ENDOUROLOGY (B SOMANI, SECTION EDITOR)



Correlation of Operative Time with Outcomes of Ureteroscopy and Stone Treatment: a Systematic Review of Literature

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Abstract

Purpose of Review To present the latest evidence related to the impact of increased operative times in retrograde intrarenal surgery and identify possible important factors that can facilitate ureteroscopy procedures.

Recent Findings Ureteroscopy constitutes the mainstay treatment of renal stones and is characterized by a huge variation in techniques and instrumentation. It has been suggested that increased operative times can mitigate the outcomes of the procedures by increasing complication rates. Nevertheless, little is known about the time limits, above which complications are likely to occur. Furthermore, complication rates in different procedure durations have not yet been assessed.

Summary Prolonged operative times are linked to increased complication rates in ureteroscopy. Stone complexity, patient risk factors, surgeon experience, bilateral surgery, and instrumentation constitute important factors that can hamper or facilitate a procedure and should be taken into account beforehand. Keeping procedural times below 90 min can dissuade potential predicaments and achieve improved stone-free rates.

Keywords Operative time · Ureteroscopy · Retrograde intrarenal surgery · Procedure time · Stone · Complication

Introduction

Ureteroscopy (URS) is a safe and effective method of treating ureteric and renal stones, and over the past two decades, the number of URS procedures performed has increased by 252% [1, 2]. The increase in kidney stone disease (KSD) has been

This article is part of the *Topical Collection on Endourology*

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Published online: 24 March 2020

due to a combination of factors including global warming, more incidental stones diagnosed on CT scan, and metabolic syndrome [3, 4, 5•]. The European Association of Urologists (EAU) guidelines have an algorithm for the treatment of stone disease to aid clinicians in their decision-making for the choice of surgical option [6].

Ureteroscopy is now being used for a wide variety of treatment conditions, and its role has expanded [6–9]. As such, endourologists have audited the outcomes in an attempt to lower their complication rates. A number of factors make surgery more challenging and can have an impact on clinical outcomes. These include stone size and location, multiplicity, patient comorbidities, and surgeon experience. All these factors have an effect on the operative time which in turn can influence patient outcome [10–20].

Whilst the operating time is affected by patient and stonerelated factors, it is also influenced by other factors such as the presence of preoperative stent, use of a ureteral access sheath (UAS), surgery for bilateral stones, the type of ureteroscope used, use of fluoroscopy, and surgeon experience [13, 16, 17, 21–28]. Previously other studies in joint replacement surgeries, laparoscopic procedures, and percutaneous nephrolithotomy (PCNL) showed better outcomes with reduced operative time duration [29–31]. We present the results of our systematic review looking at the correlation of operative times with the outcomes of ureteroscopy and stone treatment.

Methods

Evidence Acquisition

Inclusion Criteria

- 1. Studies which recorded operative times of ureteroscopy and stone treatment and correlated it with complications of the procedure
- 2. Articles written in English language

Exclusion

- 1. Paediatric studies
- 2. Animal or laboratory studies
- 3. Case reports or review articles
- 4. Older studies using the same data as a more recent study where the longest follow-up was included

The systematic review was performed according to the Cochrane review guidelines [32] and in accordance with the Preferred Reporting Items for Systematic Reviews and Metaanalyses (PRISMA) checklist [33].

The search strategy was conducted to find relevant studies from the Medline, EMBASE, Cochrane Library, CINAHL, Clinicaltrials.gov, and Google Scholar. The search terms included 'ureteroscopy', 'URS', 'Retrograde intrarenal surgery', 'RIRS', 'endoscopic', 'operative time', 'procedure time', 'laser', 'stone', 'calculi', 'mortality', 'complication', and 'death'. Boolean operators (AND, OR) were used to refine the search. Two experienced reviewers identified all studies (JL, LW). All studies that appeared to fit the inclusion criteria were included for full review. Each reviewer independently selected studies for inclusion in the review, and discrepancies were resolved by consensus with the senior author (BKS).

