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Evaluation of the clinical significance of sonographic perinephric fluid in patients with renal colic

Granat Nadav [a,*], Klang Eyal [b], Tau Noam [b], Kleinbaum Yeruham [b]

[a] Emergency Department, Rabin Medical Center, Beilinson Hospital, Petah-Tikva, Israel
[b] Department of Diagnostic Imaging, The Chaim Sheba Medical Center, Tel Hashomer, Ramat Gan, Israel

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ABSTRACT

Objective: To evaluate the significance of sonographic perinephric fluid collection on the emergent management of patients with acute urinary stone obstruction.

Methods: We conducted a prospective study with retrospective analysis. Since January 2016 through July 2017, patients admitted to our tertiary hospital's emergency department (ED) with suspected symptomatic urinary stones underwent ultrasound evaluation. Images were prospectively interpreted by experienced radiologist who analyzed each case for the following imaging features: hydronephrosis, perinephric fluid and urethral stone identification. The presence and measurements of perinephric fluid were re-evaluated by second radiologist who was blinded for the first reader's measurements. Retrospective analysis was conducted to evaluate for an association between perinephric fluid collection and the following outcome variables: need for analgesics, the number of doses of analgesics and the amount of morphine (mg) in the ED, elevation of creatinine levels, hospitalization and need for urological interventions.

Results: The need for analgesics, the number of doses of analgesics and the amount of morphine were significantly associated with the presence of perinephric fluid ($p < 0.05$). The odds ratio for the need for analgesics was 3.8 in the presence of any perinephric fluid, and 8.9 in the presence of moderate/severe perinephric fluid. No other patient outcome variables were found to be significantly associated with the presence of perinephric fluid ($p > 0.05$).

Conclusions: This study shows a correlation between sonographic evidence of perinephric fluid and more severe pain. Therefore, an emergency physician can consider the evidence of perinephric fluid, in acute urethral stone obstruction, a predictor for more severe pain.

1. Introduction

Renal and ureteral stones are a common problem in primary care practice and in the emergency department (ED) setting [1]. Diagnostic evaluation for suspected nephrolithiasis includes a detailed medical history, physical examination, appropriate imaging and laboratory tests including urine analysis [2]. When a diagnosis of nephrolithiasis is clinically suspected, imaging of the kidneys, ureters, and bladder should be performed to support the diagnosis of a stone [3].

Non-contrast computed tomography scan co (NCCT) has become the standard of care for diagnosing acute flank pain, and has replaced intravenous urography (IVU), which was the gold standard for many years [3]. NCCT can accurately determine stones' diameter and location. These features were demonstrated in several studies to be the most important parameters for predicting the need for interventional treatment [4-8]. Several studies examined whether secondary signs in the NCCT scan, such as hydronephrosis, perinephric edema/fluids or perinephric stranding, could help to predict the need for interventional versus conservative treatment, but their results were inconclusive [6-9].

Ultrasound (US) is considered an acceptable alternative to NCCT as the primary diagnostic imaging tool [3,10,11]. Ultrasound can directly identify stones located in the kidney and pyelo-ureteral and vesico-ureteric junctions, but frequently fails to detect ureteral calculi. For all stones, US has direct visualization limited sensitivity (as low as 19% in few studies) but relatively high specificity (84–100%) [12].

Regarding sonographic secondary signs, hydronephrosis is well established in the setting of point of care ultrasound (POCUS) in the ED as an important sign to assess stone size and to predict thirty day outcomes [13-16]. To the best of our knowledge, other sonographic signs have not been researched as extensively [17].

* Corresponding author.
E-mail address: nadavgr@clalit.org.il (G. Nadav).

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The aim of this study was to evaluate the significance of sonographic perinephric fluid in the emergent management of patients with acute urinary stones obstruction.

2. Materials and methods

2.1. Cohort selection

An Institutional Review Board (IRB) approval was granted for this study.

We conducted a prospective study with retrospective analysis. Over a period of eighteen months (January 2016 through July 2017) patients who were admitted to our tertiary hospital's ED with suspected symptomatic urinary stones underwent US evaluation as initial imaging, either during their ED visit or within 16 h from discharge. Two hundred twenty-six of those US examinations were prospectively interpreted by a senior experienced radiologist (with twenty four years of experience).

