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ORIGINAL PAPER



# **Emergent versus delayed lithotripsy for obstructing ureteral stones: a cumulative analysis of comparative studies**

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#### Abstract

*Objective* To analyze the current evidence on the use of ureteroscopy (URS) and extracorporeal shock wave litho-tripsy (ESWL) for the management of obstructing ureteral stones in emergent setting.

*Methods* A systematic literature review was performed up to June 2016 using Pubmed and Ovid databases to identify pertinent studies. The PRISMA criteria were followed for article selection. Separate searches were done using a combinations of several search terms: "laser lithotripsy", "ureteroscopy", "extracorporeal shock wave lithotripsy", "ESWL", "rapid", "immediate", "early", "delayed", "late", "ureteral stones", "kidney stones", "renal stones". Only titles related to emergent/rapid/immediate/early (as viably defined in each study) versus delayed/late treatment of ureteral stones with either URS and/or ESWL were considered for screening. Demographics and operative outcomes were compared between emergent and delayed lithotripsy.

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RevMan review manager software was used to perform data analysis.

*Results* Four studies comparing emergent (n=526) versus delayed (n=987) URS and six studies comparing emergent (n=356) versus delayed (n=355) SWL were included in the analysis. Emergent URS did not show any significant difference in terms of stone-free rate (91.2 versus 90.9%; OR 1.04; CI 0.71, 1.52; p=0.84), complication rate (8.7% for emergent versus 11.5% for delayed; OR 0.94; CI 0.65, 1.36; p=0.74) and need for auxiliary procedures (OR 0.85; CI 0.42, 1.7; p=0.85) when compared to delayed URS. Emergent ESWL was associated with a higher likelihood of stone free status (OR 2.2; CI 1.55, 3.17; p<0.001) and a lower likelihood of need for auxiliary maneuvers (OR 0.49; CI 0.33, 0.72; p<0.001) than the delayed procedure. No differences in complication rates were noticed between the emergent and delayed ESWL (p=0.37).

*Conclusions* Emergent lithotripsy, either ureteroscopic or extracorporeal, can be offered as an effective and safe treatment for patients with symptomatic ureteral stone. If amenable to ESWL, based on stone and patient characteristics, an emergent approach should be strongly considered. Ureteroscopy in the emergent setting is mostly reserved for distally located stones. The implementation of these therapeutic approaches is likely to be dictated by their availability.

## Introduction

Ureteral stones represent one of the most prevalent urologic disorders, and they can often cause ureteral obstruction leading to renal colic [1]. The aim of emergency treatment in patients with acute renal colic is to provide symptomatic relief, unless there are indications for immediate intervention, such as renal function impairment, and signs of urinary tract infections or sepsis [2]. Traditionally, when conservative drug therapy is not able to manage pain, the placement of a ureteral stent or nephrostomy is mandated, with no clear advantage of one over the other. Then, management of the ureteral stone is usually delayed, with options including medical expulsive therapy, extracorporeal shockwave lithotripsy (ESWL), and ureteroscopy (URS) [3]. Stone size, degree of obstruction, technical facilities, surgeon and patient preference, comorbidities and possible complications are factors that should be considered in the treatment choice [4]. URS for ureteral stones seems to be associated with a greater stone free rate and less need for ancillary adjunctive procedures, but higher complication rates and longer hospital stay when compared to ESWL [5].

Recently, both ESWL and URS have been proposed for emergent treatment of ureteral stones, as they can provide both stone disintegration and relief from obstruction in a single stage. Such early intervention may decrease the cost of care, anesthesia risk, duration of stone-related morbidity and symptoms, and ultimately translate into improved outcomes. In addition, evidence suggests that delayed relief of ureteral obstruction can translate into long-term development of renal damage [6].

Urgent ESWL was first suggested by Joshi et al. who found this to be superior to insertion of a double J stent or nephrostomy tube [7]. Since then, few other series have been published, and a cumulative analysis of over 500 cases reported in 2012 confirmed that immediate SWL for a stone-induced acute renal colic results to be a safe treatment with a high success rate [8]. Improvements in endoscopic technologies and techniques have facilitated ureteroscopic management of stones over the past decade [9]. Osorio et al. first reported a series of emergent URS for obstructive ureteral stones [10], and a cumulative analysis of over 600 cases confirmed that the procedure is safe and effective [11].