The search was limited to English language articles between 1999 and 2019; a cut-off of 10 patients was set per study to include centres with the minimum relevant endourological experience, and where more than one article was related to the same study, the longest follow-up was included.

Data Extraction and Analysis

Data was extracted for year of publication, study type, stonefree rate (SFR), sample size, age, stone size, complications, and operative time. Data was collated using Microsoft Excel (version 12.2.4).

Results

After initial screening of 680 articles, 197 abstracts were assessed for eligibility. Eventually, 8 studies met our inclusion criteria and were then included in our final analysis. Full details of the search results are depicted in the PRISMA diagram in Fig. 1.

Overall there were 32,283 patients included in the review (Table 1). All but one study [21–27] provided the mean ages of their patients, with their cumulative mean age being 50.1 years. There was a male to female predominance with 20,518 males to 11,730 females. The majority of studies provided stone size and location details [21–24, 26]. Two studies focused solely on renal stones [22, 23]. Three groups presented mean stone volumes (161.3–934.6 mm³) [22, 23, 26], two mean maximal stone diameters (7–9.3 mm; range 2.3–22 mm) [21, 24], and three did not present any information about stone size [25, 27, 28].

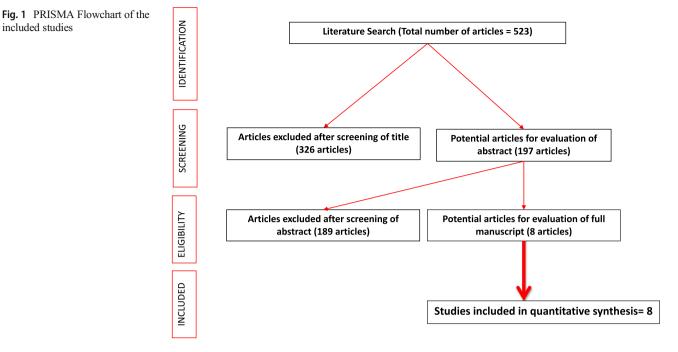
Stone-free rates were recorded in five studies [21, 22, 24, 26, 27] with an average SFR of 84%. Only three studies explained their method for determining SFR. Ozgor et al. determined SFR by repeating an abdominal CT in 1–3 months to ensure it was absent of residual fragments [26]. Knipper et al. assessed SFR with a renal ultrasound post-operatively on day one to determine the absence of hydronephrosis and/or residual stones, whereas Elashery et al. performed a plain X-ray immediately post-operatively [21, 24].

Half of the included studies categorized patients into groups depending on whether they had encountered operative complications [22, 25–27]. Their average operative time in patients who had encountered complications was 64.9 min versus 48.7 min in those without complications. All but one study [23] identified a significant link between operative time and complication rates (p = < 0.001). Sugihara et al. [28] classified the operative times into seven categories; they found that with increasing operative times, complication rates increased. Their maximum operative time at > 210 min correlated with a threefold increase in complication rates compared to the category with operative time < 59 min.

Discussion

Eight studies we identified primarily investigated operative times in URS and correlated it to complication rates [21-28]. With a high statistical significance and large sample sizes, these studies unanimously concur that lower operative times positively correlate with lower complication rates.

Whilst URS is well known to be a safe and effective way of treating renal and ureteral stones, longer operative times are associated with an increased risk of fever, bleeding, and ureteral perforation [17, 27]. This could be explained by larger stone volume and complex stones [34] demanding a more included studies



difficult and lengthy procedures [35]. Ito et al. examined operative times of 407 procedures, reviewing the total operative time and subdividing this into times before and after fragmentation [23]. The pre-fragmentation time was affected by the time it took to find the stone and thus wasn't easily predictable. The post-fragmentation time could be easily foreseen based upon the stone volume, density, absence of pre-stenting, and operator experience. The predictability of complex procedures could lead us to modify other factors that influence operative times and therefore has a direct impact upon our clinical outcomes and practice. Ozgor et al. also aimed to determine predictive factors that may reduce complication rates in URS. They reviewed 463 procedures over a 4-year period and found that operative time > 60min was positively associated with infectious complications following URS [26].