For the final analysis, we included adult patients (>age 18) with nephrolithiasis confirmed by one of the following: US/CT direct visualization of urethral stone or patient's report that the stone had been passed during ED visit or admission. We excluded four patients with final diagnosis other than nephrolithiasis (for example pyelonephritis or urinary tract obstruction unrelated to stone disease), thirty-three patients with unconfirmed nephrolithiasis diagnosis according to the inclusion criteria above, one pregnant patients and one patient with a solitary kidney.

The final cohort included 187 confirmed nephrolithiasis patients who presented to our ED with suspected nephrolithiasis and underwent a sonographic examination which was interpreted by the same experienced radiologist.

2.2. Imaging technique

Examination of the urinary system was performed by experienced ultrasound technicians with a curvilinear probe 1–5 MHz Philips IV22.

2.3. Image analysis

The sonographic evaluation included:

1. Urethral stones-presence of as well as the size (mm) and location along the ureter (1/3 proximal, 1/3 mid or 1/3 Distal)
2. Hydronephrosis – presence of hydronephrosis was defined as renal pelvic/calyx dilatation. Severity of hydronephrosis was defined according to the renal pelvic diameter: 0–10-mild, 11–20 moderate, >20 severe.
3. Perinehric fluid collection– defined as any anechoic collection adjacent to the renal cortex border. Severity of the fluid collection was defined as: mild-thin strip of fluid adjacent to less than half of renal circumference, moderate-thin strip of fluid collection adjacent to more than half of renal circumference, severe – thick layer of fluid collection adjacent to more than half of renal circumference

All the examinations were evaluated prospectively by experienced radiologist (YK with 25 years of experience). The presence and measurements of perinephric fluid were re-evaluated by second expert radiologist (NT with 7 years of experience) who was blinded for the first reader's measurements. Finally, we retrospectively compared a group of 87 cases with sonographic evidence of perinephric fluid collection to a control group of 100 cases from the same period without sonographic signs of perinephric fluid collection, with regard to different ED clinical and laboratories variables.

2.4. Analysis of clinical and laboratory variables in the ED

- Pain management: The need for analgesics as well as the mean number of analgesic doses was calculated according the documented orders for analgesics during the ED visit. The opiate doses were calculated by documented opiate medication administration, which were standardized by conversion to IV morphine (mg) according the website http://clincalc.com/opioids/
- Elevation of creatinine levels from baseline: renal function deterioration was measured by creatinine delta values (mg/dl %) between ED visit and baseline value, which was defined as the lowest value documented in the medical records.
- Hospitalization/return visits to the ED within 72 h: these parameters were analyzed according to documentation in our hospital's medical records.
- Need for urological intervention: urological interventions (including urethral stent insertion, retrograde intra-renal surgery or nephrostomy tube placement) within 45 days of the ED visit were analyzed. In addition, we separately analyzed urgent urological interventions, defined as intervention during hospitalization for the acute episode of renal colic according to the following indication: intractable pain, urinary infection/sepsis or significant deterioration in renal function (above 1.5 mg/dl %).

2.5. Statistical analysis

Calculations were performed with IBM SPSS statistic (Version 20.0) (Armonk, NY, USA). Categorical variables are reported as percentages and continuous variables are reported as the mean ± standard deviation (SD). Chi square test/Fisher's exact test were used to evaluate categorical variable and odds ratios were calculated. Student's *t*-test/Mann Whitney *U* test was used to evaluate continuous variables. $p < 0.05$ was considered statistically significant.

Cohen's kappa coefficient was used to measure inter-rater agreement between the two study readers measurements of perinephric fluid. Kappa values were categorized as follows: <0 indicating no agreement, 0–0.20 slight agreement, 0.21–0.40 fair agreement, 0.41–0.60 moderate agreement, 0.61–0.80 substantial agreement, and 0.81–1 as almost perfect agreement [18]. Statistical analysis of perinephric fluid measurement was conducted according to prospective interpretation of our first experienced reader.

We evaluated the association between the presence of perinephric fluid and the presence and severity of hydronephrosis (measured by renal pelvis size in mm), and with the size (mm) and location (proximal, middle and distal ureter) of renal stones.

We also evaluated for associations between the presence and severity of perinephric fluid with the following patient outcome variables: need for analgesics, number of doses of analgesics, amount of morphine (mg) in the ED, elevation of creatinine levels, hospitalization and need for urological interventions.

3. Results

Cohen's kappa coefficient for inter-rater agreement between the two study readers was 0.952 ($p < 0.001$).

Perinephric fluid was seen in 87/187 kidneys (46.5%), with 74/187 (39.6%) mild perinephric fluid, 11/87 (6%) moderate perinephric fluid and 2/187 (1%) severe perinephric fluid. For statistical analysis we decided to combine the groups of moderate and severe perinephric fluid to one moderate-severe group which include 13/187 (7%).