Nevertheless, the role of emergency procedures for ureteral stones treatment remains to be defined, and definitive recommendations and guidelines regarding their implementation are lacking. A recent retrospective analysis carried out on a wide database including more than 10,000 patients presenting with renal colic clearly demonstrated that early treatment is associated with a reduced mortality (0.16 versus 0.47%; p=0.002) when compared to delayed intervention [12].

The aim of this study was to systematically analyze the available evidence regarding the use of ESWL and URS as first line therapy for ureteral stones in the emergency setting.

## Materials and methods

## Search strategy

A systematic literature review was performed up to June 2016 using multiple search engines (PubMed, Ovid, and Scopus) to identify studies examining the outcomes of emergent versus delayed treatment—with either ESWL or URS—of obstructing ureteral stones.

Separate searches were done by two authors using both diagnosis (ureteral stones, kidney stones, renal stones) and intervention terms (laser lithotripsy, ureteroscopy, extracorporeal shock wave lithotripsy, ESWL, rapid, immediate, early, delayed, late). In case of disagreement, discrepancies were resolved by discussion with the senior author.

## Inclusion criteria and study eligibility

Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) criteria were used for article selection (http://www.prisma-statement.org) (Fig. 1). Only titles related to emergent/rapid/immediate/early (as viably defined in each study) versus delayed/late treatment of ureteral stones with either URS and/or ESWL were considered for further screening. Searches excluded non-comparative (single arm) studies, publications on pediatric population, and articles not written in English. Studies not having primary data (i.e. reviews, commentaries, letters) were also excluded but examined to ensure relevant citations had been included. References of included studies were manually reviewed to identify additional studies of interest.

## Assessment of study quality

Level of evidence was rated for each study according to recommendation by the Oxford Center for Evidence-Based Medicine (http://www.cebm.net). The quality of the study was determined by the Newcastle–Ottawa Scale (NOS) for nonrandomized controlled trials [13], and the Jadad scale for randomized control trials (RCTs) [14].

### Data analysis

Two separate meta-analyses were performed: one on studies with ESWL (emergent versus delayed) as modality of treatment, and the other on studies with URS (emergent versus delayed) as modality of treatment.

Extracted data included: method of treatment (ESWL or URS); stone characteristics (diameter in mm; location); outcomes (stone free rate, complication rate, auxiliary procedures).

For continuous outcomes, the weighted mean difference (WMD) was estimated. For binary variables,



Fig. 1 PRISMA flow diagram detailing search strategy and identification of studies used in data synthesis

Odds ratio (OR) was calculated with reporting of 95% confidence intervals (CIs). As only means and standard deviations are permitted for the computational portion of meta-analyses, for those studies reporting medians and ranges, a validated mathematical model was used to convert medians (ranges) to means (standard deviations) [15].

Pooled estimates were calculated with the fixed-effect model, if no significant heterogeneity was identified; alternatively, the random-effect model was used when significant heterogeneity was detected. Statistical heterogeneity was defined based on Cochrane Q p value or  $I^2$  statistics. To evaluate publication bias, Egger linear regression and funnel plots were examined. All statistical analyses were performed using Review manager software was used to performed data analyses (RevMan v.5.3).

# Results

Overall, ten studies published between 2005 and 2014 were deemed eligible and included in the analysis. In four studies (1 prospective randomized controlled and 3 retrospective case-control studies), emergent URS (n=526)was compared to delayed URS (n=987). The definition of emergency varied among the studies from 12 to 48 h from admission to the emergency room. Stone-free status was defined on postoperative imaging (KUB in 3 studies and CT scan in one), which was done at 1 month in most studies (Table 1) [16–19]. In six studies (4 prospective randomized controlled and 2 retrospective case-control studies), emergent ESWL (n=356) was compared to delayed ESWL (n=355). The definition of emergency varied among the studies from 6 to 72 h from admission to the emergency room. Stone-free status was defined on postoperative imaging (KUB in 3 studies and CT scan in 3), which was done

