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Diagnostic performance of pre-management computed tomography findings as a predictor of conservative treatment success in patients with emphysematous pyelonephritis

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Abstract

Background: Emphysematous pyelonephritis (EPN) is one of the most serious urologic emergency which should be diagnosed and treated adequately to prevent impending septic shock and death. Computed tomography (CT) is the gold standard radiologic modality for diagnosis, grading and predicting the outcome. We aimed in this study to define the initial CT radiological findings correlated with EPN conservative management success.

Results: This study involved 54 patients (42 women and 12 males) with a mean age of 48 ± 10 years. EPN grades I, II, III, and IV were noticed in 12, 17, 20, and 5 patients, respectively. Ten patients (18.5%) received successful conservative management. On the other hand, renal drainage was needed in 42 patients (77.8%). Delayed nephrectomy was required in two cases (3.7%). In univariate and multivariate analyses, the absence of hydronephrosis and decreased air locules volume were predictors of conservative treatment success ($P = 0.003$ and 0.01 , respectively).

Conclusions: Conservative therapy should be selected in certain patients of emphysematous pyelonephritis. Decreased air locules volume and the absence of hydronephrosis in pre-admission computed tomography were predictors for conservative therapy success.

Keywords: Computed tomography, Air locules, Success, Emphysematous pyelonephritis, Conservative, Management

Background

Emphysematous pyelonephritis (EPN) is one of the most common necrotizing infection of the renal parenchyma and the perinephric tissues and has been linked to increase the morbidity and mortality [1, 2]. In the previous studies, mortality rates increased up to 40–50% [3]. The presence of ureteric obstruction in accompanying with diabetes mellitus and bacterial infection (*Escherichia coli*) is the main predisposing factors [4]. EPN is

difficult to be diagnosed based solely on history, examination and laboratory investigations. So, radiological imaging is required to confirm the diagnosis.

Over time, radiological methods were evolved passing by inaccurate non-specific methods, i.e., abdominal X-ray and Ultrasound to a more accurate method, i.e., computed tomography (CT). CT allows for more precise staging and is considered the gold standard for diagnosis [2, 5]. Based on CT, two different classifications were adopted [6, 7]. Those classifications were considered a guidance for the optimal treatment for each EPN staging. In spite of that the EPN treatment has been still a matter of controversy.

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Treatment options for EPN have changed from more invasive, i.e., urgent nephrectomy which was associated with more morbidity and mortality [3], to more conservative approaches including medical treatment alone or medical treatment with urinary tract drainage (either percutaneous catheter drainage (PCD) or the use of ureteric stent). In a previous study, medical treatment with antibiotics carries the highest risk of mortality in the presence of risk factors like thrombocytopenia, shock and hemodialysis [2]. In other report [8], conservative management was recommended in case of localized disease only. Other authors recommended PCD insertion as a part of the initial management for EPN because of associated lower mortality rate than medical management [4]. In contrary, others recommended ureteral stenting in a lower stage of EPN [2].

Pre-management CT radiological findings may help in predicting treatment failure or success. In addition, identifying factors responsible for the optimal management may lower patient's mortality and morbidity. Aboumarzouk et al. [1] in a systematic review defined that medical treatment can be an appropriate management in mild cases of EPN. While in sever form drainage must be applied. But, unfortunately, the term mild or sever is not clear. EPN staging is rarely correlated significantly with treatment success or failure [9–16]

Consequently, as a gas-forming disease, air locules volume may play a role in predicting the disease severity and clinical outcome. Elbaset et al. [9] documented that increased air locules volume upsurge the risk of drainage failure of EPN. In this study, we tried to identify

pre-management CT radiological findings responsible for conservative therapy success.

Methods

Patients

All consecutive patients with EPN admitted between January 2000 and December 2016 to our tertiary center were retrospectively assessed. The study was approved by local ethical committee (R.21.06.1357). EPN was diagnosed on the absence of recent history of renal trauma, bladder catheterization or uro-enteric fistula. The clinical diagnosis of EPN is based on the presence of fever with loin pain. In addition to the presence of pyuria and positive urine culture based on laboratory findings without the presence of any other infectious foci. Radiologically, accumulation of gas locules in the kidney parenchyma, perirenal, or pararenal region is the golden sign for diagnosis [8, 9]. Patients who were managed by urgent nephrectomy, presence of uro-enteric fistula, history of renal trauma, absence of pre-management CT and patients with age less than 18 years were excluded. Patients' age, gender, presenting symptoms, associated medical comorbidities, urine culture, serum creatinine in mg/dl, leukocytic count $\times 10^3/\text{cc}$ and serum albumin in gm/dl were identified.

