsible for ureteral vascularization.

*Classification of ureteral wall injuries* Since the ureteral wall is extremely vulnerable to intraoperative injury and the latter was underreported in literature, Traxer et al. proposed an endoscopic classification of ureteral wall injuries after ureteral access sheath usage in 2013 (Table 4) [26]. In the same year, Schoentaler et al. proposed the post-ureteroscopic lesion scale (PULS), a simple grading system for the description of post-ureteroscopic lesions (Table 5) [27]. Urologists from different countries validated this scale with a video-based multicenter evaluation. Miernik et al. studied 148 prestented patients in which a 14/16 Fr ureteral access sheath was used. They found superficial lesions of the ureteral mucosa in 39.9% of patients, deeper mucosal

Table 5	Post-Ureteroscopic	Lesion	Scale	(PULS) [27]
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Grade	Complication			
0	No lesion (uncomplicated ureteroscopy)			
1	Superficial mucosal lesion and/or significant mucosal edema/hematoma			
2	Submucosal lesion			
3	Perforation with less than 50% partial transection			
4	More than 50% partial transection			
5	Complete transection			

ureteral lesions in 17.6% and a circumferential perforation in 4.7% [28]. Guzelburc et al. studied ureteral access sheath related ureteral injuries in 101 patients that were not prestented, using a 9.5/11.5 Fr or 12/14 Fr ureteral access sheath. According to PULS grading, they found grade 1 and 2 lesions in 38.6% and 2.9% of the patients, respectively. Injuries were found exclusively either in the proximal or distal ureter in 45.2% and 40.5% of the patients, respectively [29]. Following the article of Lildal et al. applying PULS, the incidence of severe ureteral access sheath-related lesions decreased when using smaller (10/12 Fr) ureteral access sheaths. The lowest incidence was seen when no access sheath was used during ureteroscopy [30].

Mucosal erosion, false passage and perforation The manipulations involved in ureteral mucosa erosion, false passage (or submucosal tunneling) and perforation are usually insertion of a guidewire, ureteral access sheath or ureteroscope, as well as lithotripsy, stone extraction and ureteral dilation. Reported incidences of mucosal erosions and false passages after ureteroscopy are between 0.13 and 9.5% [7–12, 14, 31–34]. Perforations occur between 0.3 and 7.4% of ureteroscopic procedures [2, 6–13, 31–33, 35, 36]. They may be associated with an extravasation of irrigation fluid or urine, with a reported incidence of up to 4% [31, 33, 37]. Schuster et al. reported that perforations are associated with longer operative time [35]. Traxer et al. reported incidence rates of ureteral injuries of 46.5% after ureteroscopy with a 12/14F ureteral access sheath [26]. Severe injury involving the smooth muscle layers was noticed in 13.3% of cases. The most important risk factor for severe ureteral access sheath related ureteral injury was the absence of prestenting before surgery, followed by male gender and increasing age. These high incidence rates may be explained by the fact that retrograde pyelogram and whole ureteral wall examination was routinely performed at the end of the procedure in the study by Traxer et al., and may not have been as accurate in former studies on ureteral wall injuries.

*Ureteral intussusception* Ureteral intussusception or invagination of a mucosal sleeve within the ureteral lumen can be encountered during ureteroscopy (supplementary figure) [38]. It can occur spontaneously due to the presence of a ureteral tumor or stone, or secondary to percutaneous endopyelotomy or ureteric catheter exchange. Only one case of ureteral intussusception has been directly related to diagnostic ureteroscopy in literature [39]. In that case, repeated ureteroscopy had been performed in a patient with repeatedly positive urine cytology.

Concerning localization of ureteral wall injuries, one may expect that the proximal ureter is most prone to avulsion since it has the thinnest wall structure. False passage occurs more likely at the distal ureter, with a medio-posterior entry point due to the bulky transitional layer, thick muscular backing and oblique insertion in the bladder. However, these hypothesis have yet to be confirmed [13].

*Extra-ureteral stone migration* Mucosal ureteral erosions, false passages and ureteral perforations may also be further complicated by submucosal or extra-ureteral stone migration. This was reported by Georgescu et al. in 12 out of 8150 (0.15%) semirigid ureteroscopies for ureteral stones. The fragments were left behind in 6 cases, while they were removed in 5 cases. In one case, an open surgery had been performed for stone fragment retrieval [9]. Ideally, every effort should be made to remove residual submucosal fragments to prevent chronic inflammation, which may result in later stricture formation.

*Treatment of ureteral injuries* Most authors suggest continuing the intervention when noticing small ureteral lesions and leaving a ureteral stent afterwards in a retrograde or antegrade way. In the case of documented extensive extravasation, a nephrostomy might represent an option to keep the patient dry. In massive extravasation, ureteral stent insertion and ureteroraphy should be considered [8, 9, 31, 32].

*Prevention of ureteral injuries* To prevent mucosal tears, submucosal trauma or more severe ureteral injuries, it is recommended to use small-sized instruments [40]. Instruments should always be adapted to the patient's anatomy and not vice versa. In the case of ureteral narrowing, it is recommended to place a ureteral stent and postpone the intervention for at least 1 week, allowing passive ureteral dilatation [41]. Baskets should be used with great care under direct vision and ureteral stones should be fragmented or dusted from the center towards the periphery to reduce the risk of accidental laser activation on the mucosa.

