Renal salvage, an achievable goal in patients with emphysematous pyelonephritis: Outcomes of an algorithmic renal preserving strategy

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Abstract

Introduction: Emergency nephrectomy has been the time-honored treatment of choice for emphysematous pyelonephritis (EPN), a fatal gas-forming necrotizing infection. Recent years have seen a shift toward nonextirpative approach aimed to achieve higher rates of renal salvage, limiting the indications for nephrectomy to severe grades of the disease. This study aimed at analyzing the role of initial renal preserving measures algorithmically applied across grades of EPN.

Materials and Methods: We prospectively analyzed the clinical data and outcome of 36 consecutive patients of EPN in 5 years' study period, treated by renal preserving measures, which include aggressive resuscitation, parenteral antibiotics, effective drainage of infected fluid/gas, and relieving the urinary tract obstruction. Huang-Tseng computed tomography-based classification system was used to categorize the patients as well as to employ suitable treatment modality.

Results: The mean age of the patients was 57.5 ± 12 years with female preponderance (2:1). Diabetes mellitus (97%) was the most common associated factor. *Escherichia coli* was (72%) the most frequent causative organism found. Urinary tract obstruction was seen in 27 patients (75%) attributable to ureteric calculi, renal papillary necrosis, ureteric stricture, and fungal bezoar in the descending order of frequency. Only 2 (6%) out of 36 patients managed according to our hospital renal salvage protocol required salvage nephrectomy. The overall survival rate was 94%.

Conclusion: Our hospital-based algorithmic renal preserving strategy not only improved the survival but also decreased the need for nephrectomy.

Keywords: Double J stenting, emphysematous pyelonephritis, Haung-Tseng classification, percutaneous nephrostomy

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INTRODUCTION

Emphysematous pyelonephritis (EPN) is a severe necrotizing infection of the kidney characterized by gas formation within the collecting system, renal parenchyma, and/or perirenal tissues.[1,2] In 1898, Kelly and MacCallum

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first described the gas-forming kidney infection.[3] Thereafter, various terminologies such as renal emphysema and pneumonephritis were in wide usage for this condition. Later in 1962, Schultz and Klorfein recommended the term Emphysematous Pyelonephritis which relates infective pathology of the kidney and gas formation.[4]

It occurs most commonly in patients with uncontrolled diabetes mellitus (DM), the combination which accounts for 95% of the cases. Its incidence is higher in females, probably due to increased susceptibility to urinary tract infections (UTIs). Enteric Gram-negative facultative anaerobes are responsible causative organisms in most of the cases and *Escherichia coli* remains the most common among them.[5]

Pathogenesis of EPN is multifactorial, including high-tissue glucose levels, presence of gas-forming microorganisms, poor tissue perfusion due to microangiopathy, reduced host immunity, and the presence of urinary tract obstruction. The above-mentioned factors are prevalent in patients with long-standing uncontrolled diabetes and provide a favorable microenvironment for the Gram-negative facultative anaerobic pathogens to thrive.[6] Production of the gas is due to the fermentation of tissue glucose and lactate.[7] Huang and Tseng performed image-guided needle aspiration of the gas from the EPN kidney for analysis and found carbon dioxide and hydrogen to be the main constituents.[8]

EPN often has a fulminating course and can be fatal if not recognized and treated promptly.[5,9] Earlier authors recommended emergency nephrectomy (EN) along with medical management (MM) as the treatment of choice.[10] With this approach, the mortality rate was up to 78% until 1970s.[11] In recent decades, the management strategy has gradually shifted toward renal salvage approaches such as percutaneous tube drainage (PTD) or double J stenting (DJS) along with parenteral antibiotic coverage.[9,12] Such management strategies resulted in a significant drop in the mortality rate to 21%.[9] However, nephrectomy is still being considered as a first-line modality, particularly in higher grades of EPN with the presence of high-risk prognostic factors.[8,13,14] There is no consensus on the effective management of EPN till date.[9] The current study aimed to analyze the role of initial renal salvage measures in the management of EPN.

MATERIALS AND METHODS

Study population

This was a prospective and observational study conducted at our hospital between January 2014 and June 2018. Institutional ethics and scientific committee approval was obtained. Patients who were diagnosed with EPN and managed in our hospital during the study period were included. Those who were inadequately worked up or initially received treatment at outside hospitals were excluded.