References	Study design	I oF	No of ca	ses	Definition of	Instrument	Lithotrinsv	Poston imaging	Time of assessment	Study anality
	nareau anna		10.01	626	",""""""""""""""""""""""""""""""""""""		fedmann	1 vavep. mulemb		ound dump
			Emerg	Delay	emergency (n)					
Youn [16]	Case control	3b	67	159	48	8Fr semirigid	Pneumatic	KUB	1 month	8 <sup>a</sup>
Guercio [17]	RCT	1b	139	100	12	6.5Fr semirigid; 7Fr flexible	Holmium	CT	1 month	$2^{\mathrm{b}}$
Sarica [18]	Case control	3b	76	69	24	8/9.8Fr semirigid	Pneumatic and Holmium	KUB	24 h	7 <sup>a</sup>
Matani [19]	Case control	3b	244	659	24	7.5/8Fr semirigid	Pneumatic	KUB	1 month	8 <sup>a</sup>
RCT randomize	d clinical trial, Lo	oE level	of evidence	according	to Oxford CEBM, <i>K</i>	(UB kidney-ureter-bladder X-ray	, CT computeriz	ed tomography stone	protocol	
<sup>a</sup> Newcastle Ott	awa scale									

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**Table 1** Studies comparing emergent versus delayed ureteroscopic lithotripsy for ureteral stones

up to 3 months after the treatment depending on the study (Table 2) [7, 20–24].

#### Ureteroscopic lithotripsy

#### Baseline characteristics

Delayed URS patients presented a significantly larger stone size compared to the emergent URS ones (WMD: 1.35 mm; p=0.04), whereas there was no difference in terms of stone location, which was mostly distal for both groups (60.6% emergent and 78.5% delayed; p=0.66) (Table 3).

#### Outcomes

There was no significant difference in stone-free rates between emergent and delayed URS (91.2 versus 90.9%, OR 1.04; CI 0.71, 1.52; p=0.84). In addition, there was no significant difference in terms of complication rate (8.7% for emergent versus 11.5% for delayed; OR 0.94; CI 0.65, 1.36; p=0.74) as well as need for auxiliary procedures (OR 0.85; CI 0.42, 1.7; p=0.85) (Fig. 2). Table 5 summarizes the complications graded according to Clavien–Dindo [25]. A more detailed description of the type of complications is provided in Table 6.

### ESWL

## Baseline characteristics

With regards to the ESWL, there was no difference between treatment groups for stone size (WMD 0.04 mm; p = 0.92), whereas the delayed ESWL group presented a significantly lower proportion of distally located stone (20 versus 30.9%, p < 0.001) (Table 4).

#### Outcomes

<sup>3</sup>Jadad scale

Likelihood of stone-free status after treatment was found to be higher in the emergent ESWL group (OR 2.2; CI 1.55, 3.17; p < 0.001), which also presented lower odds of need for auxiliary procedures (OR 0.49; CI 0.33, 0.72; p < 0.001). On the other hand, there was no difference in terms of risk of complications between the emergent and delayed ESWL (OR 0.79; CI 0.47, 1.32; p=0.37) (Fig. 3). Table 5 summarizes the complications graded according to Clavien–Dindo [25]. A more detailed description of the type of complications is provided in Table 6.

Table 2	Studies com	paring emerge	nt versus delayed	ESWL for	ureteral stones

References	Study design	LoE	N of ca	ses		Lithotripsy device	Postop. imaging	Time of assess-	Study quality
			Emerg	Delay				ment	
Joshi [7]	Case control	3b	16	40	Upon admission	Siemens Lithostar	KUB	After ESWL	8 <sup>a</sup>
Kravchick [20]	RCT	2b	25	28	48–72 h	Econolith	KUB	1 month	3 <sup>b</sup>
Tombal [21]	RCT	1b	50	50	6 h	Definition of "emergency" Siemens Lithostar	KUB	24–48 h	2 <sup>b</sup>
Kumar [22]	RCT	1b	80	80	48 h	Dornier Alpha compact	СТ	3 months	3 <sup>b</sup>
Uguz [23]	RCT	1b	32	31	24 h	Dornier Alpha compact	СТ	72 h	2 <sup>b</sup>
Choi [24]	Case control	3b	153	126	48 h	Dornier Compact Delta	KUB/CT	1 month	$7^{\mathrm{a}}$