**Major bleeding** Endoureterotomy or endopyelotomy are feasible treatment modalities in case of ureteral or ureteropelvic junction stenosis. It can be performed by laser incision or using an Acucise balloon [42]. These interventions are particularly prone to major bleeding. Postinterventional transfusion rates up to 10% have been reported in historical larger series because of bleeding complications after cold knife or electrocautery incision [17]. In a more recent review of 50 patients undergoing Acucise balloon endopyelotomy, transfusion rate was 8% [43]. To avoid hemorrhagic compli-

cations, the site of laser incision should be carefully chosen to avoid injury to crossing vessels. In absence of anatomical variations, an endopyelotomy or proximal endoureterotomy of the left ureter is performed at a 5 o'clock incision (posterior and lateral) to avoid damage of crossing lower pole or gonadal vessels. At the iliac vessels crossing level, the incision should be performed at 12 o'clock position. Incision of the distal left ureter is performed at 10 o'clock position (anterior and medial) to avoid injury to the internal iliac vessels and at 12 o'clock for the intramural part. For the right ureter, incisions at the aforementioned levels are performed at 7, 12, 2, 12 o'clock, respectively. It is of utmost importance to perform a contrast-enhanced CT before these interventions to evaluate the anatomical relation between the ureter and the vessels to avoid subsequent damage during procedure. When the patient is lying in a supine position, air can be injected through the ureteroscope for orientation and to define the anterior part of the ureter (12 o'clock), especially when using a digital ureteroscope or non-pendulum camera. Aberrant anatomical vessels or incisions performed at wrong locations may result in life-threatening hemorrhagic complications [43–45]. Immediate placement of a ureteral dilating balloon can tamponade the bleeding until further intervention. Depending on the damaged vessels, treatment may consist of urgent embolization or endovascular or open repair.

**Instrument malfunction or breakage** Reported incidence of instrument malfunction or breakage varies between 0.1 and 5.3% [8, 9, 32, 33, 35, 36, 46]. The type and mechanism of breakage will determine the grade of associated complications. In most cases, problems like energy generator malfunction, dilation balloon breakage or loss of view have a limited influence on the patient.

Minor malfunctions of a flexible ureteroscope include deflection loss, working channel obstruction or optical fiber breakage with subsequent image loss [47]. This may occur during manipulation or after sterilization with a peracetic-based automatic sterilizing system [48].

A frequently mentioned argument in favor of ureteral access sheath use is that this may protect and reduce the strain on a flexible ureteroscope. To date, no study on ureteroscope durability evaluated this hypothesis and rather evoked the eventual risk of ureteroscope damage at the interface between the deflected tip and the tip of the ureteral access sheath [49–51].

Prevention of instrument breakage is first of all achieved by proper instrument selection and examination before use. Instruments should be adapted to patient anatomy with particular attention to the sizing of patients' ureters. Reusable instruments should be handled with care during use, sterilization and storage. In case of malfunction or breakage of a lithotripsy probe, laser fiber, basket, forceps or ureteroscope, every effort should be made to remove and replace the equipment, since a minor defect may easily escalate into a major complication.

#### **Minor complications**

**Difficult ureteral access** Primary insertion of a ureteroscope along the upper urinary tract is not possible in 1–37% of patients without prior dilation [52, 53]. Insertion failure is defined as the surgeon's decision to resign ureteroscope insertion due to high resistance to the retrograde progression of the ureteroscope along the urinary tract. A narrow ureteral orifice or intramural part of the ureter is the main cause of access failure. This can be resolved by placing a ureteral stent for one week allowing passive ureteral dilation. Prestenting is preferred since active ureteral dilation using a serial, coaxial or balloon dilator have a 5% associated risk of ureteral perforation [54]. Disadvantages of prestenting are the need for a secondary intervention and stent-related morbidity that result in reduced quality of life in up to 80% of patients [55].

Viers et al. evaluated the association between clinical and radiographic features and the need of prestenting because of the inability of the ureter to accommodate the ureteroscope or ureteral access sheath at the time of stone treatment [56]. After multivariable analysis, they found that prior ipsilateral ureteral stenting or prior ipsilateral surgery reduced the odds for prestenting by 89% and 85%, respectively. Further, less than one-half of proximal ureteral opacification on computed tomography urography in absence of an obstructing ureteral stone was independently associated with an increased risk of prestenting. In a multicentric study, ureteroscope's size has been associated with the risk of insertion failure [52]. When a flexible ureteroscope was backloaded over a guidewire, insertion failure rate ranged from 0.9 to 37% for 7.4 F and 9.0 F instruments, respectively. After prestenting, ureteroscope or ureteral access sheath insertion failure becomes negligible and the risk of severe injury decreased by up to sevenfold [26, 41, 56]. When resistance is still encountered after prestenting, a tumor, an impacted stone or a stricture should be excluded by performing a retrograde ureterography or engaging the ureter with the smallest available ureteroscope alongside a safety guidewire. As a last resort, minimal dilation up to the size of the ureteroscope can be performed, since performing ureteroscopy with resistance has a significant risk (22%) of ureteral stricture development [57, 58].