Methodology

According to our hospital protocol, all the patients who were suspected to have EPN clinically underwent computed tomography (CT) scan to confirm the diagnosis and stage the disease. Huang-Tseng CT-based classification system was used to categorize the patients as Class I: Gas in the collecting system only; Class II: Gas in the renal parenchyma without extension to extrarenal space; Class IIIA: Extension of gas or abscess to perinephric space; Class IIIB: Extension of gas or abscess to pararenal space (beyond the Gerota fascia); and Class IV: Bilateral EPN or solitary kidney with EPN.[8] We further divided Class II into two subgroups, i.e., <50% and >50% of renal parenchyma affected. Once the diagnosis was established, irrespective of the stage of the disease and the associated risk factors, all patients were initially managed with renal salvaging measures which include aggressive resuscitation, glycemic control, parenteral antibiotic coverage followed by early drainage of the infected fluid as well as gas and release of urinary tract obstruction [Figure 1]. The drainage procedures commonly employed are percutaneous catheter drainage (PCD) or open tube drainage (OTD). To relieve the urinary tract obstruction, DJS or percutaneous nephrostomy (PCN) was performed [Figure 2]. Nephrectomy was reserved only for the patients with progressive disease or those deemed to be having refractory sepsis inspite of initial renal salvaging measures [Figure 3]. Clinical variables of the study patients including demographics, presenting features, predisposing

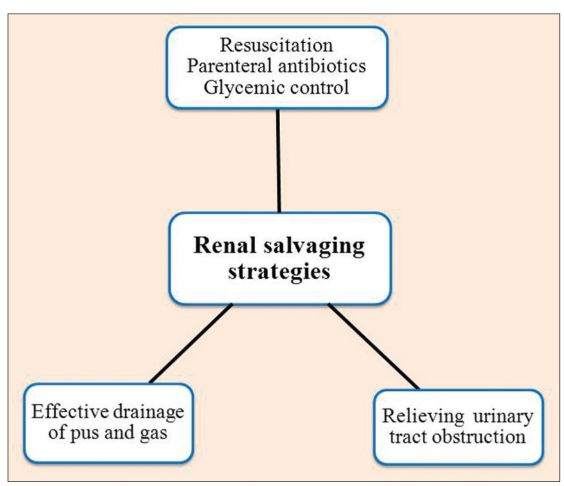

Figure 1: Various initial renal salvage strategies in the management of emphysematous pyelonephritis

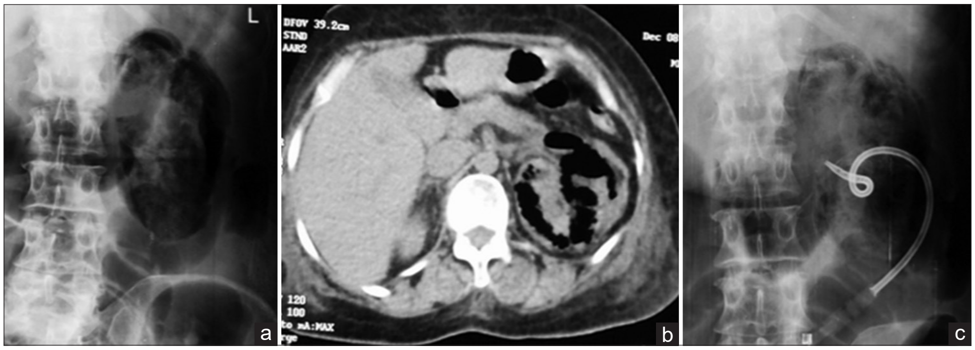

Figure 2: Diabetic patient with poor glycemic control presented with features of acute pyelonephritis (a-b) xxx, (c)