RCT randomized clinical trial, LoE level of evidence according to Oxford CEBM, Eme emergency, Del delayed, KUB kidney–ureter–bladder X-ray, CT computerized tomography stone protocol

<sup>a</sup>Newcastle Ottawa scale

<sup>b</sup>Jadad scale

Table 3 Studies comparing emergent versus delayed ureteroscopic lithotripys for ureteral stones: patients and stone characteristics

References	No. of ca	ases	Gender,	M/F	Age, years, r	nean (SD)	Stone size (SD)	, mm, mean	Stone locati distal	on, prox/mid/
	Emerg	Delayed	Emerg	Delayed	Emerg	Delayed	Emerg	Delayed	Emerg	Delayed
Youn [16]	67	159	39/28	89/70	47.8 (11.5)	51.2 (13.8)	2.4 (1.6)	4.1 (2.6)	8/4/55	36/29/94
Guercio [17]	139	100	163/81		52.7 (12.5)	50 (10.3)	8 (2.1)	8 (2.1)	13/30/68	20/25/40
Sarica [18]	76	69	45/31	51/18	34 (8.1)	44 (15.3)	8.3 (2)	11.8 (4)	29/nr/47	18/nr/51
Matani [19]	244	659	184/60	508/151	45.6 (13.2)	43.4 (15.3)	9.2 (4.4)	9.6 (5.3)	49/46/149	147/79/433

M male, F female, nr not reported, Emerg emergent ureteroscopic lithotripsy, Delayed delayed ureteroscopic lithotripsy, SD standard deviation

### Discussion

The rationale for an early therapy in patients affected by ureteral stones accompanied by colic is ureteral edema gradually develops after 24-48 h, progressing with time, and ultimately impairing the stone clearance [26, 27]. Cummings et al. demonstrated using an artificial neural network that the duration of symptoms before treatment and hydronephrosis grade represent the most important factors in predicting the passage of ureteral stones [28]. This argument holds especially true for ESWL treatment as the onset of edema determines inhibition of the expansion chamber formation and removal of the fluid layer between the stone and the tissue, reducing fragmentation rates of shockwaves [29]. According to Kumar et al., the days needed for stone clearance, the retreatment rate and the requirement of auxiliary procedures are significantly higher when treatment is performed beyond 48 h from pain onset and the more time passes, the greater is this increase [22].

Herein, we report the first meta-analysis of studies comparing emergent versus delayed lithotripsy for obstructing ureteral stones, including four studies on URS (including one randomized controlled trial), and six studies on ESWL (including four randomized controlled trials). The present analysis of a large pooled sample (over 1600 URS cases, and over 700 ESWL cases) can contribute to the ongoing debate, ultimately paving the way for further research on this topic, and also it can provide key information for contemporary evidence-based patient counseling. In this respect, a recent analysis of the Healthcare Cost and Utilization Project State Inpatient Database for Florida and California from 2007 to 2011 on over 10,000 patients admitted for obstructing nephrolithiasis revealed that early intervention occurred in 65% of cases, and this was associated with a decrease in mortality (0.16%), compared to delayed intervention (0.47%), p = 0.002) [12].