Moses et al. looked specifically at unplanned returns to hospital post-URS. Those with an operative time of > 120 min were 18 times more likely to have an unplanned return to the hospital. The majority of these were due to infection [25]. They discuss how this could be preventable by more individualized antibiotic prophylaxis and post-operative antibiotic coverage.

Somani et al. [27] reviewed all post-op complications and reviewed trends. In the CROES global study, of 11,885 patients, 874 (7.3%) encountered a complication. Those with complications on average had a longer operative time at 50 min (range, 33–75 min) compared with 40 min (range, 25-60 min) for those without a complication. It also highlighted that patients with complications were more likely to have had a preoperative stent and were performed in a low-volume centre. Surgeon volume and experience, therefore, seem to be an important factor in influencing operative time and complication rates.

Knipper et al. analysed the data of 2010 patients who had undergone a URS for stone treatment and stratified them into those with complications versus those without complications and found a statistically significant correlation (p = < 0.001)between operative time and complications [24]. Those without complications had a mean operative time of 34 min (range, 20-60 min) compared to 45 min (range, 25-76 min) for those who had a complication. However, their results were not statistically significant, and they found the correlation between operative time and the occurrence of complications very weak, thus concluding that URS can be considered a safe and effective procedure even in the context of a long procedural time.

Fan et al. retrospectively reviewed 227 patients undergoing URS with holmium laser and similarly found that operative duration was found to be closely associated with the complexity of the stone, difficult anatomy, and technical experience. Infective complication rates were higher in procedures over 90 min (p = 0.026) [22]. Elashery et al. analysed the difference in their complication rates over a total of 15 years [21]. Unsurprisingly over this time period, operative time reduced from a mean of 75 down to 36.5 min, and complication rates reduced synchronously (p = < 0.001) reflecting surgical volume and experience. Finally, Sugihara et al. reviewed a large sample size of 12,372 patients undergoing URS [17]. Of these, 2.39% suffered adverse events post-operatively. These patients had increasing complication rates with each 30-min increase in operative duration, which was statistically significant over 120 min (p = < 0.001).