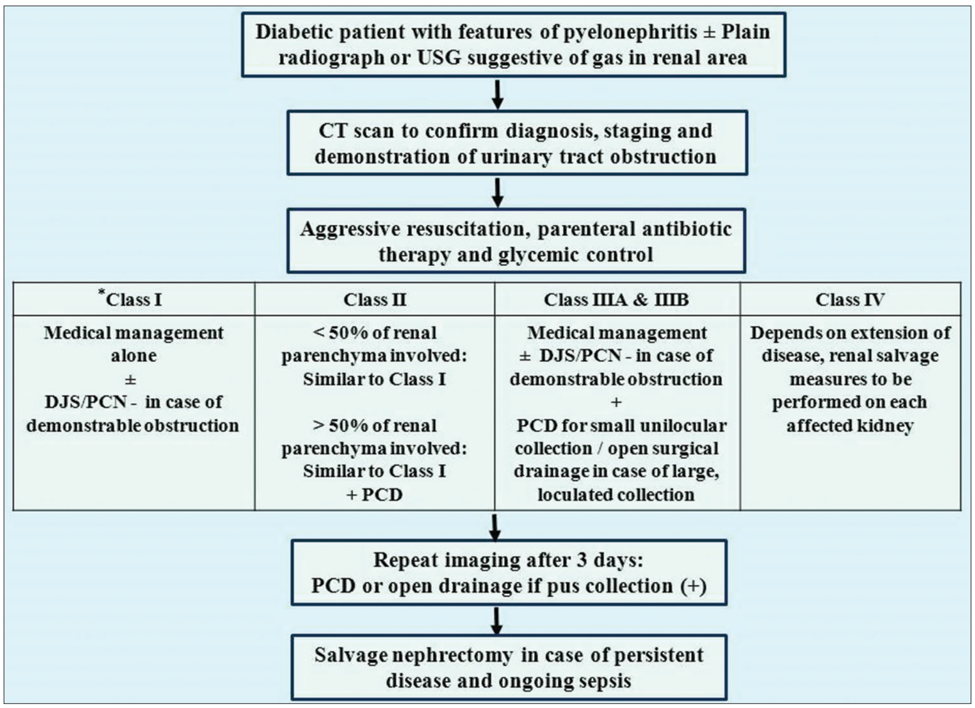

Figure 3: Algorithm of renal salvage protocol in emphysematous pyelonephritis. DJS: Double J stenting, PCN: Percutaneous Nephrostomy, PCD: percutaneous catheter drainage, USG: Ultrasonography, CT: Computerized tomography. *Class I to IV: Huang Tseng classification

factors, laboratory data, imaging findings, microbiological data, mode of treatment, and outcomes were analyzed. Patients belonging to Huang-Tseng Class I and Class II with <50% parenchymal destruction were grouped as low-grade disease. Class II with >50% parenchymal destruction, IIIA, IIIB, and IV categories were grouped as high-grade disease. High-risk prognostic variables were compared between the two groups.

Statistical analysis

Data was analysed using the Statistical Package for the Social Sciences (SPSS) version 20.0 (IBM, Armonk, New York, USA). Two group comparisons were done by unpaired *t*-test. Categorical variables were computed by Chi-square test. Results were expressed as mean ± standard deviation/standard error and percentages. $P < 0.05$ was considered as statistically significant.

RESULTS

In this hospital-based prospective study, data of a total of 36 patients who were diagnosed to have EPN and managed as per our hospital's renal salvage protocols, were analyzed. The mean age of the patients was 57.5 ± 12 years. We observed higher incidence of EPN in females than males (2:1). EPN affected predominantly left kidney (23, 64%) and one patient (3%) presented with bilateral disease. Most common predisposing factor was DM (35, 97%), and most of the study patients, 32 (89%) presented with poorly controlled diabetes, reflected by high levels of glycosylated hemoglobin (HbA1c) [Table 1]. Apart from pyuria (100%) and raised blood glucose levels (97%), other frequently observed laboratory abnormalities were anemia and elevated HbA1c in 32 (89%) patients each. Microbiological data suggest overall culture positivity from the specimens of urine, pus, and blood noted in 30 (83%) patients. *E. coli* was (*n* = 26, 72%) the most common organism detected [Table 2]. Extended-spectrum β-lactamase-producing organisms were found in 39% of the cases.

We demonstrated the cause for urinary tract obstruction in 27 patients (75%) by CT scan or during retrograde ureterography. Ureteric calculi (13, 36%) were responsible for most of the cases followed by papillary necrosis (11, 31%), ureteric narrowing (2, 6%), and fungal ball (1, 3%) in descending order of frequency [Table 1]. Based on the CT findings, the study patients were categorized into Class I (10, 28%), Class II with <50% parenchymal involvement (10, 28%), Class II with >50% parenchymal involvement (3, 8%), Class III A (3, 8%), Class III B (9, 25%), and Class IV (1, 3%). Low-grade disease (20, 56%) includes Class I and II with <50% parenchymal involvement. High-grade disease (16, 44%) includes Class II with >50% parenchymal involvement, Class III A and B, and Class IV patients [Table 2]. Incidence of septic shock ($P = 0.001$), acidosis ($P = 0.001$), haemoglobin ($P = 0.01$), leukocyte count ($P = 0.02$), serum creatinine ($P = 0.04$), and serum albumin levels ($P = 0.01$) were significantly higher in patients with high-grade disease when compared to low-grade disease [Table 3].