Our findings confirm that URS is an effective and safe procedure when performed in emergency setting (variably defined as ureteroscopy performed 12–48 h since admission to the emergency department), without significant differences in terms of stone-free rate, complication rates, and

## (a) STONE FREE RATE

	EMERG	ENT	DELAY	ſED		Odds Ratio		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	Year	M-H, Fixed, 95% CI
Sarica 2011	69	76	60	69	11.1%	1.48 [0.52, 4.21]	2011	
Guercio 2011	130	139	90	100	13.0%	1.60 [0.63, 4.11]	2011	
Youn 2012	60	67	143	159	17.0%	0.96 [0.38, 2.45]	2012	
Matani 2013	221	244	605	659	59.0%	0.86 [0.51, 1.43]	2013	
Total (95% CI)		526		987	100.0%	1.04 [0.71, 1.52]		+
Total events	480		898					
Heterogeneity: Chi <sup>2</sup> = 1	1.83, df = 3	B(P = 0.)	.61); l <sup>2</sup> = (	0%				
Test for overall effect: 2	Z = 0.21 (F	P = 0.84	)					Favours [DELAYED] Favours [EMERGENT]

## (B) COMPLICATION RATE

	EMERG	ENT	DELAY	ΈD		Odds Ratio		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	Year	M-H, Fixed, 95% Cl
Guercio 2011	2	139	2	100	4.0%	0.72 [0.10, 5.17]	2011	
Sarica 2011	9	76	2	69	3.2%	4.50 [0.94, 21.61]	2011	<b>↓</b> →
Youn 2012	3	67	15	159	14.8%	0.45 [0.13, 1.61]	2012	
Matani 2013	32	244	95	659	77.9%	0.90 [0.58, 1.38]	2013	
Total (95% CI)		526		987	100.0%	0.94 [0.65, 1.36]		+
Total events	46		114					
Heterogeneity: Chi <sup>2</sup> =	5.23, df =	3 (P =	0.16); I <sup>2</sup> =	43%				
Test for overall effect:	Z = 0.33 (	P = 0.7	4)					Favours [EMERGENT] Favours [DELAYED]

#### (C) AUXILIARY PROCEDURES

	EMERG	ENT	DELAY	ΈD		Odds Ratio		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	Year	M-H, Fixed, 95% Cl
Guercio 2011	7	139	7	100	44.4%	0.70 [0.24, 2.08]	2011	
Sarica 2011	6	76	3	69	16.6%	1.89 [0.45, 7.85]	2011	
Youn 2012	3	67	12	159	39.0%	0.57 [0.16, 2.10]	2012	
Total (95% CI)		282		328	100.0%	0.85 [0.42, 1.70]		-
Total events	16		22					
Heterogeneity: Chi <sup>2</sup> =	1.67, df =	2 (P =	0.43); I <sup>2</sup> =	0%				
Test for overall effect:	Z=0.46 (	P = 0.6	5)					Favours [EMERGENT] Favours [DELAYED]

Fig. 2 Emergent versus delayed ureteroscopy for obstructing ureteral stones: forest plots for a stone-free rate; b complication rate; c auxiliary procedures

Table 4	Studies comparing	emergent versus de	elayed ESWL	for ureteral stone	s: patients and sto	one characteristics
		6	2			

References	No. of ca	ases	Gender,	M/F	Age, years, n	nean (SD)	Stone size (SD)	, mm, mean	Stone loca mid/distal	tion, prox/
	Emerg	Delayed	Emerg	Delayed	Emerg	Delayed	Emerg	Delayed	Emerg	Delayed
Joshi [7]	16	40	12/4	28/12	54.3	49.6	8.2	9.3	6/3/7	31/4/5
Kravchick [20]	25	28	36/64	44/56	45.2 (10.6)	47.9 (11.6)	7.4 (2.4)	6.9 (2.4)	18/nr/7	25/nr/3
Tombal [21]	50	50	40/10	43/7	44	42	6 (2)	5 (2)	29/nr/21	17/nr/33
Kumar [22]	80	80	44/36	46/34	37.4 (2)	37.3 (2.5)	7.3 (1.5)	7.5 (1.7)	nr	nr
Uguz [23]	32	31	25/7	25/6	36.7 (12.7)	37.6 (12.8)	8.1 (3.1)	8.8 (2.9)	21/2/9	20/4/7
Choi [24]	153	126	108/45	96/30	43.6 (12.9)	45.1 (13.1)	7.6 (2.5)	8.3 (3.1)	93/6/54	90/6/30

M male, F Female, nr not reported, Emerg emergent SWL lithotripsy, Delayed delayed SWL lithotripsy, SD standard deviation

need of ancillary procedures when compared to delayed ureteroscopy.