Radiological evaluation using pretreatment CT was reviewed for the presence of distal obstruction, presence of hydronephrosis, grades of EPN [8] and air locules volume in cc^3 which was calculated by summing the volume of air locules using the formula ($\text{Width (W)} \times \text{Height (H)} \times \text{Length (L)} \times 0.52$) in the greatest dimensions [6] (Figs. 1, 2).

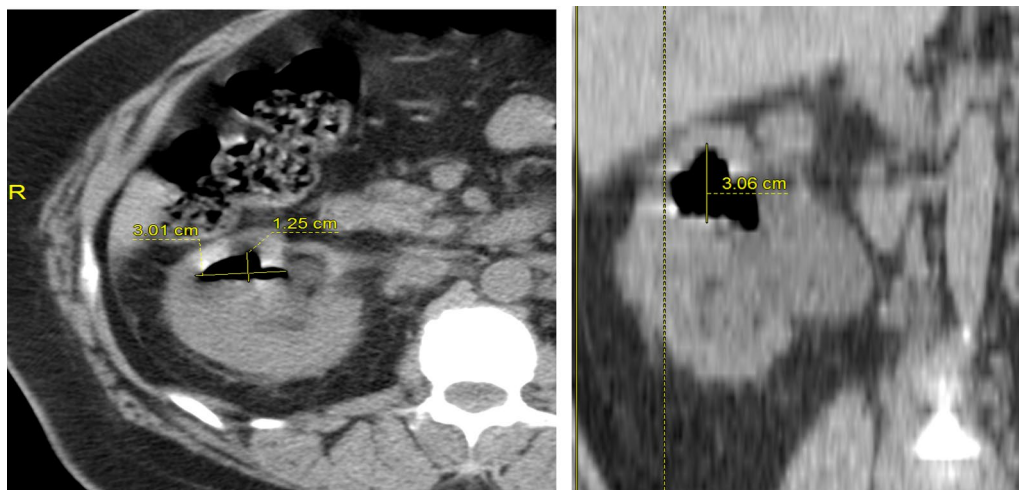


Fig. 1 A 60-years old female patient presented with fever and right loin pain. CT axial and coronal images demonstrate gas locules inside the right upper calyceal group, it measures $3.5 \times 1.2 \times 3.1$ as regard greatest axial and cranio-caudal dimensions with total air locules volume 7 cc^3 . The patient was managed with successful medical conservative therapy and discharged safely

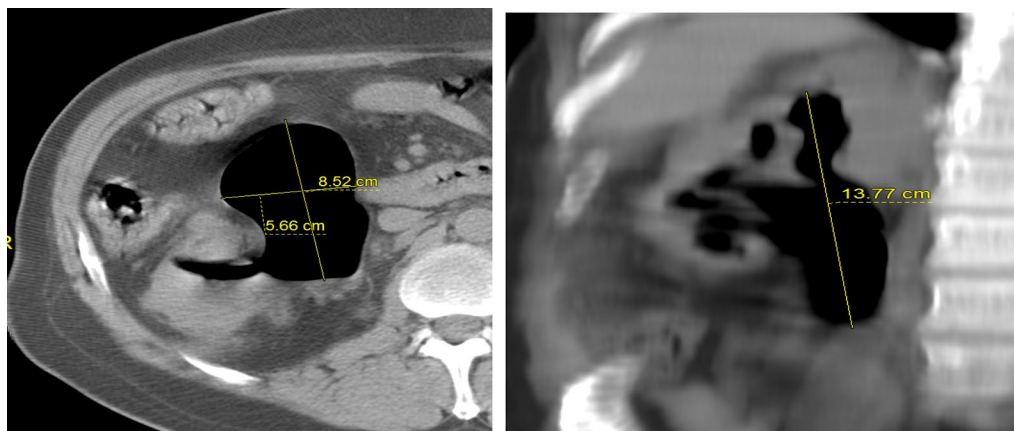


Fig. 2 A 66-years old diabetic female patient presented with high grade fever and right loin pain. CT axial and coronal images demonstrate hydronephrotic changes with gas accumulated in the right pelvicalyceal system, it measures $8.5 \times 5.6 \times 13.7$ as regard greatest axial and cranio-caudal dimensions with total air locules volume 327 cc. the patient was managed unsuccessfully by medical treatment, and drainage was done by ureteric stent