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	Comments	Statistically significant increase in operative times with increase in stone volume ($p = < 0.001$) and reduction in operator experience ($p = < 0.001$) Operative time did not impact post-operative readmission rate	Found statistically significant increase in unplanned return to the hospital rates in patients who had operating times > 120 min(< 0.001)	Patients who experience intra-/post-operative complications on average had at least a 10-min longer operation (50 (33–75) vs 40 (25–60))	Longer operative times were significantly associated with infective complications (65.3 vs 47.8 min $p = < 0.001$)	Longer operative times were significantly associated with complications (34 (20-60) vs 45 min (25-76) p = < 0.001)	Longer operative times were significantly associated with complication races (99.42 min \pm 19.08 vs 73.37 min \pm 19.37 p = 0.000 (Mam-Whiney U test)	Positive correlation found between increasing operative time and adverse post-operative events. ($p = < 0.001$)
	SFR			85.6%	85.3% - without complications 77.5% - with complications	85.4%	75.3%	
	Complication rate (%)	I	3.4%	7.4%	14.9%	14.3%	8%	≤59 - 1.25% 60-89 - 1.99% 90-119 - 2.25% 120-149 - 3.22% 150-149 - 180-209 - 4.46% 150-06.15% Overall 2.39%
	Operative time (min)	74.0 ± 32.0	No UR UR >120 min 32.6% 89.5%	WC:50 (33-75) WOC: 40 (25-60)	WIC: 65.3 ±20.9 WOIC: 47.8 ±21.2	Overall – 35 min (interquartile range (IQR) 20–61) WC: 45 min (IQR 25–76) WO2: 34 min (IOR 20–60)	WIC: 99.42 ± 19.08 WOIC: 73.37 ± 19.37	\leq 59 - 3044 (24.60%) 60-89 - 3422 (27.66%) 90-119 - 2446 (19.77%) 120-149 - 1614 (13.05%) 150-179 - 861 (6.96%) 150-209 - 448 (3.62%) \geq 210 - 537 (4.34%)
				WC WOC 209 (62.9) 8068 (73.4) 550 (23.9) 1597 (14.5) 83 (9.5) 975 (8.9)	WIC WOIC 29 1 29 7 172 9 79 5 13 0 142 9			
	Stone location	Renal: 100%		W Ureteric 20 stones 55 Renal stones 55 Combined 83 procedure			Renal: 100%	
d to outcomes	Stone size	OT < 90 min: 425.1 ± 554.9 mm ³ OT > 90 min: 934.6 ± 630.0 mm ³		1	WIC: 161.3 ± 96.6 mm ³ WOIC: 182.4 ± 152.0 mm ³	7 (5–10)mm	WJC: 206 ±43 mm ³ WOIC: 166 ±5 mm ³	
imes correlate	M:F	129:94	302:248	WC: 556:317 WOC: 7145:3842	WIC: 16:15 WOIC: 257:206	1370:640	118:109	7918:4454
Studies looking at operative times correlated to outcomes	Age	OT < 90 min: 61.6 ± 12.7 OT > 90 min: 60.0 ± 14.0	56.8 (± 14.8)	WC: 51.7 WOC: 48.4	WIC: 34.8± 14.3 WOIC: 44.7±15.2	52 (41–64)	WIC: 51.4±15.2 WOIC: 48.2±14.2	$\leq 59 - 5902 \\ (47.7\%) \\ (60-69 - 33.30) \\ (26.92\%) \\ 70-79 - 23.42 \\ (18.93\%) \\ \geq 80 - 798 \\ (6.45\%) \end{cases}$
tudies loo	No. of patients	233	550	11,885	494	2010	227	12,372
Table 1 S	Paper	Ito et al. [23]	Moses et al. [25]	Somani et al. [27]	Ozgor et al. [26]	Knipper et al. [24]	Fan et al. [22]	Sugihara et al. [28]

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Table 1 (continued)	ontinued)									
Paper No. of Age patients	No. of patients	Age	M:F	Stone size	Stone location	Operative time (min)	Complication SFR rate (%)	SFR	Comments	огог кер
Elashery et al. [21]	4512	41.9 (11.3; 17–71) 2707:1805 9.3 (2	2707:1805	9.3 (2.3; 4–22)min	Distal Ureteric 100%	43 (25–120)	Intraoperative complication rate – 6.67% Post-operative complication rate – 9.9%	94.6%	Significant association of major intraoperative complications with increased operative duration (p = < 0.001)	(2020) 21:17

WC with complications, WOC without complications, UR unplanned return to hospital, WIC with infectious complications, WOIC without infectious complications

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The Role of Increased Intrarenal Pressures (IRPs)

In pigs, renal cellular injury becomes evident within 1 h at IRPs of 20-cm H_2O or greater [36]. Especially during upper tract endourological procedures, prolonged procedure times, in combination with IRPs higher than 30 cm H_2O , have been linked to increased complication rates [37]. Of note, during URS, approximately 1 mL of irrigation fluid is absorbed per minute [38].

Operative Times Related to Endourological Interventions

Endourologists attempt to find new tools and techniques to reduce procedural times and thereby facilitate URS and reduce complications (Table 2).

Ureteral Access Sheath

The use of a hydrophilic-coated ureteral access sheath allows easy, multiple access to the ureter. They improve vision by establishing a continuous outflow and decreasing intrarenal pressure and therefore have been said to reduce operative time [41, 42]. In three studies reviewed, the access sheath reduced operative times but did not affect complication rates. However, these conclusions were not statistically significant. Conversely, a recent study shows higher operative time with the use of access sheath although no statistical difference in outcomes was noted [43]. The differences could be partly accounted for by the use of access sheath in patients with larger or more complex renal stones.