All patients were managed initially according to renal salvage protocol [Figure 3]. Among them, four patients (11%) were managed by MM alone which includes aggressive resuscitation, glycemic control, and parenteral antibiotics. DJS/PCN was performed in 16 (44%) patients. PCD ± DJS/PCN was done in seven (19%) patients and OTD ± DJS/PCN was done in 8 (22%) patients. Two patients (6%) who initially underwent PCD were subsequently subjected to undergo OTD as they had frequent clogging of the drain tube and persistence of collection in the perinephric space. Two (6%) patients with ongoing sepsis due to persistent disease in spite of initial renal salvage measures underwent salvage nephrectomy (2, 6%) [Table 1].

The overall survival rate was 94% (34). There were two deaths, one patient died during postoperative period of salvage nephrectomy due to intractable sepsis. Another patient with severe septic shock and acute respiratory distress syndrome at the initial presentation died in spite of aggressive resuscitation and PCD [Table 1].

DISCUSSION

EPN runs a fulminant course due to its association with

Table 1: Demographics, clinical profile, laboratory parameters, treatment modalities, and outcome (*n*=36)

Variable	Number of cases (%)
Age	57.52±12
Female/male	24:12 (2:1)
Affected side (right vs. left vs. bilateral)	13:23:1
Comorbidities	
DM	35 (97)
Hypertension	16 (44)
Chronic kidney disease	5 (14)
Ischemic heart disease	6 (17)
Symptoms	
Fever	29 (81)
Flank pain	35 (97)
Vomiting	11 (31)
Dysuria	10 (28)
Hematuria	1 (3)
Pneumaturia	1 (3)
Abdominal examination	
Flank tenderness (+ve)	27 (75)
Palpable mass (+ve)	7 (19)
Crepitus (+ve)	1 (3)
Cause for obstruction	
Papillary necrosis	11 (31)
Ureteric calculus	13 (36)
Ureteric stricture	2 (6)
Fungal ball	1 (3)
Laboratory data	
Anemia (<11 g/dl)	32 (89)
Hypoalbuminemia (<3 g/dl)	25 (70)
Thrombocytopenia (<1,20,000/µL)	16 (44)
Acidosis (PH <7.4)	7 (19)
Uncontrolled diabetes (HbA1c >7%)	32 (89)
CT classification[a]	
I	10 (28)
II with (<50% parenchyma involved)	10 (28)
II with (>50% parenchyma involved)	3 (8)
IIIa	3 (8)
IIIb	9 (25)
IV	1 (3)
Treatment modalities	
MM alone	4 (11)
DJS/PCN	16 (44)
PCD±DJS/PCN	7 (19)
Open-surgical drainage±DJS/PCN	8 (22)
Salvage nephrectomy	2 (6)
Mortality	2 (6)

[a]CT classification is based on Huang-Tseng classification system. Depending on extent of parenchymal involvement, Class II was subdivided into two groups. MM: Medical management, DJS: Double J stenting, PCN: Percutaneous Nephrostomy, PCD: Percutaneous tube drainage, DM: Diabetes mellitus, CT: Computed tomography, HbA1c: Glycosylated hemoglobin

Table 2: Causative organisms isolated from pus, urine, and blood

Organism	Pus culture	Urine culture	Blood culture	Overall (%)
Escherichia coli	10	20	4	26 (72)
Klebsiella pneumoniae	1	1	1	1 (3)
Enterococcus faecalis			1	1 (3)
Candida albicans		1		1 (3)
Polymicrobial[a]	1			1 (3)
Total (%)	12 (33)	22 (61)	6 (17)	(30 (83)

[a]Citrobacter and Acinetobacter

Table 3: Comparison of various clinical and laboratory prognostic factors between low-grade and high-grade diseases

Parameters	Low Grade[a] (*n*=20; 56)	High Grade[b] (*n*=16; 44)	*P*
Septic shock (+ve)	2	10	0.001*
ESBL producer(+ve)	7	7	0.59
Hemoglobin	10±1.62	8.5±1.19	0.01*
Total leukocyte count[#]	14310±1261	21755±3311	0.02*
Platelet count[#]	259500±29898	163437±41384	0.07
Creatinine[#]	2.06±0.30	3.18±0.45	0.04*
Albumin	3±0.67	2.39±0.69	0.01*
HbA1c	9.76±1.77	9.66±2.51	0.9
Bicarbonate	20±2.91	13±3.58	<0.001*

