

Preoperative risk factors in patients with xanthogranulomatous pyelonephritis undergoing nephrectomy

Factores de riesgo preoperatorios en pacientes con pielonefritis xantogranulomatosa sometidos a nefrectomía

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Abstract

Objective: To identify preoperative risk factors associated with major complications in patients with xanthogranulomatous pyelonephritis undergoing total nephrectomy. **Method:** Retrospective analysis of patient's charts with xanthogranulomatous pyelonephritis who underwent nephrectomy. Risk factors included for analysis were gender, body mass index, Charlson comorbidity index, American Society of Anesthesiologists physical status classification, Malek's stage, leukocyte count and creatinine levels. Postoperative complications were stratified in minor and major according to Clavien-Dindo's classification. Univariate and bivariate analysis using Fisher's exact test, Pearson's chi-squared and odds ratio (OR) was performed. **Results:** 72 patients were analyzed, 83% women, mean age of 50 years, 58.3% positive urine cultures and 66% kidney stones. Major complications were present in 32% of cases, and 15% were admitted to the intensive care unit. Elevated creatinine (OR: 3.8; 95% confidence interval [95%CI]: 1.1-13; $p = 0.02$) and Malek's stage II to III (OR: 4.5; 95%CI: 1.2-17.5; $p = 0.02$) were associated with major complications. **Conclusion:** The Malek Stage and elevated creatinine increases the risk of major complications in patients undergoing nephrectomy due to xanthogranulomatous pyelonephritis.

Keywords: Xanthogranulomatous pyelonephritis. Nephrectomy. Postoperative complication. Prognosis.

Resumen

Objetivo: Identificar factores de riesgo asociados a complicaciones mayores en pacientes con pielonefritis xantogranulomatosa sometidos a nefrectomía. **Método:** Análisis retrospectivo de expedientes clínicos de pacientes con pielonefritis xantogranulomatosa sometidos a nefrectomía. Se analizaron el sexo, el índice de masa corporal, el índice de comorbilidad de Charlson, la clasificación del estado físico de la American Society of Anesthesiologists, la etapa de Malek, el conteo leucocitario y los valores de creatinina. Las complicaciones se estratificaron en menores y mayores según la clasificación de Clavien-Dindo. Se realizó análisis univariado y bivariado usando las pruebas exacta de Fisher y ji al cuadrado de Pearson, y se establecieron medidas de riesgo utilizando la odds ratio (OR). **Resultados:** Se analizaron 72 pacientes con una edad media de 50 años, el 83% mujeres, el 58.3% con urocultivo positivo y el 66% con litiasis renal. El 32% tuvieron alguna complicación mayor y el 15% requirieron admisión a la unidad de cuidados intensivos. Los valores elevados de creatinina (OR: 3.8; intervalo

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de confianza del 95% [IC95%]: 1.1-13; $p = 0.02$) y la etapa Malek II-III (OR: 4.5; IC95%: 1.2-17.5; $p = 0.02$) se asociaron con complicaciones mayores. **Conclusión:** El estadio de Malek y los valores elevados de creatinina incrementan el riesgo de desarrollar complicaciones mayores en los pacientes con pielonefritis xantogranulomatosa sometidos a nefrectomía.

Palabras clave: Pielonefritis xantogranulomatosa. Nefrectomía. Complicaciones posoperatorias. Pronóstico.

Introduction

The incidence of xanthogranulomatous pyelonephritis is low and has been reported to range from 0.03% to 0.06%^{1,2}. The study of this pathology is mainly composed of case reports, which is why much of the natural evolution of the disease and patient prognosis are unknown¹⁻⁶.

Malek and Elder¹ proposed a histopathological staging system composed of three stages that vary depending on the degree of renal and extrarenal involvement. By computed tomography, it has been demonstrated that it is possible to properly classify patients in one of the three stages⁷.

The clinical relevance of Malek's classification lies in that it helps decision-making; for example, in pediatric population at stage I or II, partial nephrectomy is suggested, while patients at stage III require management with total nephrectomy. As for the type of intervention, both laparoscopic nephrectomy and the open technique have shown similar results⁸⁻¹⁰.

The incidence of postoperative complications is high, with 48% of cases being classified as minor complications (Clavien < 3), and 19%, as major complications (Clavien $\geq$ 3)⁹.

The purpose of this study is to identify preoperative risk factors related to major complications in patients with histopathological diagnosis of xanthogranulomatous pyelonephritis who underwent nephrectomy.

Method

After authorization was granted by the ethics committee, a retrospective analysis of the medical records of patients with histopathological diagnosis of xanthogranulomatous pyelonephritis who underwent total nephrectomy during the period from 2010 to 2016 was carried out. Incomplete medical records were excluded.

