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Kidney preservation protocol for management of emphysematous pyelonephritis: Treatment modalities and follow-up

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KEYWORDS

Emphysematous
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ABBREVIATIONS

EPN, emphysematous pyelo-
nephritis;
NCCT, non-contrast CT;
US, ultrasonography;
PCN, percutaneous
nephrostomy;
PCD, percutaneous tube
drain

Abstract Objectives: To present treatments for kidney preservation in the management of emphysematous pyelonephritis (EPN), and to evaluate the functional outcome of preserved kidneys during the follow-up.

Patients and methods: The computerized files of patients with EPN from 2000 to 2010 were reviewed. After initial resuscitation, ultrasonography-guided percutaneous tubes were placed for drainage of infected fluid and gas. A radio-isotopic renal scan was done after stabilization of the patients' condition. Preservation of the affected kidney was attempted when the differential function was >10%. A renal isotopic scan was taken during the follow-up to evaluate renographic changes in preserved kidneys.

Results: The study included 33 kidneys in 30 consecutive patients (mean age 51.7 years, SD 10.9). Kidney preservation was applicable for 23 kidneys (20 patients). Preservation methods included percutaneous nephrostomy for 12, percutaneous tube drain for two and conservative treatment for nine kidneys (six patients). Nephrectomy was performed for 10 kidneys (emergency in three and delayed in seven). The frequency of post-treatment septic shock after kidney preservation (10%) was significantly lower than after nephrectomy (20%, $P = 0.005$). The overall mortality rate

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was 7% (two patients). The follow-up was completed for 13 patients with 15 preserved kidneys for a mean duration of 21 months. During the follow-up, differential renographic clearance of the affected kidney was stable in 13 of 15 while two kidneys showed improvement.

Conclusions: Kidney preservation should be the primary goal in the treatment of EPN when the differential renal clearance is > 10%. It was associated with fewer complications than nephrectomy and the follow-up showed a favourable functional outcome of the preserved kidneys.

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Introduction

Emphysematous pyelonephritis (EPN) is a rare, severe infection of the kidney that results in formation of gas in the collecting system, renal parenchyma, or perinephric tissue [1]. It is most commonly seen in diabetics and immunocompromised patients [2]. The clinical features of EPN are indistinguishable from those of severe acute pyelonephritis and the diagnosis can be suspected after a poor response to conventional antibiotic treatment [3]. It is a life-threatening condition, with mortality rates of 11–42% [1–4].

The radiological diagnosis depends on detecting gas in or around the kidney by plain X-ray film of the abdomen or by ultrasonography (US), which can also diagnose obstruction and associated stones or collections. Non-contrast CT (NCCT) can be used to confirm the diagnosis and various radiological classifications have been suggested based on CT. Wan et al. [3] described two distinct radiological classifications of EPN, while Huang and Tseng [1] classified EPN into four categories.

The treatment of EPN has been a subject of controversy. Emergency nephrectomy after medical control of septicemia and diabetes was reported [5,6]. The availability of effective antibiotics and advances in image-guided procedures resulted in the use of less aggressive surgical approaches such as percutaneous drainage [7–9]. Moreover, some authors suggested medical treatment alone [10]. In recent years the goals of treatment included improving the survival rate and preserving the affected kidney whenever possible [11].

Risk factors for death from EPN were previously assessed in a meta-analysis [2], but studies discussing risk factors for nephrectomy are scarce [12] and, to the best of our knowledge, there is no study evaluating differential renal functional changes after preserving the affected kidney. The current study was conducted to present kidney preservation protocols for managing EPN, to determine risk factors predicting the need for nephrectomy, and to show differential renographic changes during the follow-up of patients with preserved kidneys.

Patients and methods

The computerized files of patients with acute pyelonephritis who were treated in our centre from January 2000 to December 2010 were reviewed retrospectively. The study included patients with EPN who had evidence of gas in the kidney, perinephric or pararenal spaces by NCCT. We excluded patients with possible external introduction of gas into the urinary system (e.g. fistula with gastrointestinal system, recent ureteric catheterization or recent percutaneous renal procedures).

The patients' files were reviewed for medical and surgical history, clinical presentation, predisposing factors, laboratory and radiological investigations, treatments, complications and outcomes. Laboratory investigations included urine analysis and

culture, serum creatinine estimation, complete blood count, and random blood sugar and liver function tests. Radiological investigations included abdominal US and NCCT, done to confirm the diagnosis and for classification.