Intervention

Medical management including intravenous broad-spectrum antibiotics (third generation cephalosporin) with adequate intravenous fluids and good glycemic control were initiated then changed according to the urine culture result. A wide bore urethral catheter was inserted at the time of hospital admission and usually removed after clinical and radiological improvement. Successful conservative therapy defined by an improvement in clinical status (absence of fever, improved leukocytic count, and discharged alive without intensive care unit (ICU) admission). In addition to clinical improvement, air locules clearance at follow up imaging was a radiological finding for improvement in X-ray, ultrasound or CT if needed. Persistence of symptoms for ≥ 3 days or more is considered failure of conservative medical treatment and patients were either managed by PCD or ureteric stent according to urologist's preference. Patient discharge was considered if there was no fever for more than 48 h with stable vital parameters.

Clinical outcome

Primary outcome was to define radiological findings responsible for conservative treatment success without the need for urinary tract drainage.

Statistical analysis

When appropriate, continuous data were reported as mean SD or median and range. The chi-square test, Mann–Whitney *U* test or Student's sample *t* test were utilized in univariate analysis to detect predictors for conservative medical management success. The receiver operating characteristics (ROC) curve was used to

determine the cutoff values with the best sensitivity and specificity for significant continuous variables in univariate analysis. Logistic regression test was utilized to carry out multivariate analysis. All statistical tests were performed by IBM "SPSS" statistics version (21), and a *P* value of less than 0.05 was considered significant.

Results

The study involved initially 62 patients admitted with a picture coping with EPN. Eight patients were excluded (four patients due to the absence of pre-management CT, two patients were managed by urgent nephrectomy and other patients were presented post-abdominal trauma). Lastly, 54 patients (42 women and 12 men) were included with a mean age (\pm SD) of (48 ± 10) years. Pre-management CT imaging showed that I, II, III, and IV EPN grades were noted in 12, 17, 20, and 5 patients, respectively. In ten cases (18.5%), conservative therapy was successful without need for further intervention (Table 1).

In case of conservative management failure, renal drainage was required in the other 42 cases (77.8%) due to persistent symptoms, where 25 patients were managed by using PCD and 17 patients were managed by ureteric stents. Twenty patients (37%) admitted to ICU due to septic shock and five of them (25%) died after ICU admission. Delayed nephrectomy post-drainage was required in two cases (3.7%) both were stage III EPN.

In univariate analysis, decreased renal air locules volume in addition to the absence of hydronephrosis were statistically significant predictors of conservative therapy success ($P=0.002$ and 0.04 , respectively) (Table 1).

To detect the best cutoff value of air locules volume with the best sensitivity and specificity, ROC curve

Table 1 Univariate analysis for successful conservative management in patients with EPN

Variables	Conservative treatment success (N = 10)	Conservative treatment failure (N = 44)	P value
A. patient's demographics and clinical data			
Age* (years) (mean \pm SD)	46 \pm 10.7	49.6 \pm 9.9	0.5
Gender** (no. of pts.) (%)			
Male	2 (20)	10 (22.7)	0.5
Female	8 (80)	34 (77.3)	
Fever** (no. of pts.) (%)			
Yes	8 (80)	42 (95.5)	0.2
No	2 (20)	2 (4.5)	
Uncontrolled DM ** (no. of pts.) (%)			
Yes	6 (60)	36 (81.8)	0.2
No	4 (40)	8 (18.2)	
B. Laboratory findings at admission			
Urine Culture** (no. of pts.) (%)			
A. Polymicrobial	2 (20)	12 (27.3)	0.1
B. E.coli	5 (50)	18 (40.9)	
C. klebsiella	2 (20)	11 (25)	
D. others (Candida Albicans)	1 (10)	3 (6.8)	
Serum creatinine* (mg/dl) (Median (range))	1.5 (1–6.1)	1.6 (1.2–8.4)	0.8
WBCS $\times 10^3$ /cc # (Mean \pm SD)	12.9 \pm 4.4	14.1 \pm 5.1	0.06
Albumin* (gm/dl) (Mean \pm SD)	2.6 \pm 0.7	2.4 \pm 0.6	0.4
C. CT radiological data at admission			
Presence of hydronephrosis** (no. of pts.) (%)			
Yes	2 (20)	31 (70.5)	0.04
No	8 (80)	13 (29.5)	
Presence of distal obstruction** (no. of pts.) (%)			
Yes	4 (40)	30 (68.2)	0.1
No	6 (60)	14 (31.8)	
Renal air locules volume cc ³ # (median (range))	17 (4.4–89)	112 (2–1440)	0.002
Types** (no. of pts.) (%)			
Type I	5 (50)	7 (15.9)	0.4
Type II	3 (30)	14 (31.8)	
Type III	1 (10)	19 (43.2)	
Types IV	1 (10)	4 (9.1)	