Baseline characteristics that were included for statistical analysis were body mass index ≥ 25 kg/m², moderate to severe Charlson comorbidity index (CCI), physical status ≥ 3 according to the American Society of Anesthesiologists (ASA) classification, white

blood cell (WBC) count $\geq 12,000$ μ /mL, moderate to severe anemia (hemoglobin < 11 g/dL), creatinine ≥ 2.5 mg/dL and Malek II-III stage as preoperative factors associated with higher risk of postoperative complications. All variables were analyzed as dichotomous or polytomous.

All complications that occurred to each patient were documented, i.e., a patient may experience one or more minor or major complications. For statistical analysis, only the most serious complication was considered. Postoperative complications were stratified, according to Clavien-Dindo classification, into minor and major¹¹.

For quantitative variables descriptive analysis, means ($\pm$ standard deviation) and medians (25th-75th percentiles) were used, according to the type of distribution. Qualitative variables were described using measures of frequency and proportions.

To determine statistically significant differences between exposed and unexposed groups, Pearson's chi-square test and Fisher's exact test were used. A p-value < 0.05 was considered to be statistically significant. To establish the magnitude and direction of the associations, the odds ratio (OR) was calculated with a 95% confidence interval (CI). The SPSS package, version 25 (IBM Chicago, IL, USA), was used.

Results

A total of 72 patients were included, out of whom 83% were women. Mean age was 50 years (± 14.5). Positive urine cultures were identified in 58.3%, out of which, 50% (21/42) were positive for extended-spectrum beta-lactamase-producing microorganisms. Some degree of anemia was documented in 66.6% of patients, with the distribution by gender being 41/60 (68.3%) and 7/12 (58.3%) for women and men, respectively. The demographic characteristics are presented in table 1.

Overall prevalence of complications, both intraoperative and postoperative, was 92%. Six intraoperative complications were documented: three vascular lesions and three colon perforations.

Table 1. Demographic characteristics

Variable	n = 72
Age, mean (SD)	50 ± 14.5
Females, n (%)	60 (83.3)
Diabetes mellitus, n (%)	26 (31.9)
Renal lithiasis, n (%)	48 (66)
ASA physical status, n (%)	
1	12 (16.6)
2	20 (27.7)
3	29 (40.3)
4	11 (15.4)
Charlson comorbidity index, n (%)	
Mild	56 (78)
Moderate	8 (11)
Severe	8 (11)
BMI, n (%)	
< 25 kg/m ²	31 (43)
25-29.9 kg/m ²	22 (30.6)
≥ 30 kg/m ²	19 (26.4)
General urinalysis	
Abnormal results	61 (84.7)
Positive nitrites	22 (30.6)
Leukocyte esterase	53 (73.6)
Pyuria	60 (83.3)
Erythrocytes	51 (70.8)
Positive urine culture	42 (58.3)
ESBL microorganisms	21 (29.2)
Chronic kidney disease, n (%)	12 (16.6)
Anemia in females	41 (68.3)
Mild	9 (15.1)
Moderate	22 (36.6)
Severe	10 (16.6)
Anemia in males	7 (58.3)
Mild	3 (25)
Moderate	3 (25)
Severe	1 (8.6)
WBC ≥ 12,000 μ/mL, n (%)	31 (43.1)
Creatinine ≥ 2.5 mg/dL, n (%)	12 (16.7)
Laterality, n (%)	
Left, n (%)	42 (68.3)
Right, n (%)	30 (41.7)
Malek stage*	
I	22 (30.5)
II	26 (36.2)
III	24 (33.3)

ASA: American Society of Anesthesiologists; BMI: body mass index; ESBL: extended-spectrum beta-lactamase; SD: standard deviation.

*Malek stage was established by computed tomography.

Table 2. Complications according to Clavien-Dindo classification

Minor complications	n (%)
I	Fever 9 (13)
II	Blood transfusion 29 (40)
Major complications	
IIIA	Pneumothorax 1 (1)
IIIB	Surgical site abscess 4 (6)
	Retroperitoneal hematoma 3 (4)
	Enterocutaneous fistula 1 (1)
IVA	Organ dysfunction 7 (10)
IVB	Septic shock with multiple organ failure 4 (6)
V	Acute myocardial infarction 3 (4)
	Septic shock 2 (3)

of packed red blood cells (PRBC) was required in 40% of cases; out of them, 72% (21/29) required two or more PRBC units.

Most complications classified as Clavien 3 were due to admission to the intensive care unit (ICU). All Clavien 4B complications were secondary to septic shock with multiple organ failure. The rest of the complications are presented in table 2.

After the bivariate analysis, creatinine values ≥ 2.5 mg/dL (OR: 3.8; 95% CI: 1.1-13; p = 0.02) and Malek stage II-III (OR: 4.5; 95% CI: 1.2-17.5; p = 0.02) were associated with a higher risk of postoperative complications. A tendency was found to exist between WBC counts ≥ 12,000 μ/mL and moderate to severe CCI in relation to the development of major complications (Table 3).

Discussion

To the best of our knowledge, this study represents the largest cohort reported in the literature and is the first to identify prognostic factors in patients with xanthogranulomatous pyelonephritis.

