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ORIGINAL ARTICLE

Asymptomatic bacteriuria prior to partial and radical nephrectomy: To screen or not to screen? Results from the national and multicenter TOCUS database

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Abstract

Introduction In the era of increased bacterial resistance, the main strategy is to reduce the prescription of antibiotics when possible. Nowadays, it is highly recommended to screen for asymptomatic bacteriuria (ABU), prior to urological surgery with potential mucosal breach or urine exposure. Screening and treating urinary colonization is a strategy widely adopted before radical and partial nephrectomy but without any evidence. Our main end point in this study is to analyze the relationship between preoperative urine culture and the risk of postoperative febrile urinary tract infection (UTI) or surgical-site infection (SSI) in partial or radical nephrectomy patients.

Methods We conducted a multicenter retrospective cohort study between January 2016 and January 2023 in 11 French tertiary referral hospitals (TOCUS database). We collected the data for 269 patients including several pre-, intra-, and postoperative variables that could potentially increase the risk of postoperative UTI and SSI including preoperative urinary culture results.

Results The incidence rate of postoperative UTI and SSI was 8.9% in our study. After conducting a logistic multivariate analysis, a propensity score matching analysis, and a subgroup analysis, we found no significant correlation between the urine culture and the postoperative UTI risk [OR = 1.2 (0.5–2.7) ($p = 0.7$)]. Only the postoperative non-infectious complications were related to a higher risk of postoperative UTI [OR = 12 (4–37), $p < 0.001$)].

Conclusion Our research shows that screening and treating for ABU prior to radical or partial nephrectomy seems to be unnecessary to prevent postoperative UTI and SSI.

Keywords Nephrectomy · Urinary tract infection · Surgical-site infection · Asymptomatic bacteriuria · Urine culture

Introduction

Nowadays, bacterial resistance has become a major concern in medical field. The excessive use of antibiotic seems to be the major cause of this resistance [1]. In addition, new data seem to show an increase in the rate of infectious postoperative complication and even oncological progression related to the use of excessive antibiotics [2–4].

In a recent study published by Cassini et al. in 2018, the increase of highly resistant infection in Europe is reported, among which 64% are related to nosocomial infection [5]. In France, the rate of *E. coli* resistant to 3rd-generation cephalosporin is around 8.3% [6].

Asymptomatic bacteriuria (ABU) is defined as a positive urine culture in a patient without symptoms. The treatment of ABU is still controversial, indicated in pregnant women and prior to selected surgeries [7]. The EAU guidelines recommend screening and treatment of ABU prior to urological surgeries with urothelium breach [7]. The antibiotics should be initiated peri-operatively, targeting the bacteria found in

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the urine culture with no clear guidelines for the duration of such antibiotics nor any stratification based on the type of surgery [7]. The SFAR (Société Française d'Anesthésie-Réanimation) guidelines state that urological surgery should be performed in patients with negative urine culture or adequately treated positive urine culture [8]. These guidelines do not precise any details about the time of screening nor the duration of the treatment. The French Association of Urology highly recommends to treat the ABU, 48 h prior to urological intervention for a maximum duration of 7 days [9].

Thus, it is obvious that the management of this ABU is unclear with controversial data and is even different between surgeons working in the same hospital. The main concern of a urologist, related to ABU, is the postoperative infection that can impact healing and hospital stay and increase morbidity and even mortality [10].

Recent data show a rate of 2–12% of postoperative infectious complications, of which about 25% are caused by urinary sepsis [11].

Screening and treatment of ABU has shown a decrease in postoperative urinary sepsis in percutaneous nephrolithotomy, flexible ureteroscopy, and transurethral prostate resection [12–14].

Nephrectomy (partial and radical surgery) is a type of urological surgery with a low risk of urothelium breach and screening ABU is probably unnecessary. Nevertheless, no studies have been conducted on this subject.

This strategy could be interesting in the ecological perspective of fighting against bacterial resistance. On the contrary, the cost of urine culture for patients who are subject to nephrectomy and the cost of the potential antibiotic treatment can cause a high burden on the health-care system, which could be omitted if the preoperative urine culture is to be shown as unrelated to postoperative urinary infection.