*Independent sampled t test, **Chi-square test and # Mann–Whitney test and No. of pts. = number of patients

was used. Air locules volume ≤ 54 cc was the best cut-off value as a predictor for treatment success (sensitivity and specificity of 70% and 90%, respectively) (Fig. 3).

In a multivariate analysis, the same predictors were significantly increased the risk for treatment success (absence of hydronephrosis and decreased air locules volume ≤ 54 cc) with a 5.5- and 12-fold risk of conservative therapy success, respectively ($P = 0.003$ and 0.01 , correspondingly) (Table. 2). Neither distal ureteric obstruction nor the grades of EPN was a significant predictor of conservative treatment success.

Discussion

Awareness to EPN diagnosis and proper management is required due to life-threatening nature of associated septic complications. Proper initiation of medical treatment using adequate intravenous fluid, antibiotics in addition to electrolyte resuscitation and glycemic control can be helpful. Further treatment is either to continue conservative medical treatment with antibiotics alone, drainage with PCD or ureteral stent under the umbrella of antibiotic therapy or urgent nephrectomy may be required according the clinical situation and the disease severity.

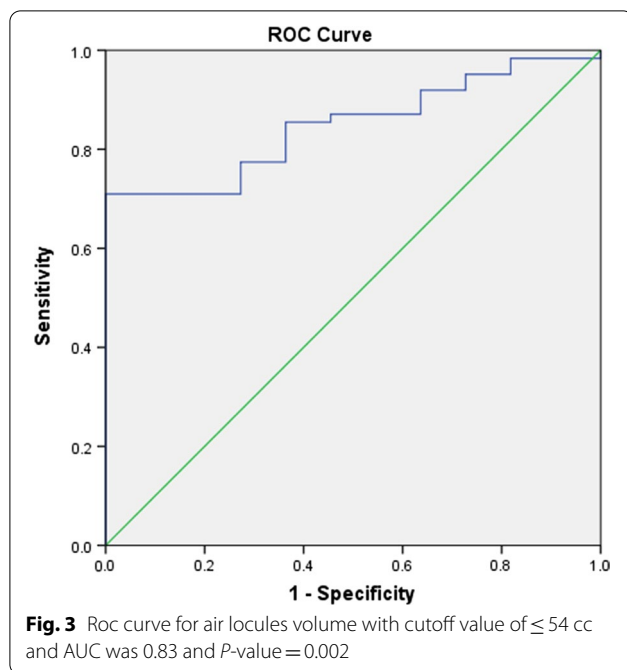


Table 2 Multivariate analysis of factors affecting the success of conservative management in patients with EPN

Variable	Logistic regression analysis	
	95% CI (lower–upper)	P-value
Absence of hydronephrosis	5.5 (1.3–9.57)	0.003
Renal air locules volume ≤ 54 cc	12 (1.96–21.65)	0.01

The management of EPN has been progressed from invasive approach to more conservative treatment. Historically, Ahlering et al. [5] reported higher mortality rate among patients with EPN managed by urgent nephrectomy reaching 42%. Recently, PCD becomes one of the most effective treatment for EPN in association with medical management. This combination lowers the risk of mortality as a rapid noninvasive drainage method with preserving renal units.

In a retrospective study, it was reported that the successful EPN management with antibiotics alone treatment was noted in 40%, and in combined medical treatment with PCD drainage, treatment was successful in 80%. Conservative management failure was noted with associated clinical risk factors as thrombocytopenia, shock, and hemodialysis. In the absence of the previously mentioned risk factors, the success rate with conservative management was 100% [2].

Huang and Tseng [6] reported that conservative management could be successful in case of mild cases (class I and class II) EPN in addition to massive EPN (class

III and IV) with <2 risk factors (thrombocytopenia, increased serum creatinine, shock and confusion) [6]. In a previous multicenter study, it was reported that medical management success was observed in 93.3% of patients (14 out of 15 patients) [7]. In another study, the failure rate of conservative management was observed in nearly one third (32.6%) of patients (14/43). Severe hypoalbuminemia, renal injury with hemodialysis, and polymicrobial infections were significantly associated with failure of conservative treatment [8].