Hydronephrosis was seen in the majority of the patients 177/187 (94.7%). Mild hydronephrosis (pelvic diameter ≤ 10 mm) was seen in 106/187 (56.7%) patients, moderate hydronephrosis (pelvic diameter 11–20 mm) was seen in 67/187 (35.8%) patients and severe hydronephrosis (pelvic diameter > 20 mm) was seen in only 3/187 (1.6%) patients.

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The presence of perinephric fluid was found to be associated with hydronephrosis (p = 0.002). Although the frequency of perinephric fluid was not statistically different between severity groups of hydronephrosis (mild hydronephrosis: 51/106, 48.2%, moderate hydronephrosis: 34/67, 50.7%, severe hydronephrosis: 2/3, 66.7%), mean pelvic diameter was higher in kidneys with perinephric fluid (mean pelvic diameter with absence of perinephric fluid 9.8 ± 5.3 mm vs. mean pelvis diameter with perinephric fluid 11.9 ± 3.6 mm, p = 0.005) (Figs. 1 and 2).

Stones were seen in 135/187 (72.2%) of the patients, with 19/187 (10.2%) proximal ureter stones, 9/187 (4.8%) middle ureter stones and 105/187 (56.1%) distal ureter stones. Mean stone size was similar in kidneys with and without perinephric fluid (stone size without perinephric fluid 7.3 ± 3.7 mm vs. stone size with perinephric fluid 6.3 ± 2.3 mm, p = 0.112). There was no association between the stone's location along the ureter and the presence of perinephric fluid (p = 0.103) (Table 1).

Table 2 summarizes the associations between the presence and severity of perinephric fluid and patients' outcome variables. As can be seen in the table, the need for analgesics, the number of doses of analgesics and the amount of morphine (mg) are all associated with perinephric fluid (odds ratio 3.8 for analgesics with perinephric fluid), and all of them increase in moderate/large perinephric fluid (odds ratio 8.9 for analgesics with severe perinephric fluid). All other patient outcome variables were not found to be significantly associated with perinephric fluid.

4. Discussion

Perinephric fluids collection is a well described pathological finding in the setting of acute urethral stone obstruction as well as in other causes of urinary obstruction(including pelvic mass, retroperitoneal fibrosis and posterior urethral valves) [19]. Regarding pathophysiology, there are two main theories in the literature: according to one theory, the perinephric collection results from a urinary leak secondary to forniceal rupture. In acute urethral stone obstruction, there is often a sharp rise in intra-pelvic pressure and the collecting system may rupture at its weakest location—the fornices [20,21]. According to the second theory, one of the kidneys responses to the increased pressure in the ureter is urine absorption, which then infiltrates the perinephric space along the bridging septa [22].

Established literature concerning the significance of perinephric fluid collection in the management of acute urethral stone obstruction is absent. Therefore, therapeutic approach in these cases is controversial. A literature review revealed only few observational studies that described different management approaches: conservative treatment which included observation with or without alpha blockers and/or antibiotics vs urgent intervention such as ureteral stenting, percutaneous drainage, or nephrostomy tube placement [19,23-26]. Moreover, there are conflicting reports regarding the rate of delayed perinephric fluid complications such as renal abscess or sepsis [25-29].

Recently, Thom C et al. published a case series of perinephric fluid collection complicating simple renal colic, diagnosed by POCUS along with a literature review on the topic. He also concluded that “there are no randomized control or large prospective trials available to help inform decision making in these cases” [30].

To our knowledge, our study is the first prospective study to investigate the significance of sonographic perinephric fluid collection secondary to acute urethral stone obstruction. We investigated the relevant aspects of the management in the ED including need for analgesics, admission rates, return visits to the ED within 72 h, renal function deterioration and need for urgent intervention.