Patients were classified according to Huang and Tseng [1], who classified EPN as: Class I, gas in the collecting system only; class II, gas inside the renal parenchyma with no extension into the extrarenal space; class IIIa, extension of gas into the perinephric space; class IIIb, extension of gas into the pararenal space; and class IV, bilateral disease or EPN in a solitary kidney.

Treatment started by resuscitation of patients in shock, and blood sugar control for diabetic patients. Intravenous antibiotics (third-generation cephalosporins) were administered for all patients at time of presentation. In patients with obstruction or extensive gaseous collections, the infected fluid and gas were drained using an US-guided percutaneous nephrostomy (PCN) or percutaneous tube drain (PCD). The response to treatment was monitored using a plain abdominal film and US for some patients, or NCCT in others. After stabilising the patient's condition, a renal radio-isotopic scan using ^{99m}Tc – MAG3 was taken to estimate the differential function of the affected kidney. Preservation of the affected kidney was attempted when the differential function was > 10% [13].

Patients with preserved kidneys were recruited for follow-up; they had a clinical examination, urine analysis, plain film, US and renal isotopic scan to evaluate changes in differential function of the affected kidney. A change in renographic clearance of > 5% of the pretreatment value was considered as improvement or deterioration, while changes within 5% were defined as stable function [13].

The data were analysed using standard methods; to determine significant prognostic factors for nephrectomy, univariate analysis (chi-square test) and multivariate (logistic regression analysis) were used, with $P < 0.05$ taken to indicate statistical significance.

Results

The study included 33 renal units in 30 consecutive patients, as three patients had bilateral EPN. The mean (SD, range) patient age was 51.7 (10.9, 22–80) years. The patients' demographics, presentations, predisposing factors and CT classes are shown in Table 1. Six patients needed admission to the intensive care unit to manage septic shock and three presented with acute renal failure. Urine cultures were positive in 18 patients (60%); the most frequently isolated organism was *Escherichia coli* in 11 patients (60%), while *Klebsiella* species were responsible for the remaining positive cultures.

Kidney preservation was attempted for 23 kidneys in 20 patients; preservation methods included PCN for 12 kidneys, conservative (medical) treatment for nine (six patients) and

Table 1 Demographics, presentations and predisposing factors of 30 patients with EPN.

Variable	N (%)
Gender	
Male	8 (27)
Female	22 (73)
Affected side	
Right	12 (40)
Left	15 (50)
Bilateral	3 (10)
Presentation	
Fever and loin pain	21 (70)
Shock	6 (20)
Acute renal failure	3 (10)
Predisposing factors:	
Diabetes mellitus	23 (77)
Renal calculi	2 (7)
Ureteric calculi	3 (10)
Immunocompromise	2 (7)
CT Class:	
I	7 (23)
II	8 (27)
IIIa	7 (23)
IIIb	3 (10)
IV ^a	5 (17)

^a Three patients had bilateral disease and two had solitary kidneys.

PCDs for extensive para-renal gaseous collection in two (Fig. 1). Nephrectomy was used for 10 kidneys (emergency in three and delayed after PCN in seven). Table 2 summarizes the results of the univariate statistical analysis of risk factors for nephrectomy. Thrombocytopenia was the only statistically significant factor ($P = 0.009$) on univariate analysis, but there was no significant factor on multivariate analysis.

Post-treatment septic shock developed after emergency nephrectomy in two of 10 patients, and after kidney preserva-

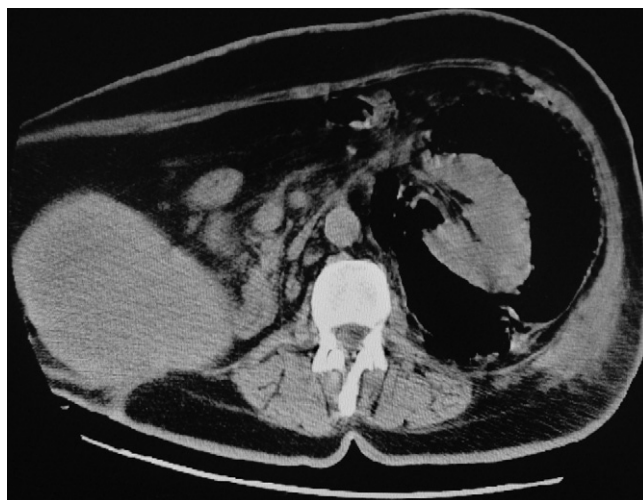


Figure 1 NCCT (axial scan) showing extensive gaseous collection affecting the parenchyma of the left kidney and extending to the para-renal space (class IIIb).