Our aim is to evaluate a possible relationship between the rate of postoperative infection (UTI or SSI) in the 30 days' period following partial and radical nephrectomy and preoperative urine culture.

Methods

Population

We conducted a multicenter retrospective study between January 2016 and January 2023 in 11 French tertiary referral hospitals. We extracted data about patients operated for partial or radical nephrectomy, already collected in the TOCUS database ("To Treat Or not to treat a Colonization prior to Urologic Surgery") between January 2016 and January 2023 ("Appendix 1").

Inclusion criteria

Patients included in this study should be above 18 years old and hospitalized in any of these 11 centers for partial or radical nephrectomy (including nephro-ureterectomy surgeries) who have been screened preoperatively (10 days maximum) for bacteriuria with a urine culture.

Exclusion criteria

Patients who have not had a preoperative urine culture, who had an active urinary infection (symptomatic or associated with systemic infection), or who had a concomitant surgery not related to the kidney were excluded from the study.

Data collection

We collected the age, BMI, the presence or absence of preoperative urinary stent, and any history of symptomatic urinary infection in the year preceding the operation (in a 12-month period from the day of surgery). We also collected any data related to the urine culture, including the presence of leukocyturia or hematuria, the count and type of germs, and the resistance profile of each germ.

We also noted whether the ABU was treated or not and the duration of that treatment.

Peri-operative data consisted of the type of surgery, the surgical approach (robotic, laparoscopic, or open), the duration, the administration of antibiotic prophylaxis, and the intra-operative stenting (urethral or ureteral catheter).

Finally, we reported postoperative UTI in the 30-day period postoperatively and all other complications with its Clavien–Dindo grade.

This study is a "real-life study" and that is why we collected all partial and radical nephrectomy with screening of ABU even if it was not recommended. All included patients were screened for ABU, 4 to 10 days prior to nephrectomy. The treatment of this ABU was based on the surgeon preference.

Primary end point

The primary end point is the occurrence of postoperative UTI or SSI in a 30 days' postoperative period in patients operated for partial or radical nephrectomy with positive preoperative ABU.

Postoperative urinary tract infection (prostatitis and pyelonephritis) is defined as a combination of fever (> 38 °C) with urine symptoms associated with clinical, radiological, and biological infectious signs.

Surgical-site infections are defined as superficial infections at the incision or deep tissue infections at the operation site.

This diagnosis was reported by the surgeon if it was diagnosed during initial stay or by the general practitioner if it was diagnosed after discharge.

Secondary end point

The secondary end point is to detect the presence of any predictive risk factor for the development of postoperative UTI and SSI in patients operated with partial or radical nephrectomy.

Statistical analysis

Continuous variables were represented by its mean and its 95% confidence interval. Categorical variables were represented by a percentage of each category.

Our analysis started with a univariate regression to detect all potential cofactors associated with the development of postoperative UTI. For categorical factors, results were reported by its odds ratio with a confidence interval of 95%, calculated through a univariate logistic regression. For continuous variables, we reported the mean in each subgroup with its standard deviation.

Then, we studied the correlation between the diagnosis of a postoperative UTI and the preoperative urine culture in a multivariate logistic regression.

Variables with a p-value < 0.2 were included in our multivariate regression. The p-value, calculated in the univariate regression, were not reported in the result section since it was considered insignificant in the analysis of our end point.

We took into consideration $p < 0.05$, in the multivariate regression, as a significant result. We also calculated a propensity score to control any confounding factor. We finally analyzed the relationship between preoperative ABU and postoperative UTI in a subgroup analysis (radical vs. partial nephrectomy group). Patients with missing data were omitted from our statistical analysis. All statistical analyses were conducted through R studio software® version 2021.09.0.

Results

Between January 2016 and January 2023, and after omitting 5 patients (1.8%) with missing data, we found 269 patients operated for partial or radical nephrectomy in the 11 hospitals noted above. The patients' characteristics are reported in Table 1.

Seventy-five patients (27.9%) had a positive urine culture, 1 week prior to their surgery, and 55% had concomitant leukocyturia.