Osorio et al. reported the first series of emergency ureteroscopy in 2007 [10]. They performed a retrospective analysis on 144 patients performed mostly (90%) for distal stones (mean stone diameter 9 mm), and they had an overall stone-free rate of 92.4%. They observed that greater stonefree rate was achieved in patients with stones < 10 mm

# (a) STONE FREE RATE

	EMERG	ENT	DELAY	(ED		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI Ye	ar M-H, Fixed, 95% Cl
Joshi 1999	13	16	28	40	7.3%	1.86 [0.45, 7.73] 199	99
Tombal 2005	37	50	31	50	19.6%	1.74 [0.74, 4.09] 200	05
Kravchick 2005	18	25	18	28	11.5%	1.43 [0.45, 4.58] 200	
Kumar 2010	69	80	64	80	21.4%	1.57 [0.68, 3.63] 20	10
Uguz 2012	17	32	12	31	13.9%	1.79 [0.66, 4.89] 20	2
Choi 2012	135	153	84	126	26.3%	3.75 [2.03, 6.94] 20	12
Total (95% CI)		356		355	100.0%	2.21 [1.55, 3.17]	•
Total events	289		237				
Heterogeneity: Chi <sup>2</sup> = 4	1.53, df = 5	6 (P = 0.	48); l <sup>2</sup> = (	0%			
Test for overall effect: 2	Z = 4.35 (F	<b>P</b> < 0.00	01)				Favours DELAYED Favours EMERGENT

## (B) COMPLICATION RATE

	EMERG	ENT	DELAY	ΈD		Odds Ratio		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	Year	M-H, Fixed, 95% Cl
Kumar 2010	36	80	44	80	74.8%	0.67 [0.36, 1.25]	2010	
Choi 2012	11	153	8	126	25.2%	1.14 [0.45, 2.93]	2012	
Total (95% CI)		233		206	100.0%	0.79 [0.47, 1.32]		-
Total events	47		52					
Heterogeneity: Chi <sup>2</sup> =	0.86, df=	1 (P =	0.35); l² =	0%				
Test for overall effect:	Z = 0.90 (	P = 0.3	7)					Favours [EMERGENT] Favours [DELAYED]

# (C) AUXILIARY PROCEDURES

	EMERG	ENT	DELAY	ΈD		Odds Ratio		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	Year	M-H, Fixed, 95% Cl
Kravchick 2005	7	25	8	28	7.6%	0.97 [0.29, 3.22]	2005	
Tombal 2005	11	50	8	50	8.7%	1.48 [0.54, 4.06]	2005	
Kumar 2010	13	80	26	80	30.3%	0.40 [0.19, 0.86]	2010	
Uguz 2012	2	32	6	31	8.0%	0.28 [0.05, 1.50]	2012	· · · · · · · · · · · · · · · · · · ·
Choi 2012	15	153	33	126	45.5%	0.31 [0.16, 0.60]	2012	
Total (95% CI)		340		315	100.0%	0.49 [0.33, 0.72]		•
Total events	48		81					
Heterogeneity: Chi <sup>2</sup> =	8.48, df =	4 (P = 1	0.08); I <sup>z</sup> =	53%				
Test for overall effect:	Z = 3.58 (	P = 0.0	003)					Favours [EMERGENT] Favours [DELAYED]

Fig. 3 Emergent versus delayed ESWL: forest plots for a stone-free rate; b complication rate; c auxiliary procedures

Table 5         Complications rate           according to Clavien–Dindo         grading system	Clavien grade	URS		ESWL	
		Emergency $(n=526)$	Delayed $(n=987)$	Emergency $(n=233)$	Delayed $(n=206)$
	Ι	17 (3.2%)	35 (3.5%)	41 (17.6%)	41 (19.9%)
	II	12 (2.3%)	42 (4.2%)	-	_
	IIIa	15 (2.8%)	36 (3.6%)	1 (0.4%)	1 (0.5%)
	IIIb	2 (0.4%)	1 (0.1%)	-	_
	Graded n/a	-	-	5 (2.1%)	10 (4.8%)
	Total	46 (8.7%)	114 (11.5%)	47 (18%)	52 (20.4%)