Pre-stenting

Many studies have looked into the role of pre-stenting before URS [11, 14]. Stents are most commonly placed if the patient has a compromised renal function, intractable pain, or obstructed infected kidneys; however, some institutions have routinely pre-stented patients prior to URS. Similar to the UAS, they found that pre-stenting improves the stone-free rate and intraoperative complications [27]. In our review, Lumma et al. found that pre-stenting actually increased the length of the operation by 4 min yet made no difference to the complication rate [14]. Chen et al. also found the operative time to be shorter in patients who were pre-stented, on average by 15 min, yet no significant difference in complications [11].

Bilateral Surgery

Bilateral URS can be an option to treat bilateral urolithiasis, especially in high-volume centres [44]. It allows simultaneous URS procedures rather than being staged, as the later increases the overall cumulative procedural time. It not only reduces the

Table 2 Studies lo	Studies looking at interventions which reduce operative times	ich reduce operative times						
Paper	Journal	Intervention	Total no. of patients	Study type	Overall mean stone size (mm)	Stone location	Op time (min)	Complication rate
Pradere et al. [16]	European Urology Sumulements	Access sheath	400	Retrospective	17.4 vs 16.4	Ι	$63 \pm 29 \text{ vs } 85 \pm 34$	12 vs 9%
Kourambas et al. [13]	The Journal of Urology		59	Prospective	13.7 vs 10.1	Renal: 23 Ureteral: 28 Renal, ureteral: 2	43 vs 53.5	Decrease in post-operative symptoms in patients who underwent access sheath vs balloon dilatation
Schuster et al. [17]	Schuster et al. [17] The Journal of Urology		322	Prospective	8±4	Renal: 108 Upper ureteral: 95 Lower ureteral: 119		
Chen et al. [11]	Urologia Internationalis	Pre-stenting	199	Retrospective/ prospective	14	Renal: 86 Proximal ureter: 64 Multinle: 49	$30.553 \pm 8.9645 \text{ vs}$ 45.969 ± 19.4732	3.5 vs 1%
Lumma et al. [14]	Lumma et al. [14] World Journal of Urology		550	Retrospective	5.3	Renal pelvis: 103 Proximal ureter: 70 Mid ureter: 81 Distal ureter: 204 Multinler 97	38.4 vs 43.3	3.1 vs 3.5%
Alkan et al. [10]	Central European Journal of Urology	Bilateral surgery	06	Retrospective	ı	Ureter: 45 Multiple: 45	$61.9 \pm 3.4 \text{ vs } 29.4 \pm 2.2$	17.8 vs 15.5%
Galal et al. [12]	International Brazilian Journal of Urology	Rigid vs flexi URS	135	Retrospective	13.5 vs 12.9	Proximal ureter: 135	$40.9\pm16.4\ vs\ 48.4\pm13.8$	No statistical significance in complication rates
Wolff et al. [20]	Urolithiasis	Increased surgeon experience	307	Retrospective	6	Renal: 117 Ureter: 188 Multinle: 68	36 (24–56) vs 30 (20–49)	14.5 vs 9.5%
Usawachintachit M et al. [19]	Journal of Endourology	Single-use flexible ureteroscope (LithoVue)	142	Prospective	15.2 ± 10.7		$54.1 \pm 25.7 \text{ vs} 64.5 \pm 37.0$ $5.4 \text{ vs} 18\%$	5.4 vs 18%
Singh et al. [18]	Urology Annals	Fluoroscopy	82	Prospective	41.75 ± 13.44	Upper ureter: 11 Middle ureter: 19 Lower ureter: 50	43.90 ± 12.99 vs 45.61 ± 11.62	4 vs 3.6%
Manzo et al. [15]	Arab Journal of Urology		100	Retrospective	78.5		94.33 vs 98.29	24.2 vs 10.4%
Somani et al. [39]	Urology	Digital versus conventional flexible URS	118	Prospective	12.8 vs 12 mm	I	$44.5 \pm 14.9 \text{ vs } 53.8 \pm 15.2$	0.9 vs 1%
Humphreys [40]	J Urol	Dusting vs Fragmentation	159	Prospective	96.1 vs 63.3 mm ²	I	35.9±17.8 vs 67.4±53.3 No difference	No difference