Table 1 Patients' general, preoperative, intra-operative, and postoperative characteristics

Variables	Total *n* (%)
Sex	
Male	177 (65.8)
Female	92 (34.2)
Age (years)/mean (CI 95%)	63.7 (62.3–65.1)
BMI (kg/m^2)/mean (CI 95%)	28.4 (27.6–29.2)
History of UTI (1)	
Yes	25 (9.3)
No	244 (90.7)
Preoperative urological stents (2)	
Yes	24 (8.9)
No	245 (91.1)
Type of surgery	
Radical	69 (25.7)
Partial	200 (74.3)
Surgical approach	
Open	29 (10.8)
Laparoscopic	75 (27.9)
Robotic	165 (61.3)
Preoperative urine culture	
Positive	75 (27.9)
Negative	194 (72.1)
Preoperative leukocyturia	
Positive (3)	94 (34.9)
Negative	175 (65.1)
Preoperative antibiotic therapy	
Yes	60 (22.3)
No	209 (77.7)
Intra-operative antibiotic prophylaxis	
Yes	58 (21.6)
No	211 (78.4)
Skin antiseptic	
Alcoholic betadine (5%)	184 (68.4)
Dermal betadine (10%)	48 (17.8)
Other	37 (13.8)
Intra-operative urinary stent (2)	
Yes	228 (84.8)
No	41 (15.2)
Postoperative UTI and SSI (4)	
Yes	24 (8.9)
No	245 (91.1)
Postoperative complications (5)	
Yes	40 (14.9)
No	229 (85.1)
Operating time (min.)/mean (CI 95%)	176 (167.7–184.3)

(1): UTI in the 12 months prior to surgery

(2): including bladder catheter, nephrostomy, ureteral stent

(3): considered positive if > 1000 colonies/mm^3 mono or polymicrobial

(4): including prostatitis, pyelonephritis, obstructive pyelonephritis, urosepsis, and SSI

(5): Hematuria, urinary fistula, digestive fistula, hematoma, abscess, lymphocele, acute urinary retention, acute renal failure, blood transfusion, pneumonia, or pulmonary embolism, excluding urinary infection

Study	OR	95%CI	p-value
Age	-	-	0.27
BMI	-	-	0.5
Sex	1.9	[0.7-5]	0.2
History of UTI	2.4	[0.6-8]	0.18
Preoperative Urinary stent	0.6	[0.17-2.3]	0.4
Type of surgery	0.4	[0.02-2.7]	0.45
Surgical approach	1.1	[0.35-3.2]	0.87
Open surgery	0.5	[0.12-1.5]	0.19
Laparoscopy	-	-	0.9
Robotic	Ref	-	-
Urine culture	0.8	[0.14-5]	0.8
Leucocyturia	0.6	[0.16-3.2]	0.55
Preoperative antibiotic	2.5	[0.75-9]	0.13
Antibiprophylaxis	0.8	[0.17-2.7]	0.7
Antiseptic	-	-	0.5
Alcoholic betadine	Ref	-	-
Dermal betadine	2.3	[0.44-10]	0.3
Other	0.9	[0.16-3.6]	0.85
Operating time	-	-	0.75
Postoperative urinary stent	2.5	[0.6-15]	0.24
Non infectious complications	12	[3.9-37]	<0.001

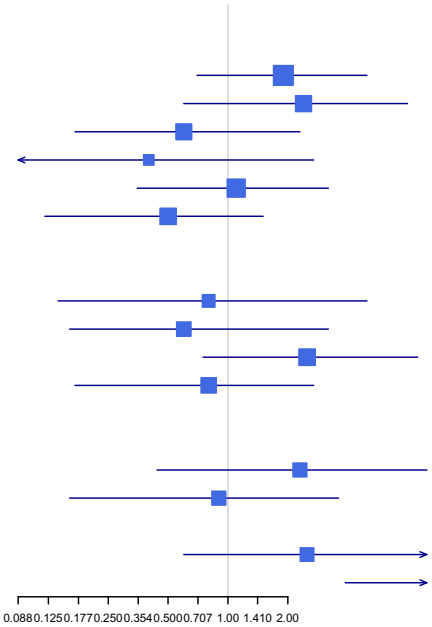

Fig. 1 Forest plot representation of the multivariate analysis results. This forest plot represents graphically the OR (odds ratio) calculated between postoperative UTI and SSI and the potential risk factors, with its respective 95%IC (95% confidence interval). The *p*-value evaluates the strength of this correlation and its potential significance

Among these 75 positive UC, 8 patients (10.6%) were polymicrobial, whereas the other cultures were mono or bimicrobial. The main bacterium identified was *E. coli* (62.7%), followed by *E. faecalis* (18.7%).