(95.8% versus 89%; p = 0.002) and in those presenting with stones in distal ureter (94.6 versus 71.4%; p = 0.004). The role of stone location and size as key factors in determining the success of URS was also confirmed by Youn et al. who found a higher stone-free rate when only distal ureteral stones were considered (97.6 versus 89.8%), and fewer complications when only stones <10mm were taken into consideration (2.7 versus 7.96%) [16]. Picozzi et al. estimated that every 1mm of increased diameter over 8mm determine a reduction of stone-free rate of 5% in distal ureter and 8.1% in proximal ureters [11]. Al Ghazo et al. stratified their 244 cases by stone location, and they found

	Complication type (Clavien grade)	Emergency URS	Delayed URS
Youn [16]	Mucosal Injury (I)	3 (4.5%)	9 (5.6%)
	Haematuria (I)	_	6 (3.7%)
Guercio [17]	Haematuria (I)	1 (0.7%)	_
	Urinary tract infection (II)	1 (0.7%)	1 (1%)
	Ureteral stricture (I)	_	1 (1%)
Sarica [18]	Mucosal injury (I)	6 (7.9%)	2 (2.9%)
	Haematuria (I)	3 (3.9%)	_
Matani [19]	Flank pain (II)	7 (2.9%)	26 (3.9%)
	Hematuria (I)	4 (1.6%)	17 (2.6%)
	Urinary tract infection (II)	4 (1.6%)	15 (2.3%)
	Ureteral injuries		
	Perforation	7 (2.9%)	21 (3.2%)
	(IIIa)	6	20
	(IIIb)	1	1
	Avulsion (IIIb)	1 (0.4%)	_
	False passage (IIIa)	7 (2.9%)	15 (2.3%)
	Stricture (IIIa)	2 (0.8%)	1 (0.1%)
	Complication type (Clavien grade)	Emergency ESWL	Delayed ESWL
Kumar [22]	Steinstrasse <sup>a</sup>	5 (6.2%)	10 (12.5%)
	Haematuria (I)	31 (38.7%)	34 (42.5%)
Choi [24]	Steinstrasse		
	Asymptomatic (I)	2 (1.3%)	1 (0.8%)
	Symptomatic (IIIa)	1 (0.7%)	1 (0.8%)
	Gross Haematuria (I)	2 (1.3%)	1 (0.8%)
	Severe Pain (I)	6 (3.9%)	5 (4.0%)

 Table 6
 Detailed description of complications graded according to Clavien–Dindo

<sup>a</sup>Clavien grading not possible due to lack of data in the study

higher stone-free rates for mid (95.8%) and distal ureter (96.6%) compared to distal (69.4%) [30]. Conversely, in the only randomized trial comparing emergent versus delayed URS, Guercio et al. found that neither stone size nor location had any impact on stone-free rate [17]. This finding could be explained by the fact that this was the only group to use a flexible scope (besides the semirigid one), and therefore one might expect that a more aggressive pursuit of residual or migrated fragments was implemented.

No significant difference in terms of complication was found in our analysis and this finding is similar to the 7.6% complication rate reported in the cumulative analysis of 681 by Picozzi et al. [11]. An overall 5% complication rate was reported by a recent large audit form New Zealand [31]. In the four comparative studies, we identified and included only two major complications, which were reported by Matani et al., who had one ureteral perforation and one avulsion caused by stone basket [19].

Our findings also support the concept that emergent ESWL is more effective (than delayed ESWL) in terms of stone-free rate, and it requires less ancillary maneuvers.