[a]Huang-Tseng Class I and II with <50% parenchymal involvement, [b]Huang-Tseng Class II with >50% parenchymal involvement, IIIa, IIIb, and IV EPN. All results were expressed as mean±SD. # Mean±SEM, *$P<0.05$ was considered significant. HbA1c: Glycosylated hemoglobin, SD: Standard deviation, ESBL: Extended-spectrum β-lactamase, EPN: Emphysematous pyelonephritis, SEM: Standard error of mean

severe septic complications and demands high level of its awareness among clinicians as it can be fatal if not recognized and treated promptly.[5,15] The clinical profile and demographics of our cohort were similar to those reported previously. For instance, it is more common in females and left kidney is most commonly affected. Female preponderance can be attributed to increased susceptibility to UTIs.[5]

It occurs typically in patients with DM, which accounts for 95% of the reported cases.[5] Very rarely it can occur in nondiabetics in whom the reported predisposing factors were obstructed upper urinary tracts, polycystic kidney disease, renal tumors, end-stage renal disease, drug abuse, and neurogenic bladder.[5,16-19] We came across only a single case of nondiabetic presented with EPN secondary to large ureteric calculus.

As per our protocol, any patient with uncontrolled diabetes and features of acute pyelonephritis underwent CT imaging to look for gas in the renal region and to stage the disease [Figure 3]. In a systematic review including 32 studies and 628 patients by Aboumarzouk *et al*.[12] noted 100% detection rate by using CT scan. It also aids in demonstrating urinary tract obstruction, an another important predisposing factor for EPN.[20]

The reported risk of developing EPN secondary to obstruction is 20%–40%.[5,9] However, we could demonstrate urinary tract obstruction in 27 (75%) of patients. Its higher rate of detection in our study is probably due to routine use of CT scan and retrograde ureterography prior to drainage procedures at our center. Ureteric calculi followed by renal papillary necrosis were found to be responsible for most of the obstructions. Ureteric narrowing and fungal ball were also found in others. We found a high incidence of underlying urinary tract obstruction in patients with EPN in this study compared to what is reported in the literature. It is possible that this higher incidence of obstruction is even more than what we have found. This is probably due to the difficulty in demonstrating certain obstructive causes such as renal papillary necrosis and fungal ball by the commonly employed imaging methods for EPN.[21,22] For example, CT scan is relatively less sensitive than intravenous urogram in detecting papillary necrosis. The sensitivity might even drop when the underlying renal dysfunction precludes the contrast administration.[21] On the other hand, magnetic resonance imaging can be used to detect papillary necrosis when contrast administration is contraindicated, but insensitivity in detecting ureteric stones limits its utility in this setting.[23] Accumulation of the gas in cases of unrelieved urinary tract obstruction can lead to raised intrapelvicalyceal pressure, which can further impair the renal circulation resulting in poor tissue perfusion and infective parenchymal destruction. This would not only provide favorable microenvironment for the offending organism but also make antibacterial therapy ineffective.[7] Hence, it appears that some obstructive mechanism is operational in most cases and relieving obstruction leading to better renal salvage observed in this study strengthens this hypothesis.

Our therapeutic goal was not only to improve survival but also to preserve the renal function by employing different renal salvage measures with respect to the stage of disease. In the past, most of the authors recommended EN along with MM to reduce the mortality rate and shorten the recovery period.[10] This management strategy has been rejected by many in the recent decades. Renal salvage approaches such as PTD or DJS along with parenteral antibiotic coverage have emerged as first-line therapeutic strategies.[9,12] In 1986, Hudson *et al*.[24] first reported a case of EPN treated successfully with fluoroscopically guided percutaneous drainage. Since then, various authors have described successful results with percutaneous drainage.[9,25,26] As DJS can be done endoscopically with minimum morbidity, Das and Pal[27] preferred this as the choice of drainage procedures. Aswathaman *et al*.[28] found that the mean relative function of the conservatively managed EPN kidney was 42%. Therefore, the remaining nephrons in the affected kidney might still function after the eradication of infection.