**Minor bleeding** Following the MCCS, Mandal et al. did not consider hematuria lasting less than 6 h as a complication of ureteroscopy [2]. Hematuria resolving spontaneously by 48 h was considered as "transient hematuria". "Persistent hematuria" was defined by its persistence for more than 48 h and when additional medication or interventions were needed [2]. Transient hematuria after ureteroscopy is reported with an incidence of 0.2% to 19.9%, while persistent hematuria is reported with an incidence of only 0.1-5.7% [2, 6-10, 12-14, 31-34, 36, 37]. Secondary complications such as urinary clot retention may arise in up to 1.6% of patients [2, 14, 59]. Blood transfusion may be required in up to 0.7% of ureteroscopic cases [2, 6, 13]. Seldom, endourological or angiographic techniques are necessary to treat live threatening bleeding as discussed above [34].

Intraoperative bleeding can occur during ureteroscopy following iatrogenic ureteral wall trauma, excessive intrarenal pressure or applying energy (laser, ultrasonic, electrohydraulic) on the mucosa. Iatrogenic trauma following inappropriate instrument usage may be prevented by gently using small-caliber ureteroscopes and instruments [40]. When vaporizing urothelial carcinoma of the upper tract, bleeding may be prevented with the "non-contact technique" with a low energy, low frequency and long pulse duration for Ho: YAG laser or using a Tm: YAG laser [60]. Bleeding may also occur as a consequence of forniceal rupture because of increased intrarenal pressure. It may be prevented by keeping the intrapelvic pressure as low as possible (below 50 mmHg) [61]. This may be achieved by applying low-pressure irrigation and using a ureteral access sheath that lowers irrigation pressures transmitted to the renal pelvis [62]. The impact on pressure decrease will depend on the outer diameter of ureteroscope and the inner diameter of the sheath [41]. Increasing irrigation pressure during bleeding may further worsen the situation. Minor bleeding usually stops spontaneously after a couple of minutes of low-pressure irrigation. In case of prolonged poor vision caused by bleeding, it may be advisable to place a ureteral stent and postpone the intervention.

Westerman et al. studied the effect of anticoagulation and antiplatelet agents on bleeding-related complications following ureteroscopy. They found that continuing antiplatelet therapy in patients on chronic therapy did not increase the risk of bleeding-related complications [63]. In contrast, they reported in another study that continuation or bridging of anticoagulants increased the risk of perioperative bleeding [64]. In a recent meta-analysis on complications following ureteroscopy with or without the holmium laser, Sharaf et al. found that patients on anticoagulants, on antiplatelet agents or with bleeding diatheses had an increases risk of bleeding-related complications, but not of total complications. They concluded that the increased risk of procedure-related bleeding was significant and that a patient-centered approach should be taken with regards to continuing these agents or not correcting bleeding diatheses [65].

#### Early postoperative complications

#### **Major complications**

**Death** Even though ureteroscopy is generally considered as a safe procedure, fatal events may occur. Most frequently reported cause of death is urosepsis [2, 6, 36, 66–68]. Other causes include multiple organ failure, arrhythmia, cardiac death and lung thromboembolism. These complications are frequently secondary to mistakenly safe interpretation and wrong management of severe situations such as treatment of infected urolithiasis without antibiotic coverage, bleeding or perirenal hematoma [6, 34, 35]. Chang et al. reported a gas embolism as a cause of death [69]. Possible explanatory mechanisms may be air bubbles generated during Ho:YAG laser lithotripsy, air pushed into the upper urinary tract during repeated ureteroscope extraction and insertion, air bubbles from irrigation, or peripheral venous catheter-related air embolism.

**Renal pseudoaneurysm** A renal pseudoaneurysm is an uncommon, but serious condition that is caused by an arterial perforation which is only surrounded by connective tissue and a hematoma. This vascular lesion may become life-threatening when the arterial pressure surpasses the tamponade effect of the surrounding tissue. It has been reported following endopyelotomy or lithotripsy with various energy sources (laser fragmentation and electrohydraulic energy), and with or without the use of a ureteral access sheath [70–75]. It may be asymptomatic or present as unexplained anemia, abdominal pain, fever or hematuria. A renal pseudoaneurysm is diagnosed with contrast enhanced computed tomography or renal angiography. Treatment consists of embolization or surgical intervention [70–75].

**Arteriovenous fistula** A few authors reported the development of intrarenal arteriovenous fistula after Ho:YAG or electrohydraulic lithotripsy. These fistulae are probably caused by damage of tissue and small interlobar arteries and veins during lithotripsy, leading to a connection between a high-pressure artery and a low-pressure vein. All cases presented with hematuria and were treated by selective embolization [67, 76–78].

**Uretero-iliac fistula** Uretero-iliac fistula is a very rare complication of ureteroscopy with only two documented cases in literature so far [79, 80]. The first case was secondary to dilation of a ureteral stenosis [79]. The second case occurred during laser-lithotripsy in spinal anesthesia, as the patient suddenly got nauseous and made a flexion of the spine to vomit. Because the ureteroscope was still inserted at the level of the iliac vessels, this caused a uretero-iliac fistula with rapid hypotension. This case could successfully

be treated by emergency open laparotomy and suture of the vessel injury.