Notably, four of the six comparative studies we included were RCTs, which further corroborate these findings. However, these studies were of intermediate quality (Jadad score 2-3). Also for ESWL, the definition of "emergency" procedure varied among studies (anywhere from 6 to 72h). In their pioneering work, Joshi et al. pointed out that treating the stone emergently with ESWL can minimize the energy-absorbing effects derived from progressive wall changes related to stone impaction, ultimately translated into high success rate of the procedure [7]. Choi et al. pointed out that significantly better treatment outcomes in the emergent group were noticed only for patients with stone size  $< 10 \,\text{mm}$  and proximal ureteral stones [24]. In the study by Uguz et al., the stone-free rate was also significantly higher for immediate SWL only for upper ureteral stones (p = 0.019), regardless of the stone size [23]. In their pooled analysis of six studies (including 570 cases), Picozzi et al. did not register a difference in terms of stone-free rate between upper ureteral stones (79%) versus mid (78%) or distal (78%) stones [8]. In their RCT, Kumar et al. showed no significant difference in stone-free rate between delayed

and early ESWL (86.3 versus 80%; p = 0.31), although they only included upper ureteral stones <10 mm. Notably, in this study, the need of auxiliary procedure and number of ESWL sessions was significantly lower when ESWL is performed within the first 48 h [22]. More recently, a group from UK reported another retrospective series of 97 patients with an overall success rate of 73%, and they identified stone size and stone density (as determined by Hounsfield units) as factor predicting the outcomes of the emergency ESWL procedure. Others have reported the role of non-contrast CT scan to determine the attenuation values of urinary calculi before ESWL to predict treatment outcome [32]. As far as complication rates, no differences between emergent and delayed ESWL were noticed in our meta-analysis (p=0.58).

Our study is not devoid of limitations. First, despite meta-analyses being a robust statistical tool, controversies exist regarding their relative role in surgical decisionmaking [33]. However, it has been argued that to minimize the biases, meta-analyses should be performed within the frame of systematic reviews [34], as it is the case of our work. Moreover, it should be pointed out that the analysis on URS outcomes was based on only one RCT, and this was of low quality; therefore, this should be taken into account when interpreting the results. Second, the variability in the definition of "emergent" procedure might account for some bias. Third, success rate of ureteroscopy, and ESWL can also depend on the technology and instrumentation used. This holds especially true for ESWL, where the implementation of more portable second, and third, and fourth generation machine has come to the place [35], and for which the results might be machine specific, and also depend on fine tuning of technical factors (focal zone, pulse rates, ramping strategies, coupling) [36]. Fourth, SFR was defined as absence of stone in 7 out of 11 studies, while in four studies fragments  $\leq 3 \text{ mm}$  were considered as a successful outcome. Moreover, imaging technique for defining the SF status (KUB and/or CT scan) and follow-up time (range 24h-4weeks) widely varied among analyzed series. Fifth, we could not perform a sensitivity analysis based on stone location and size as stratified outcomes for these variables were not available in most of the included studies.

Last, this analysis does not allow a formal assessment of the cost-effectiveness of emergency lithotripsy. However, it can be speculated that achieving rapid decompression of the obstruction and pain relief in only one step can translate into a benefit in terms of decrease hospital stay, and reduction of readmissions in emergency room. In a large (over 5000 cases) data sample using claims data, Hollingsworth et al. found that men placed on medical expulsive therapy experienced higher repeat emergency department visits compared to those undergoing immediate endoscopic stone removal (68.8 versus 39.6%, respectively, p=0.025) [37]. A more recent study from the same group suggested that patients receiving conservative therapy may actually file fewer short-term disability claims, and experience less income loss within the first 42 days [38]. However, these claims data are limited by the lack of information about stone size and location which may impact these findings and conclusions [39].

## Conclusions

Current evidence suggests that emergent lithotripsy, either ureteroscopic or extracorporeal, can be offered as an effective and safe treatment if a patient presents with a symptomatic ureteral stone. If amenable to ESWL, based on stone and patient characteristics, an emergent approach should be strongly considered. Ureteroscopy in the emergent setting is mostly reserved for distally located stones. The implementation of these therapeutic approaches is likely to be dictated mostly by their availability in the emergency setting. The findings of the present cumulative analysis should be interpreted by taking into account its limitations. Further investigation in this area is desirable.

#### Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

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