In our study, success rate of conservative medical management was observed in only 18.5% of total included patients. Lower rate of medical management success may be related to increase the incidence of drug resistance due to increasing the global use of antibiotics before admission. By other words, the causative bacteria that produce extended-spectrum beta-lactamase (ESBL) can reduce the efficacy third generation cephalosporins and make medical treatment alone usually ineffective [9].

Vast of the previous studies discussed mainly patient's clinical status in addition to laboratory findings at the time of admission and their relationship with conservative management success or failure. On contrary, the relationship between CT-based radiological findings and treatment outcome is seldom discussed and is still a matter of debate.

Huang and Tseng [6] noted that higher mortality correlated with higher EPN stage. Furthermore, Falagas et al. [10] concluded that bilateral renal affection and EPN type I category (according to Wan radiological classification) were associated with higher mortality. In another study, it was concluded that EPN staging of 3B or 4 was the most reliable predictor of poor outcome [11]. On the other hand, some authors did not find any correlation between radiological staging and initial success with conservative management [12]. Boakes et al. [13] suggested that radiological grade of EPN alone was not sufficient to determine the pattern of treatment. The same conclusion was adopted by other studies [14, 15].

Subsequently, air locules volume calculation at admission can be a reliable marker for disease severity. As postulated that the mechanism of gas formation in EPN is "the gas chamber theory". This theory was based on the presence of gas-forming organisms, poor diabetic control, and poor renal vascularity in addition to immune insufficiency [6]. Increased the volume and the number of renal air locules may be linked to the severity of EPN infection, increased the bacterial load and impaired glucose control.

In a previous study, Elbaset et al. [16] documented that higher air locules volume may be associated with different drainage methods failure (either PCD or ureteral stent) and poor clinical outcome [16]. In our

study, lower air locules volume $\leq 54 \text{ cc}^3$ was a predictor for conservative medical treatment success. In the latter group, the majority of patients were presented with lower EPN staging (EPN stage I and II), only six patients presented with uncontrolled diabetes, the majority of isolated culture was *E.coli* and the minority was polymicrobial infection, in addition the total leukocytic count was lower in patients with successful conservative treatment compared with patients who failed conservative treatment. All previous clinical and laboratory data, while they are statistically insignificant, indicate that the load of infection was lower in patients with successful conservative management and may be reflected by lower air locules volume in affected renal unit.

The presence of hydronephrosis and urinary stasis provide the time and opportunity for bacteria to adhere to the urinary tract epithelium, multiply, and infect the host [16]. The presence of hydronephrosis increase the risk of gas chamber theory by increased the pelvicalyceal system pressure and compromised renal circulation with impaired gas transportation [6]. In the absence of stone obstruction, necrosis of renal tissue may predispose to more pelvicalyceal system obstruction which by its turn increase the rate of infection [6]. In-line with these theories, we found that the absence of hydronephrosis was a predictor for conservative management success.

The main limitation is the retrospective nature of the study with inherent selection bias. Small sample size is another limitation. In spite of these limitations, our study highlights the importance of CT markers for patients who can get benefit from medical management safely without time delay without the need for urinary drainage. Further studies are needed to confirm our findings.

Conclusion

Pre-management computed tomography characteristics can help in the optimal patient selection for successful conservative treatment without time delay. Conservative therapy can be selected in certain patients of emphysematous pyelonephritis with lower bacterial load with mild pattern of the disease. Lower air locules volume ($\leq 54 \text{ cc}^3$) and the absence of renal hydronephrosis were predictors of conservative therapy success.

Abbreviations

CT: Computed tomography; EPN: Emphysematous pyelonephritis; ROC: Receiver operating characteristic; AUC: Area under the curve; PCD: Percutaneous drainage; ICU: Intensive care unit.

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Members of radiology department and Urology department members of Urology and Nephrology Center, Mansoura University, Egypt.

Author contributions

Contributed in data collection: MA, MZ, FKG, MIA and AE. Data analysis and Writing: MAB and AA. Manuscript has been read and approved for submission by all named authors.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Research Ethics Committee of the Faculty of Medicine at Mansoura University in Egypt. After receiving approval from the institutional review board number R.21.06.1357.

Consent for publication

All patients included in this research gave written informed consent to publish the data contained within this study.

Competing interests

The authors declare that they have no competing interests.

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