tion in two of 20 patients (10%); the difference was statistically significant; $P = 0.005$). The overall mortality rate was 7% (two patients); the first presented with septic shock after a trial medical treatment of acute pyelonephritis for many days before presentation to our centre, and trial resuscitation in the intensive care unit failed. The second death was due to failed treatment of septic shock after emergency nephrectomy of the affected kidney.

Among patients who survived, the kidney was preserved in 23 of 31 affected kidneys (74%). Any calculi were treated after 2 weeks of infection control and stabilization of the general condition, with percutaneous nephrolithotomy in two and ureteroscopy in three patients. The follow-up was completed for 13 patients with 15 preserved kidneys for a mean (range) of 21 (3–55) months. The function of the affected kidney was stable in 13 of 15 while two kidneys showed an improvement in selective clearance from 25% and 50% before treatment to 37% and 60% during the follow-up, respectively.

Discussion

EPN is a life-threatening infection characterized by the presence of gas in the renal parenchyma and the surrounding tissues. Diabetes mellitus was the most frequently reported predisposing factor for developing EPN, as it constituted 80–100% of patients [5,14,15]. Of the present patients, 77% were diabetic, and the second predisposing factor was urolithiasis; the same was reported by Kapoor et al. [12].

The clinical presentations of EPN among the present patients were similar to those reported previously, with loin pain and fever (70%) being the predominant symptom [7,8,16]. Patients who had delayed treatment presented with septic shock, and those with a solitary kidney presented with acute renal failure. Urine culture was positive in 60% of the present cases, unlike the value of 98% reported by Huang and Tseng [1]. With the virtually unlimited access of patients to antibiotics without prescription, most were likely to have tried self-medication or would have received antibiotics from the referring doctor. This ultimately might give false-negative cultures. *E. coli* was the predominant organism in cases with positive cultures, and these findings were consistent with the other reports [4,9,17].

Radiological detection of gas in and around the kidney is diagnostic for EPN; US is a good screening method, and it is useful in the diagnosis of stone disease and upper urinary tract obstruction. A plain X-ray of the abdomen can also detect gas in the renal region. NCCT was reported to have the highest diagnostic accuracy (100%) for EPN [9]. Therefore, NCCT was the investigation of choice, not only for diagnosing EPN but also for classifying patients into different categories [1,3,9].

Previously EPN was considered as a surgical emergency because of the high mortality rate. Falagas et al. [2] conducted a meta-analysis of seven reports including 175 patients with EPN to identify risk factors for mortality. They found an overall mortality rate of 25% (11–42%). Factors associated with increased mortality rate were conservative treatment alone, bilateral EPN, type I EPN according to the classification of Wan et al., and thrombocytopenia. More recently, Kapoor et al. [12] reported a mortality rate of 13% of 39 patients with EPN. They concluded that altered mental status, thrombocytopenia, renal failure and severe hyponatraemia at presenta-

Table 2 Univariate statistical analysis of risk factors for nephrectomy in 33 kidneys with EPN.

Factor	Preserved kidney <i>n/N</i> (%)	Nephrectomy, <i>n/N</i> (%)	<i>P</i>	Odds ratio (95% CI)
Gender			0.396	2.133 (0.363–12.54)
Male	8/10	2/10		
Female	15/23 (65)	8/23 (35)		
Age, years			0.441	0.533 (0.119–2.408)
< 50	8/13	5/13		
> 50	15/20 (75)	5/20 (25)		
Side			0.779	1.250 (0.263–5.936)
Right	11/15	4/15		
Left	12/18	6/18		
Diabetes mellitus			0.911	1.111 (0.177–6.990)
No	5/7	2/7		
Yes	18/26 (69)	8/26 (31)		
Obesity			0.909	1.091 (0.247–4.817)
Not obese (BMI < 30)	12/17	5/17		
Obese (BMI > 30)	11/15	5/15		
Renal obstruction			0.853	1.154 (0.255–5.223)
No	10/14	4/14		
Yes	13/19 (68)	6/19 (32)		
CT class			0.730	0.769 (0.174–3.409)
I or II	10/15	5/15		
III or IV	13/18	5/18		
Serum creatinine, mg/dL			0.198	0.325 (0.056–1.880)
< 2	13/21 (62)	8/21 (38)		
≥ 2	10/12	2/12		
Leukocytosis ^a			0.383	1.950 (0.431–8.828)
No	13/17	4/17		
Yes	10/16	6/16		
Thrombocytopenia ^b			0.009	14.67 (1.371–156.9)
No	22/28 (79)	6/28 (21)		
Yes	1/5	4/5		