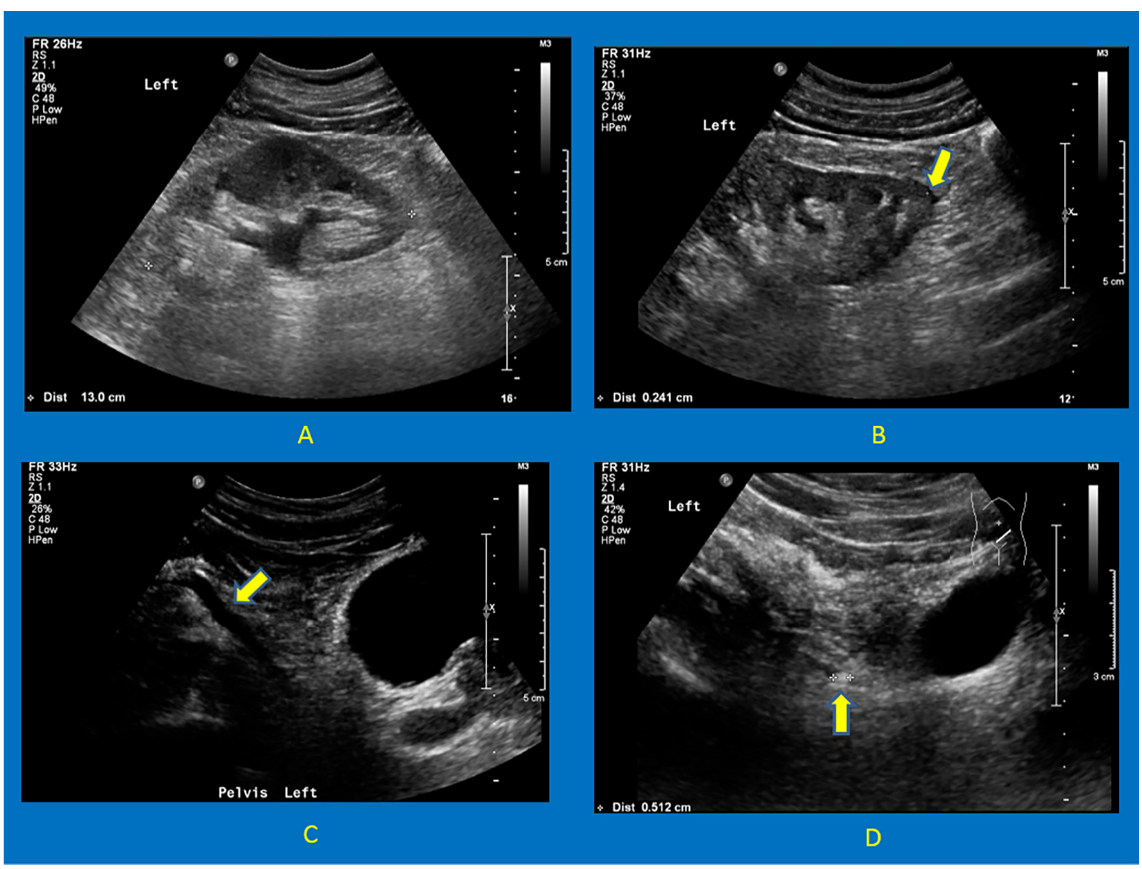

Fig. 1. 63 y/o male with left flank pain. A: longitudinal image of the left kidney demonstrated moderate hydronephrosis. B: longitudinal image of the left kidney demonstrated small amount of fluid extravasation around the lower pole of the kidney (arrow). C: image of the left pelvis demonstrated left hydro ureter (*arrow*). D: image of the left pelvis demonstrated small ureteral calculi (*arrow*).