Urinoma, perirenal abscess and subcapsular, perirenal and retroperitoneal hematoma Urinoma, perirenal abscess and subcapsular, perirenal and retroperitoneal hematoma after ureteroscopy have been reported by several authors, with an incidence up to 2.2% (supplementary figures) [2, 8, 14, 36, 67, 81–90]. These authors suggested that high intrarenal pressure during ureteroscopy and iatrogenic trauma of the pelvicalyceal system during instrumental manipulations are the most probable mechanisms that lead to these possibly life-threatening complications. Inappropriate ureteral stent placement has also been reported as a cause of renal parenchyma perforation and may be associated with the use of traumatic guidewires [91, 92]. Patients may present with lumbar pain, macroscopic hematuria, fever, septic or hypovolemic shock. Diagnosis is usually made by contrast-enhanced computed tomography or angiography. Depending on the clinical situation, patients can be treated conservatively, with a drain, by selective embolization or by drainage with repair of the ruptured pelvicalyceal system. Seldom, patients must be treated with a nephrectomy [8, 36, 67].

In a retrospective study on 2848 patients, Bai et al. reported 11 cases (0.4%) of subcapsular renal hematoma after Ho:YAG laser lithotripsy [81]. This complication was associated with larger stones (1.4 vs. 0.9 cm, P < 0.001), more severe ipsilateral hydronephrosis (P < 0.001), longer operation duration (41 vs. 33 min, P < 0.001), and higher perfusion pressure of hydraulic irrigation (176.8 vs. 170.2 mmHg, P < 0.001).

**Urosepsis** Urosepsis is defined as sepsis (life-threatening organ dysfunction caused by a dysregulated host response to infection) caused by a urogenital tract infection. It has an incidence between 0.1 and 4.3% after ureteroscopy [2, 6, 8, 10, 13, 14, 32, 34–36, 93–95]. In rare cases, this complication may become fatal, especially in cases of delayed initiation of supportive care, antibiotics and appropriate drainage or decompression of the urinary tract [67, 96].

Urosepsis after ureteroscopy mostly results from a urinary tract infection caused by *Escherichia coli*, Proteus, Pseudomonas species, Serratia and group B Streptococci, as well as Candida species [97–99]. Risk factors include recent urinary tract infection, infectious stones, prolonged preoperative stent dwelling time, chronic drains, immunocompromised status (e.g. post-transplantation, diabetes mellitus), elderly, female gender and anatomic abnormalities of the collecting system [94, 100–102]. The influence of the use of a ureteral access sheath on sepsis is debatable [41]. The Clinical Research Office of the Endourological Society (CROES) examined prospective data of 2239 patients that underwent ureteroscopy over 1 year. After analyzing their data, sepsis rate was 0.63% (14 out of 2239 patients). Sepsis occurred more frequently in the absence of a ureteral access sheath (0.94% vs. 0.47%) [103]. These findings support the assumption that a ureteral access sheath may decrease post-operative sepsis rates by decreasing intrapelvic pressure. Of note, the authors of that study did not record the reason why a sheath was used or not, which may have led to a selection bias.

Diagnosis relies on the recognition of symptoms associated with sepsis. Intraoperative stone culture may be more informative than preoperative urine culture [104]. Procalcitonin is a biomarker of a systemic response to infection. It accurately predicts the presence of bacteremia and bacterial load and may be a helpful biomarker to limit the use of blood cultures [105]. Treatment consists of early recognition, immediate resuscitation, source control with appropriate drainage of the urinary tract and culture-based antibiotic therapy.

Preventive measures include treating urinary tract infections prior to ureteroscopy, giving preoperative antibiotic prophylaxis [106–108] and sending stones for culture [104]. More studies are necessary to evaluate the possible influence of reusable versus disposable instruments and ureteroscopes on post-operative sepsis [109, 110].

**Fever and urinary tract infection** Fever is a known early complication following ureteroscopy, with an incidence varying from 0.2 to 15% [2, 6, 7, 13, 14, 31, 32, 34, 36, 37, 46, 59, 83, 95]. This wide range is explained by the fact that some authors report fever as an apart entity, while others include it under predisposing factors like urinary tract infection, urinoma, subcapsular hematoma, perforation or urosepsis. In the absence of underlying factors, it is treated conservatively with antipyretics.

Urinary tract infections following ureteroscopy also occur in 0.2–15% of cases [2, 6, 7, 13, 14, 31–37, 83, 108, 111]. Only in a minority of cases and when not treated appropriately, they may evolve to more morbid complications such as pyelonephritis and urosepsis.

Risk factors for infectious complications and fever include female gender, Crohn's and cardiovascular disease, ASA score of II or higher, preoperative bacteriuria, hydronephrosis, struvite stones, proximal ureteral stones, a high stone burden, and the presence of a urethral catheter, ureteral stent and percutaneous nephrostomy [111, 112]. Ureteral stent extraction strings seem not to add to the risk of infection [113, 114].