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combined procedural time but could be relevant for the patient's quality of life and have huge financial savings to all healthcare systems. Nonetheless, Alkan et al. found little difference in complication rates when treating bilateral upper tract stones [10].

Increased Surgeon Experience

It may seem intuitive for increased surgeon experience correlating with a decreased operative time; however, there is limited evidence to suggest that this decreased complication rates [45, 46]. Wolff et al. found that specialist urologists had a lower operative time and complication rate; however, neither of these were statistically significant [20]. However, other studies have shown that post-operative complications can be predicted based upon stone volume, density, absence of prestenting, and operator experience [23].

It is therefore prudent that surgical procedures are vetted beforehand so that the more complicated procedures can be identified and performed by a surgeon of appropriate experience.

Single-Use Flexible Ureteroscopes

One study in our systematic review has looked into whether single-use ureteroscopes (LithoVue) are superior to reusable scopes. Usawachintachit M et al. found that single-use ureteroscopes correlated with almost a 15-min reduction in operative time [19]. The paper did not specify how LithoVue reduced operative time; however, both groups had similar complication rates.

Use of Fluoroscopy

The use of fluoroscopy is a standard aspect of all URS procedures; however, this exposes the patient and theatre staff to radiation. Two studies looked into whether ultrasound-guided URS with holmium laser lithotripsy can achieve the same results as fluoroscopy [15, 18]. Despite the longer operative times associated with ultrasound-guided URS, complication rates between them were not significantly different, and thus the authors recommended clinicians to consider reducing radiation dosage with URS.

Digital Versus Fibreoptic Ureteroscope

The use of digital flexible ureteroscope was shown to reduce the operative time compared to fibreoptic conventional ureteroscope [39].

Dusting Versus Fragmentation

When comparing dusting with fragmentation, the former was noted to reduce the operative time significantly $[40\bullet]$. Similarly, dusting and pop-dusting seem to be the new benchmark for treating large or multiple stones in a single setting without the need for a secondary procedure in most cases [47].

Strengths, Limitations, and Areas of Future Research

Operative time is positively associated with complication rates. The fewest complications appear to happen with procedural time under an hour; however, this might be biased towards straightforward URS procedures. Conversely, difficult or larger stones would have a higher risk of complication and also need longer procedural time. Hence, procedural time itself may not be the sole cause of increased complication rates. Based on our data, we would recommend limiting procedural time to under 90 min to reduce infectious complications and unplanned returns to the hospital. In difficult cases, a planned second-look URS might be necessary, and the patients need to be counselled accordingly.

Our review is based on published data which always has a publication bias attached to it. Future work should include a focus on the cost and quality of life of these patients [48•, 49•, 50•]. With new thulium laser and smaller scopes promising to reduce the operative times further, the landscape of URS will change further and lead to a wider uptake and use in difficult patients [51, 52•].

Conclusion

Longer procedural time seems to be associated with a higher risk of post-ureteroscopy complications. The use of ureteral access sheath, preoperative stent, and surgeon experience all influence procedural times. The size and complexity of stone and patient risk factors also need to be understood and stratified for planning ureteroscopy, patient counselling, and shared decision-making. Ultimately the principle of 'ALARA - as low as reasonably achievable' and keeping the procedural time as short as possible would lower complication rates and seem to be a good strategy provided the SFR is not compromised.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict(s) of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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