^a Blood leukocyte count > 12,000 dL⁻¹.

^b Platelet count < 140,000 dL⁻¹.

tion were significantly associated with death. In the present study the mortality rates were significantly lowered to 7%. The better mortality rate in our series and that of Aswathaman et al. [11] was the result of efficient resuscitation followed by early percutaneous drainage if there was obstruction or no improvement of the patient's condition on conservative treatment alone.

Emergency nephrectomy was considered by some authors as the surgical treatment of choice and a life-saving procedure for treating EPN [5,6]. This taboo was also rejected in recent years and a new treatment strategy of kidney preservation emerged [8–11]. The reasons for this change were the high mortality rates of emergency nephrectomy (17.6–40%) [5,6] and advances in image-guided procedures for drainage of the gas and infected fluids, using PCDs [9,10]. Chen et al. [8], in their experience with 25 patients, suggested that percutaneous drainage is safe and effective for EPN, and that can result in cure. Moreover, surgical intervention often poses a substantial risk for patients with haemodynamic instability. In the present patients, methods of kidney preservation were associated with a significantly lower complication rate (10%) than for nephrectomy (20%), whether these nephrectomies were early or delayed after drainage.

Somani et al. [9] published a systematic review of 10 studies on 210 patients with EPN. They found that the highest mortality rate (50%) was with medical treatment alone, followed by emergency nephrectomy (25%), while percutaneous drainage was associated with a 13.5% mortality rate and the lowest

mortality (6.6%) was reported with percutaneous drainage then elective nephrectomy. They concluded that percutaneous drainage should be part of the initial management for EPN because it was associated with a lower mortality rate than medical management or emergency nephrectomy. The advantages of percutaneous drainage include stabilization of patients' condition, treatment of underlying contributory factors, and a decreased risk associated with nephrectomy should surgery later be required. Our results support these conclusions, as there was one death due to prolonged medical management and another after emergency nephrectomy.

Conservative (medical) treatment for EPN was suggested by some authors [7,10,11]. Aswathaman et al. [11] reported complete success for conservative treatment in patients who had no risk factors such as thrombocytopenia, shock, altered sensorium, and haemodialysis. Among the present patients, it was successful in six patients with nine diseased kidneys. We recommend considering this method for patients with localized disease (class I or II in the Huang classification) who have no renal obstruction. When patients have EPN in a solitary kidney or bilateral EPN, conservative treatment, and drainage if there is a poor response, should be tried before embarking on nephrectomy; this might help to obviate life-time renal dialysis [8].

Risk factors for nephrectomy were studied by Kapoor et al. [12] in a retrospective study of 39 patients. They found that extensive renal parenchymal destruction of > 50% (based on CT) significantly predicted the need for nephrectomy (*P* < 0.001). In the present series there was no statistically significant factor (on multi-

variate analysis), possibly because there were too few nephrectomies (10 kidneys) or failure of all preoperative factors to affect the decision for nephrectomy. Based on our observations, we believe that the primary goal in treating EPN should be preservation of the affected kidney unless its renographic clearance is < 10%.

The main limitation of our study is the retrospective nature, but this was the main limitation of all previously published series of EPN. The main advantage of this study is that it confirmed objectively, for the first time, that kidney preservation in patients with EPN is beneficial because the preserved kidneys maintained their function during the follow-up.

In conclusion, kidney preservation should be the primary goal in treating EPN when the differential renal clearance is > 10%, because it was associated with fewer complications than nephrectomy. The kidney-preservation protocol includes adequate resuscitation, diabetic control and antibiotic coverage, followed by early drainage of obstructed systems or para-renal infected fluid and gas. The follow-up showed a favourable functional outcome of the preserved kidneys.

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