Preoperative antibiotic prophylaxis decreases the incidence of pyuria after ureteroscopy. However, it does not significantly reduce the rate of bacteriuria, postoperative urinary tract infection and fever [112, 115]. In spite of these data, EAU and AUA guidelines recommend a single preoperative dose of antibiotics. Additional postoperative antibiotics does not seem to decrease infection rates after ureteroscopic stone treatment [108].

**Ureteral obstruction and steinstrasse** Ureteral obstruction or Steinstrasse after ureteroscopy have an incidence between 0.3 and 2.5% [2, 6, 13, 31, 35, 36, 83, 93]. This can result from mucosal edema or aggregation of stone fragments or blot clots in the ureter. It is characterized by flank pain that can be relieved with ureteral stenting or nephrostomy in expectation of another ureteroscopy in case of residual fragments.

**Vesicoureteral reflux** Transitory vesicoureteral reflux can be noticed with indwelling ureteral stents. Vesicoureteral reflux can also be persistent as reported by Geavlete et al. after two out of 2735 ureteroscopies. They did not report the mechanism of this complication [8]. One may expect that this occurred after dilatation of the ureterovesical junction, which may cause reflux in up to 10% and 20% of cases when dilating up to 13.5 F and 24 F, respectively [116, 117]. Early vesicoureteral reflux after ureteroscopy is of low grade and temporary in most cases. In case of persistence, treatment consists of conservative management or submucosal collagen injection [8, 116].

**Pretern labor** Urolithiasis and renal colic during pregnancy may result in obstetric complications such as preterm labor. This is defined as regular uterine contractions that result in thinning and dilation of the cervix before 37 weeks of pregnancy. Uterine contractions measured by cardiotocography are significant when they occur three or more times in ten minutes at high intensity. This risk of this complication increases when the time to intervention is delayed [118].

Ureteral obstruction may be treated conservatively, by drainage via ureteral stenting or percutaneous nephrostomy. Considering the morbidity associated with ureteral stents and nephrostomies and because ureteral stents are prone to encrustation (gestational hyperuricosuria and hypercalciuria) and therefore require frequent replacement, primary ureteroscopy can be proposed in case of obstructive urolithiasis [119]. Until now, no prospective comparison of obstetric complications resulting from ureteroscopy versus stent placement has been performed. Buttice et al. reported preterm labor in 8.7% of 208 patients following ureteroscopy. All patients were in the second or third trimester of pregnancy [120]. Johnson et al. reported two obstetric complications after 46 ureteroscopic procedures (4.3%), including 1 preterm labor managed conservatively and one preterm labor resulting in preterm delivery [121]. They concluded that a multidisciplinary approach to the pregnant patient is recommended and with both fetal monitoring and obstetrical services available, especially in the third trimester when the risk of preterm labor is increased.

**Stone migration and residual fragments** Stone migration from the ureter to the pelvicalyceal system during ureteroscopy has a reported incidence between 0.1 and 7.4% [2, 7–10, 14, 32–34]. When residual fragments are larger than 4 mm, this is associated with increased stone growth, complications (59%) and reinterventions (38%) [122]. Stone migration may be reduced using low-pressure irrigation, applying laser lithotripsy instead of pneumatic lithotripsy, or using anti-retropulsion devices [123–125]. Residual fragments should be excluded by inspecting the whole pelvicalyceal system and the urinary tract after lithotripsy.

**Ureteral stent migration** Ureteral stents are produced with a memory of a pigtail or double-J shape to prevent migration. Nevertheless, ureteral stent migration has a reported incidence between 0.1 and 26.3% [2, 8, 9, 14, 32, 34, 36, 46, 93, 126]. Migration usually occurs upwards due to incorrect positioning, incorrect size selection or ureteral peristalsis. Treatment consists of repositioning or stent removal, which may implicate another intervention when migration occurs postoperatively. Preventive measures include choosing a sufficiently long stent, placing the proximal curl in the pelvis instead of the upper calyx, and the presence of an appropriate distal curl in the bladder [127].

Intravascular ureteral stent migration Several cases of intravascular ureteral stent migration have been reported so far [128–140]. In all cases, ureteral stents were mistakenly placed either directly in the inferior vena cava or through iliac veins towards the inferior vena cava. Most cases were diagnosed postoperatively and presented with persisting gross hematuria, thromboembolism, dyspnea, obstructive uropathy, or were asymptomatic. In two cases, the ureteral stent migrated up to the pulmonary artery [128, 133]. Most stents could be successfully extracted by endovascular access. Eventually, some cases required open surgical removal. Absence of intraoperative fluoroscopy was acknowledged by the authors as a possible risk factor. Other preventable risk factors include those discussed earlier relating to intraoperative ureteral wall disruption.

**Forgotten ureteral stent** Complications from forgotten ureteral stents seem to be time-related and are secondary to stent encrustation, fragmentation and obstruction [141]. They include infectious complications, obstructive uropathy and prolonged morbidity from lower urinary tract symptoms. Catastrophic complications such as renocolic fistula from perinephric abscess formation or even death have been reported [142, 143].