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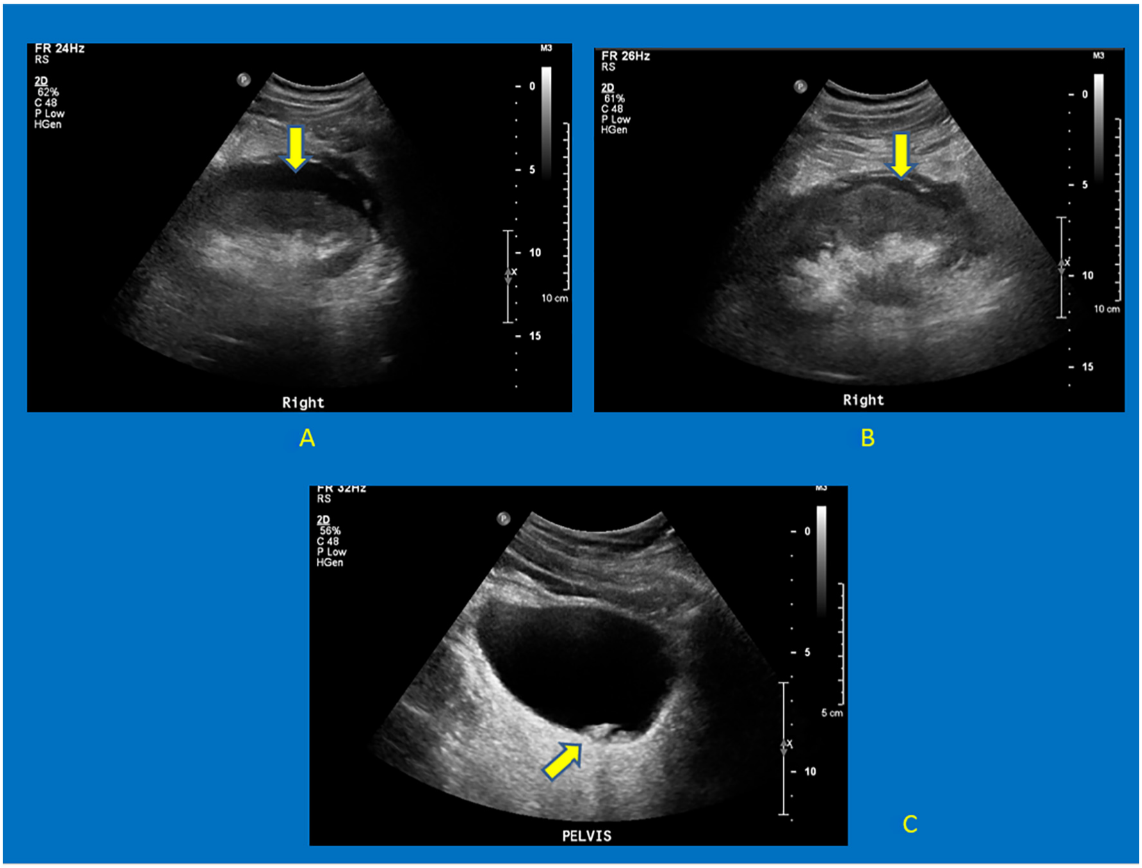

Fig. 2. 63 y/o male right flank pain. A: longitudinal image of the right kidney demonstrated large amount of fluid extravasation around the kidney (*arrow*). B: longitudinal image of the right kidney demonstrated mild hydronephrosis and fluid extravasation around the kidney (*arrow*). C: longitudinal image of the urinary bladder demonstrated two urinary bladder calculi (*arrow*).

According to our results, there is a strong and consistent correlation between perinephric fluid collection and aspects of pain management including the need for analgesics, the number of doses of analgesics and the amount of morphine. Moreover, this correlation was even stronger in the cases of significant (moderate-large) perinephric fluid collection. We did not find any other description of this correlation in the literature.

Table 1
Demographic data for the study cohort.

	Perinephric fluid (N = 87)	Without perinephric fluid (N = 100)
Age (years, mean)	45	49
Sex (M:F) % (n)	85:15 (74/13)	84:16 (84/16)
Symptoms% (n):		
Right abdominal/flank pain	48 (42)	44 (44)
Left abdominal/flank pain	36 (38)	53 (53)
Diffuse abdominal pain/urinary symptoms	16 (7)	3 (3)
US pathological findings% (n)		
Right kidney	50.5 (44)	46 (46)
Left kidney	49.5 (43)	54 (54)
Perinephric fluid collection% (n)		
Small	85 (74)	–
Moderate-large	15 (13)	–
Hydronephrosis % (n)	100 (87)	90 (90)
Hydronephrosis severity% (n)		
Absent	0 (0)	10 (10)
Mild	59 (51)	56 (56)
Moderate	39 (34)	33 (33)
Severe	2 (2)	1 (1)
Sonographic urethral stone identification% (n)	68 (59)	74 (74)
Stone size mm (mean)	6.3	7.3
Urethral stone location% (n)		
Proximal	20 (12)	9.5 (7)
Mid	4 (2)	9.5 (7)
Distal	76 (45)	81 (60)

We suggest that the correlation between perinephric fluids collection and increased pain reflects a higher degree of intra-urinary collection system pressure secondary to urethral obstruction. This results in physiological adaptation of the kidney either by forniceal rupture or urine absorption (as described above).

Nevertheless, all other patient outcome variables including admission rates, return visits to the ED within 72 h, renal function deterioration and urgent intervention were not found to be significantly associated with the presence of perinephric fluid collection.

In contrast to our results, Chapman JP et al., who compared 21 patients with perinephric fluid extravasation to 94 patients with obstructive urography but without extravasation found a trend to lower admission rates of admission in patients with perinephric fluid extravasation [25]. The small size of the group of the patients with perinephric extravasation as well as the different imaging modality (US vs IV uretrography) make it difficult to compare the two studies or draw any conclusions with regard to the conflicting results.