The mortality rate in patients with EPN was 78% until the late 1970s.[5,11] In the late 1980s, with EN and/or open surgical drainage together with antibiotic therapy as principal therapeutic interventions, it remained at 40%–50%.[5] The improvements in imaging modalities for detection of EPN in early stages, availability of good parenteral antibiotics, multidisciplinary approach of managing sepsis-related complications, and a paradigm shift toward preference for minimally invasive drainage procedures resulted in reduced mortality rate to 21%.[5,9] Early recognition of the condition, prompt resuscitation, adequate drainage of gas as well as infected fluid and effectively relieving the urinary tract obstruction reduced mortality rate to 6% in our study cohort. Besides, the striking overall survival rate (94%), we also found decreased need for nephrectomy. Salvage nephrectomy was performed only in two patients (6%) in our cohort due to ongoing sepsis in spite of initial renal salvaging measures. In a systematic review by Somani *et al*.,[9] including ten retrospective studies on 210 patients with EPN, the reported mortality from MM alone was 50%, MM combined with EN was 25%, and MM combined with percutaneous drainage was 13.5%. Of the patients who underwent medical treatment with percutaneous drainage, a small number (15 out of 118, 13%) subsequently underwent elective nephrectomy and the mortality was 6.6% (1 of 15). They recommended percutaneous drainage should be part of initial treatment strategy for EPN.

However, percutaneous drainage is not without shortcomings. Drainage can be grossly inadequate in cases of large loculated or noncommunicating abscesses containing thick pus.[9] OTD via flank incision is the best alternative to nephrectomy, particularly when percutaneous drainage fails.[29] Our protocol advocates institution of open drainage and placement of large caliber tube in such cases [Figure 3]. We use a gentle finger controlled division of the loculations which not only allows better drainage but also reduces the chance of injury to adjacent viscera. We also observed that opening the gerota fascia in case in cases of perinephric collections is a crucial and rewarding step to drain the gas and infected fluid. We performed OTD in 8 (22%) patients. We also considered OTD for two patients who underwent PCD but failed to drain the infected fluid adequately.

Various risk factors associated with mortality in patients with EPN have been identified.[30,31] Falagas *et al*.[30] assessed the risk factors associated with mortality in a meta-analysis of seven study cohorts including 175 patients with EPN. According to their report, conservative treatment alone, bilateral EPN, Type 1 EPN (Wan's classification), and thrombocytopenia were associated with increased mortality rates. They also found that systolic blood pressure of <90 mmHg, serum creatinine level >2.5 mg/dl, and altered consciousness were associated with increased mortality rates. In a retrospective analysis, Lu *et al*.[31] found that hypoalbuminemia, shock at initial presentation, bacteremia, the need for hemodialysis, and polymicrobial infection were associated with mortality in patients with EPN. Presence of more than two of these prognostic factors had the highest risk of mortality. We found the incidence of septic shock, acidosis, anemia, leukocytosis, hypalbuminemia, and serum creatinine were significantly higher in patients with high-grade disease when compared to low-grade disease.

Relatively small patient pool is one limitation of the study. Lack of objective evaluation of renal function by renographic studies of the affected kidney managed by renal preserving strategies, is the another limitation. Hence, larger and multicenter prospective studies which include objective measurement of preserved renal function are necessary to corroborate the results of the current study.

The time-honored approach to treating EPN has always been aimed at patient salvage followed renal salvage. Our study shows that a clinician should make every effort to achieve renal salvage with preparedness to undertake more invasive procedures such as open drainage as well as nephrectomy in selected patients. This management strategy also decreases the morbidity associated with nephrectomy and prolonged general anesthesia. As a significant number of EPN patients have impaired renal function, nephrectomy would render them dialysis dependent. Hence, renal salvage along with improving survival should be the primary goal in management of EPN. An algorithmic approach of our center helps in achieving both the goals by early institution of renal salvage measures.

CONCLUSION

Renal salvaging protocol including aggressive resuscitation, parenteral antibiotic therapy, early drainage of the infected fluid as well as gas and relieving the urinary tract obstruction is effective way of initial management of EPN, which not only improves the survival but also helps in salvaging renal function. Based on our study results, the following recommendations can be made:

- Primary goal of the management of EPN is to preserve the renal function to the possible extent while improving the survival by employing the initial renal preservation strategies irrespective of the stage of the disease and high-risk prognostic factors
- Effort should be made to demonstrate urinary tract obstruction and when present should be relieved promptly
- Threshold for OTD, especially for large, loculated perinephric or pararenal collection and in cases of failed PCD should be low

- Salvage nephrectomy should be considered only in patients with progressive disease and ongoing sepsis in spite of initial renal preserving strategies
- We suggest subdivision of Huang-Tseng Class II disease depending on extent of renal parenchyma affected for the better treatment plan, i.e., <50% and >50% parenchyma affected.

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Conflicts of interest

There are no conflicts of interest.

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