The largest prospective observational study to date included 68 cases presenting in a single institution with forgotten ureteral stents with a mean dwell time of 17 months [144]. Most patients presented with urinary tract infection (60%) and/or elevated creatinine levels (25%). A majority of all forgotten ureteral stents (62%) could not be removed by simple cystoscopy and needed a complex endourological intervention, including ureteroscopy, percutaneous nefrolitholapaxy or open surgery. In another study from an expert center, a majority of patients (98%) with forgotten ureteral stents could be managed endoscopically by ureteroscopy and Holmium:YAG laser (supplementary figure) [145].

To prevent such complications, patients with ureteral stents should be monitored closely by the means of digital local or web-based stent registries [146].

Stents should be removed or changed after a maximal dwell time recommended by manufacturers. Multiple authors suggest monitoring of patients with ureteral stents by the means of digital local of web-based stent registries [146].

**Deep venous thrombosis** Deep venous thrombosis is very rarely reported after ureteroscopy [147]. However, it is conceivable that patients are at increased risk during a long-lasting ureteroscopic procedure in lithotomy position. International guidelines on thromboprophylaxis recommend pharmacological or mechanical prophylaxis with low molecular weight heparin or anti-embolism stockings in high-risk patients until complete mobilization of the patient is achieved [148].

**Cerebrovascular accident and transient ischemic attack** Cerebrovascular accident and transient ischemic attack are severe complications that are rarely reported after ureteroscopy [6, 13, 34]. These authors did not mention if these vascular complications were associated with other complications or risk factors. Patients with stroke-like symptoms should be imaged urgently. Rapid and appropriate management are necessary to minimize the detrimental neurological effects.

#### Minor complications

**Pain and renal colic** Distension of the upper urinary tract provokes pain, due to stimulation of mechanoreceptors in the ureter and kidney [149]. Pain following ureteroscopy is usually located in the flank or lower abdomen. In most cases (incidence between 1.1 and 10.2%), it can be treated conservatively with analgesics [7, 13, 33, 35, 37, 46]. In up to 2.2% of patients following ureteroscopy, analgesics are insufficient in pain management and ureteral stenting is required [2, 8, 34].

Oğuz et al. prospectively investigated factors related to severe early postoperative pain after retrograde intrapelvic

surgery in 250 patients. They found that female gender, larger stone burden and ureteral access sheath time were correlated with severe pain. They found no association with side of surgery, stone location, pre-operative stenting, size of ureteral access sheath or post-operative stenting [150]. In another prospective trial, Kourambas et al. found that patients who required ureteral dilatation experienced more postoperative pain when dilation was performed with a ureteral balloon dilator compared to dilation with a ureteral access sheath [151].

**Urinary retention** Urinary retention following ureteroscopy has a reported incidence between 0.1 and 1.4% [32, 34, 35, 46, 83]. It is mainly seen in elderly male patients. Predisposing factors include bladder outlet obstruction or neurogenic bladder dysfunction. Treatment consists of temporary placement of a Foley catheter.

**Post-obstructive diuresis** Post-obstructive diuresis is a potentially lethal complication that can occur following relief of a prolonged urinary obstruction. Ibrahim et al. reported post-obstructive diuresis in two out of 148 patients. Both cases presented with an obstructed solitary kidney [32]. This potentially serious complication is classified as a grade I complication using the MCCS despite its important impact on hospital stay, management and costs of monitoring and laboratory investigations. Factors predicting post-obstructive diuresis include high serum creatinine, high serum bicarbonate and urinary retention on admission. Urgent drainage is necessary to reduce the risk of severe chronic renal failure [152].

**Transient serum creatinine elevation** Transient elevation of serum creatinine is frequently seen after ureteroscopy but seldom reported. Ibrahim et al. and Mandal et al. reported it in their prospective studies with an incidence rate of 1.4% and 1.6%, respectively [2, 32]. Since minor, self-limiting complications are rarely reported, its real incidence rate is probably underestimated.

**lleus** Elashry et al. reported post-operative ileus lasting more than one day in 22 out of 5133 cases (0.4%) [7]. Predictive factors of this rare complication are unknown.

**Urethral injury** Fuganti et al. are the sole authors that report one urethral injury in their retrospective series of 1235 semirigid ureteroscopies [11]. This complication is probably underreported. Prospective studies are necessary to evaluate the impact of bleeding and false passages in the urethra following ureteroscopy on the development of strictures.

**Ureteral stent discomfort** The CROES reported complications in 11,885 patients after ureteroscopy. From the 9669 patients that were stented, 112 (1.1%) reported ureteral stent discomfort. This is in contrast to other reports that report stent-related symptoms (e.g. flank pain, urgency, dysuria) in up to 88% of cases with the need of analgesics in over 70% of cases [55, 153, 154]. Stent-related symptoms and their associated costs feed the debate about obviating routine stenting after uncomplicated ureteroscopic stone removal [46, 155, 156]. Cases for which post-operative stenting may be recommended are patients with larger stone size, longer operation duration, solitary kidney and recurrent renal colic. Ureteral stent extraction strings does not seem to alter stentrelated symptoms [113]. Use of a ureteral access sheath does not routinely require post-operative stenting [36, 157].