The prevalence of xanthogranulomatous pyelonephritis in women was three times higher than in men, with a ratio of 4:1, which is similar to that reported in other series^{2,5,10}.

The prevalence of patients with diabetes mellitus was lower in our population^{12,13}. However, it continued to be the most common comorbidity, with an occurrence of three out of every ten cases. We believe that,

According to the Clavien-Dindo classification, the incidence of minor and major complications was 53% and 35%, respectively. Transfusion of at least one unit

Table 3. Bivariate analysis: prognostic factors associated with major complications

Variable	Minor complications (n = 49)	Major complications (n = 23)	OR (95 CI%)	p
Gender				
Females	9 (75)	3 (25)	1	
Males	40 (66.7)	20 (33.3)	1.5 (0.3-6.1)	
BMI				
< 25 kg/m ² (%)	21 (67.7)	10 (32.3)	1	
≥ 25 kg/m ² (%)	28 (68.2)	13 (31.8)	0.9 (0.3-2.6)	0.5 [†]
CCI				
Mild (%)	41 (73.2)	15 (26.8)	1	
Moderate-severe %)	8 (50)	8 (50)	2.7 (0.8-8.5)	0.07*
ASA physical status				
≤ 2 (%)	24 (77.4)	7 (22.6)	1	
≥ 3 (%)	25 (61)	16 (39)	2.1 (0.7-6.2)	0.1 [†]
WBC ≤ 12,000 µ/mL				
Present (%)	31 (75.6)	10 (24.4)	1	
Absent (%)	18 (58)	13 (42)	2.2 (0.8-6.1)	0.09 [†]
Hemoglobin < 11 g/dL				
Present (%)	23 (63.9)	13 (36.1)	1	
Absent (%)	36 (72.2)	10 (27.8)	1.4 (0.5-3.9)	0.4 [†]
Creatinine ≥ 2.5 mg/dL				
Present (%)	5 (41.6)	7 (58.4)	1	
Absent (%)	44 (66.6)	16 (33.3)	3.8 (1.06-13.8)	0.03*
Malek stage				
I (%)	20 (87)	3 (13)	1	
II-III (%)	29 (59.2)	20 (40.8)	4.5 (1.2-17.5)	0.02 [†]

ASA: American Society of Anesthesiologists; BMI, body mass index; CCI: Charlson comorbidity index; CI: confidence interval; OR: odds ratio.

*Fischer's exact test.

†Pearson's Chi-square test.

as described in the literature, diabetes mellitus plays a determining role in the development of xanthogranulomatous pyelonephritis, although larger series need to be available in order for a statistical association to be established.

Of all positive urine cultures in our series, in more than 50% did an extended-spectrum beta-lactamase-producing bacteria develop. Although we do not have specific growth patterns available, more than 50% of patients with xanthogranulomatous pyelonephritis have been reported have a positive urine culture prior to surgery^{1,2,6,14}. This finding could be related to inappropriate antibiotic therapy for the treatment of recurrent urinary tract infections, which are common in these patients^{1,6,9}.

Most minor complications consisted of PRBC transfusions. The high rate of blood transfusions found in our series may be due, in part, to the high preoperative prevalence of moderate and severe anemia. Information regarding intraoperative

bleeding was not available for analysis, but Shah et al.⁹ report a mean bleeding of 257 mL in patients undergoing open nephrectomy. We consider that, although this value does not represent clinically significant bleeding, it might be reduced by the laparoscopic approach.

The only series reported in the literature that uses the Clavien-Dindo classification is that by Shah et al.⁹, in which an incidence of complications higher than 13.5% was found, which is lower than in our series. This difference may be attributed to a higher prevalence of comorbidity in our population, as shown by the trend found between CCI and the risk of major complications.

Most major complications consisted of ICU admissions. Among the indications for ICU admission, the most common were single organ failure and septic shock. These findings suggest that delaying surgical intervention until clinical parameters (anemia, resolution of urinary tract infection, renal function, etc.) are

optimized, as well as preoperative assessment by the ICU, may be feasible behaviors for prognosis to be improved.

Patients with creatinine values ≥ 2.5 mg/dL were found to have three times the risk of major complications; however, patients with Malek stage II-III are at even greater risk. Creatinine values are modifiable, but it is not the same scenario with Malek stage.

Most limitations of this study are related to the low incidence of this disease, which makes it difficult to recruit a more representative sample that allows a multivariate analysis and adjustment for a larger number of confounding factors. Another important limitation is the methodological design.

Given that this is a rare disease with high rates of comorbidity and postoperative complications, we believe it is relevant to develop prospective, multicenter studies that allow to clarify the prognosis of these patients.

Conclusions

Malek stage and elevated creatinine values increase the risk of developing major complications in patients with xanthogranulomatous pyelonephritis undergoing nephrectomy.

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Conflicts of interest

All authors declare that there are no conflicts of interest of any kind.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments have been performed on humans or animals for this research.

Confidentiality of data. The authors declare that they have followed the protocols of the work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained informed consent from the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

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