Further research is needed to understand the pathophysiology of perinephric fluid accumulation in the setting of acute urinary stones obstruction. Furthermore, large prospective studies are required to evaluate the correlation between perinephric fluid collection and different clinical and laboratory aspects and to clarify the significance of this finding for acute ED management. This study emphasizes the importance of integration between the sonographic assessment of the radiologist and the clinician evaluation in the ED.

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Table 2
Associations between the presence and severity of perinephric fluid and patients' outcome variables

Entire cohort (N = 187)	Any perinephric fluid (N = 87)	Moderate-large perinephric fluid (N = 13)
Need for any analgesics in the ED (N = 144)	77/87 (88.5%) vs. 67/100 (46.5%), $p < 0.001$, Odds ratio = 3.8	13/13 (100%) vs. 131/174 (75.3%), p = 0.042, Odds ratio = 8.9
Number of doses of any analgesics in the ED	1.3 ± 1.2 doses vs. 2.1 ± 1.4, $p < 0.001$	1.6 ± 1.4 doses vs. 2.4 ± 0.9 doses, p = 0.017
Morphine (mg)	4.0 ± 5.8 mg vs. 8.1 ± 7.8 mg, $p < 0.001$	5.6 ± 7.1 mg vs. 9.6 ± 5.6 mg, $p = 0.049$
Elevation of creatinine levels from baseline (delta from baseline in mg%)	0.1 ± 0.4 mg% vs. 0.1 ± 0.3 mg%, p = 0.654	0.1 ± 0.4 mg% vs. 0.2 ± 0.4 mg%, p = 0.803
Hospitalization	41/100 (41.0%) vs. 44/87 (50.6%), p = 0.190, Odds ratio = 1.5	7/13 (53.8%) vs. 78/174 (44.8%), p = 0.529, Odds ratio = 1.4
Return visits to the ED within 72 h	16/87 (18.4%) vs. 15/100 (15.0%), p = 0.534, Odds ratio = 1.3	3/13 (23.1%) vs. 28/174 (16.1%), p = 0.455, Odds ratio = 1.6
Either hospitalizations or return visits to the ED within 72 h	49/87 (56.3%) vs. 48/100 (48.0%), p = 0.245, Odds ratio = 1.4	9/13 (69.2%) vs. 88/174 (50.6%), p = 0.194, Odds ratio = 2.2
Need for urological intervention	29/87 (33.3%) vs. 31/100 (31.0%), p = 0.692, Odds ratio = 1.1	4/13 (30.8%) vs. 56/174 (32.2%), p = 0.905, Odds ratio = 0.9
Need for urgent urological intervention	6/87 (6.9%) vs. 11/100 (11.0%), p = 0.446, Odds ratio = 0.6	0/13 (0%) vs. 17/174 (9/8%), p = 0.612, Odds ratio = 0.3

5. Limitations

The sonographic definition we used for perinephric severity is not based of previously established radiological definitions. Nevertheless, to our knowledge there aren't such established radiological definitions for the severity of this sonographic findings, so we had to rely on the definitions of our experienced radiologist for the severity definitions as described above.

6. Conclusions

The significance of the presence of perinephric fluid collection in the management of acute urethral stone obstruction is not well established. Our study results suggest that sonographic evidence of perinephric fluid collection reflects more severe pain in comparison with patients without fluid collection. Up-to-date, the assessment of renal colic with POCUS by an emergency physician, generally centers on the identification of hydronephrosis. This study results suggest perinephric fluid collection as an additional important finding with possible clinical impact. Therefore, an emergency physician should be aware to the presence of perinephric fluid, as part of patient's POUCS evaluation for acute urethral stone obstruction in the ED, and to consider it as a predictor for more severe pain. Further research is required to investigate the significance of perinephric fluid collection with regard to pain management as well as to other aspects of acute management.

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An Institutional Review Board (IRB) approval was granted for this study.

Conflicts of interest

The authors have no conflict of interest to declare.

Author contributions

Granat N and Kleinbaum Y conceived the study and designed the trial. Kleinbaum Y supervised the conduct of the trial and data collection. Tau N re-evaluated the presence and measurements of perinephric fluid. Granat N undertook recruitment of patients and managed the data, including quality control. Klang E provided statistical advice on study design and analyzed the data. Granat N wrote the paper. Kleinbaum Y and Klang E drafted the manuscript, and all authors contributed substantially to its revision. All authors were responsible for the final approval of the version to be published.

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