#### Late postoperative complications

#### **Major complications**

**Ureteral stricture** Ureteral strictures occur in up to 3% of patients after ureteroscopy [6–8, 11, 13, 14, 36, 46]. The mechanism of stricture formation remains to be elucidated. Hypothetical mechanisms include direct mechanical trauma or perforation of the ureteral wall (e.g. guidewire, lithotripter, ureteroscope), foreign body (e.g. guidewire introducer), thermal injury (e.g. laser) or ischemia (e.g. impacted stone) leading to inflammatory processes in the ureteral wall [158–160]. Delvecchio et al. analyzed the long-term association between the use of a ureteral access sheath and ureteral stricture formation in 71 ureteroscopic procedures. They found only one stricture (at the ureteropelvic junction) after a mean follow-up of 332 days. They concluded that the use of a ureteral access sheath was not a contributing factor [161].

Kidney function deterioration, flank pain or hydronephrosis after ureteroscopy are reminiscent of stricture formation. Treatment should be initiated in time to prevent other complications such as infection or renal damage. Definitive treatment may consist of stricture dilation, incision, resection, buccal ureteroplasty, ureteral reimplantation or renal autotransplantation [7, 11, 46, 162, 163]. Based on a retrospective assessment of 114 patients with benign ureteral strictures with intact or compromised vascular supply, Richter et al. found that balloon dilation was effective (89%) in the management of short strictures with intact vascular supply. For a long ureteral stricture, ureteropelvic junction stenosis and a short ureteral stricture with compromised vascular supply, they recommended endoureterotomy with stenting [164]. Wolf et al. reported an 80% success rate of endoureterotomy of benign ureteral strictures [165]. In case of endourological treatment failure, open or laparoscopic surgical repair is required.

Based on the hypothetical mechanisms of stricture formation, preventive measures may consist of using miniaturized ureteroscopic armamentarium [7, 166, 167]. Also, impacted stones should be entirely removed, since chronic inflammation may lead to stone granuloma formation which in turn has been associated with stricture formation [168–170]. This also forms the rationale for authors recommending not to perform lithotripsy in the same session as endopyelotomy [171].

**Post-operative hydronephrosis** Authors rarely report ipsilateral hydronephrosis as a complication following ureteroscopy. Therefore, four groups evaluated the predictors of ipsilateral hydronephrosis with non-contrast enhanced CT or ultrasound following ureteroscopy during the last four years (Table 6) [157, 172–174]. Follow-up varied between 3 weeks and 6 months. Incidence rates of postoperative hydronephrosis varied between 15.1 and 32.1%. After multivariate analysis, independent predictors of postoperative hydronephrosis were prior ipsilateral ureteroscopy in three studies, impacted stones in two studies, and multiple stones, increasing stone diameter, increasing preoperative diameter of the hydronephrotic kidney, perioperative ureteral injury, longer operative duration and postoperative renal colic symptoms in one of these studies.

Sutherland et al. reported an incidence rate of silent obstruction of 1.9%. This prolonged obstruction may result in subsequent loss of kidney. Therefore, they performed a cost-analysis of routine postoperative imaging after ureteroscopy. They found routine postoperative imaging costeffective in preventing renal loss and its attendant morbidity [175]. When postoperative hydronephrosis is detected,

 Table 6
 Predictors of ipsilateral hydronephrosis [157, 172–174]

Authors	Patients	Imaging	Period	Hydrone- phrosis (%)	Predictors
Gokce et al. (2017)	455	СТ	>3 weeks	17.8	Prior ipsilateral ureteroscopy, multiple stones
Gokce et al. (2017)	116	CT or US	>3 weeks	27.6	Prior ipsilateral ureteroscopy, impacted stone, perioperative ureteral injury
Kim et al. (2016)	137	CT or US	6 months	32.1	Increasing preoperative hydronephrosis, impacted stone
Barbour et al. (2015)	324	CT or US	4-12 weeks	15.	Prior ipsilateral ureteroscopy, increasing stone diameter, longer operative duration, renal colic symptoms

future imaging should be based on these results, along with patient's risk for complications or stone recurrence.

# Overall risk factors for complications related to ureteroscopy

Sugihara et al. studied complications after ureteroscopic lithotripsy, based on a Japanese inpatient administrative claims database. They analyzed severe complications that occurred in 296 out of 12,372 patients (2.4%). After multivariate analysis, they found that severe complications following ureteroscopy were associated with longer operative duration (more than 90 min), lower hospital volume (less than 15 ureteroscopic procedures per year), female gender, older age (over 80 years old), Charlson Comorbidity Index more than 1, general anesthesia and emergent admission [68]. Daels et al. concluded from the CROES database that the risk of complications is the highest among elderly patients presenting with comorbidities (diabetes, cardiovascular disease, obesity, anticoagulants) [65].

In a prospective study of 120 patients, Mandal et al. reported that stones greater than 10 mm, impacted stones, midureteral stones (vs. lower ureteral stones) and surgeon experience (resident vs. consultant) were associated with complications following ureteroscopy for ureteral stones. They did not find an association with patient sex, stone laterality or lithotripter type [2]. As well, Maghsoudi et al. found no difference in complication rate comparing stone lithotripsy with Ho:YAG laser energy or pneumatic energy [123]. Schuster et al. found a higher complication rate for stones treated in the kidney compared to ureteral stones [35].

The finding that complications occur more frequently during long-lasting procedures and when performed by less experienced surgeons was also reported by other authors [31, 35, 176, 177]. However, it remains unclear whether complications happened due to prolonged surgery or that surgery lasted longer because of complications [2].

Atis et al. reported that a small ureteroscope can reduce the need for ureteral balloon dilation complications like mucosal injury and postoperative hematuria [40]. Another factor that seemed to increase complications is the presence of congenital renal abnormality (e.g. bifid pelvis, complete ureteral duplication, calyceal diverticulum, horseshoe kidney, pelvic ectopia, malrotation) [36].

In a retrospective study, Youssef et al. evaluated 69 patients that initially presented with urosepsis before ureteroscopy and matched paired them with 69 patients without prior urosepsis. In patients with prior urosepsis, they found higher complication rates (20% vs. 7%), longer hospital length of stay (2.5 days vs. 0.6 days) and longer courses of postoperative antibiotics (1.7 days vs. 0.4 days) following intervention [178]. This was not confirmed in a prospective study by Pietropaolo et al. that found only complications in 3 out of 76 patients (4%) that underwent elective ureteroscopy for ureteric stones with prior urosepsis and emergency drainage [179]. Similarly, Kanno et al. found in a retrospective study that patients treated by ureteroscopy with or without preoperative pyelonephritis had similar complication rates (10% vs. 12%) [180].

Huang et al. recently published a meta-analysis on the usefulness of a ureteral access sheath during ureteroscopy. Based on four studies, they found a higher incidence of post-operative complications with the use of a ureteral access sheath. Its use was not associated with intraoperative complications and hospitalization duration [181]. Therefore, inserting a ureteral access sheath should not be a systematic step when performing flexible ureteroscopy. The decision should be made on a patient-specific basis [41].

Rashahmadi et al. evaluated the effect of preoperative Tamsulosin (oral doses within 24 h prior to surgery) on complications of ureteroscopy in a prospective, double-blinded, randomized controlled trial. They found a significant risk reduction of ureteral wall injuries in favor of Tamsulosin (7%), compared to the control group (19%). Tamsulosin also allowed for significantly higher ability to access the upper urinary tract and perform the surgery (95% vs. 87%).

There is sufficient evidence that placing an indwelling stent after uncomplicated ureteroscopy is not decreasing post-operative complications. Moreover, they increase costs, hospital readmission rates and result in stent-related symptoms in terms of flank pain, frequency and dysuria, without influencing stone-free rate. This supports the practice of omitting a ureteral stent after an uncomplicated ureteroscopic procedure [156, 182–185].

Kumar et al. recently analyzed risk factors for readmission after ureteroscopy. The most common etiology for readmission was sepsis/fever (1.7%), followed by stent-related symptoms (0.7%). After bivariate analysis, risk factors for readmission included diabetes mellitus and ASA class greater than 2 [186].

## Discussion

Complications during and following ureteroscopy are not uncommon despite the enormous evolution of instruments in the ureteroscopic armamentarium during the last two decades. Ureteral stent discomfort, ureteral wall injury and stone migration are the most reported complications. Incidence rates on these and other complications vary extensively between the reviewed reports. This may be because many complications usually not require intervention and standardized reporting systems are seldom used. Even though minor complications occasionally require intervention, they increase the cost and duration of the intervention or hospitalization and may result in major complications if not recognized. Severe complications like urosepsis, multiorgan failure and death are rare but may be underreported as well with only 21 death cases reported worldwide to date for the latter [187]. This may give urologists an unwarranted sense of security when performing a ureteroscopy.

It is important that all sequelae associated with ureteroscopy are reported since minor complications like perioperative stone migration, Steinstrasse, ureteral stent migration or urinary obstruction increase the cost and duration of the intervention or hospitalization. As well, every urologist should be aware of possible complications of ureteroscopy to prevent and manage them and to put them in perspective to other treatment modalities like shock wave lithotripsy and percutaneous nephrolithotomy.

In contrast to many other types of surgery, ureteroscopic intervention can always be prematurely aborted. Since complications mostly occur unexpected, we support the presence of a safety guidewire during every ureteroscopy. This enables the possibility of placing a ureteral stent at any moment, to prevent further aggravation of the situation and to postpone the intervention. The safety guidewire can be considered as seat belt: it serves rarely but in case of an accident, nobody regrets to have it.

In conclusion, ureteroscopy seems to be associated with more complications than currently reported. To prevent these complications, every urologist performing ureteroscopy should be aware of all technical characteristics of the available instruments, with its according weaknesses and strengths. When encountering complications, the surgeon should be able to recognize and solve them to prevent devastating aggravation of the situation. Therefore, future randomized prospective studies using standardized systems for classifying complications are warranted to compare results among different studies, to conduct meta-analyses, inform surgeons and counsel patients correctly about possible risks.

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## **Compliance with ethical standards**

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Bhaskar Somani, Silvia Proietti, Moises Rodriguez-Socarras, Maria Rodríguez-Monsalve and Eugenio Ventimiglia declare that they have no conflict of interest.

**Research involving human participants and/or animals** This article does not contain any studies with human participants or animals performed by any of the authors.

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