Not all patients with a positive urine culture had preoperative antibiotic therapy. The treatment of the asymptomatic bacteriuria was based on the surgeon preference. In fact, only 48% with positive urinary culture had a targeted antibiotic therapy. We found that 13.5% of patients with leukocyturia were treated with antibiotics, even though no bacteria were identified.

The rate of postoperative infections that were diagnosed in the 30-days' period postoperatively was 8.9%: 8% in partial nephrectomy subgroup versus 11.5% in the radical nephrectomy subgroup.

In our research, 45.8% of patients who developed a postoperative UTI or SSI had a preoperative ABU, among whom we found two patients (18.2%) with polymicrobial UC, seven (63.6%) patients with monobacterial identification, and two patients (18.2%) with bimicrobial identification.

The comparison of the microorganisms detected on the preoperative UC with the microorganisms detected on the postoperative UC in patients who developed a postoperative infection found a similarity rate of 58.3%.

All patients who had a peri-operative antibiotic prophylaxis had a pre-operative ABU.

We reported 14.9% of non-infectious postoperative complications, mainly hematuria, urinary fistula, hematoma, acute urinary retention, and acute renal failure.

The results of the univariate analysis are presented in "Appendix 2".

In the univariate analysis, a positive preoperative urine culture and postoperative non-infectious complications were associated with a higher risk of postoperative infection with an OR of 1.8 (1.02–4) and 7.7 (3–19), respectively.

In the multivariate analysis, only the presence of non-infectious postoperative complications was associated with higher risk of postoperative UTI and SSI (OR = 12 (4–37), $p < 0.001$). None of the preoperative and intra-operative variables were significantly related to the postoperative risk of UTI. Preoperative urine culture was not significantly correlated with postoperative UTI or SSI (Fig. 1).

After weighing with the propensity score, the relationship of preoperative urine culture and postoperative UTI or SSI was estimated with an OR of 1.2 (0.5–2.7) ($p = 0.7$).

We also performed a subgroup analysis in the partial and radical nephrectomy groups. We could not reveal a significant association of preoperative UC and postoperative UTI or SSI ("Appendix 3").

Discussion

In our study, we detected a rate of 8.9% of urinary tract infection or SSI after partial and radical nephrectomy. We also found a relatively lower incidence of urinary infection after robotic surgery (7.8%) compared to open (14.3%) and laparoscopic approaches (9.3%) in concordance with previous data showing lower rate of complications in mini-invasive surgery [15].

Concerning our primary end point, after matching with a propensity score, no significant effect of the UC on the risk of developing a postoperative UTI or SSI was detected in patients operated for radical or partial nephrectomy [OR = 1.2 (0.5–2.7) ($p = 0.7$)].

The lack of association could be hypothetically due to a higher risk of urinary breach in patients operated for partial nephrectomy compared to patients operated for radical nephrectomy for whom the urinary tract is usually clamped intra-operatively.

Thus, we conducted a multivariate subgroup analysis between these two types of surgery, which revealed a higher non-significant risk of postoperative infection in the radical nephrectomy group (OR = 3 with $p = 0.3$ vs. 1.1 in the partial nephrectomy group with a p-value = 0.5).

On the contrary, we noticed that patients treated with preoperative antibiotics (based on the results of urine culture) seem to have an increased risk of developing postoperative urinary infection [OR = 2.1 (0.9–5)]. Even though statistically non-significant, this result was also found in the multivariate analysis. This observation is concordant with earlier published research showing an increase in the risk of highly aggressive microorganism in patients treated with unnecessary antibiotics [2, 3].

The administration of intra-operative antibiotic prophylaxis is not recommended in both surgeries according to the French Anesthesiologist Society recommendation, updated in 2018 [8]. Nevertheless, 21.6% of patients had antibiotics intra-operatively. The decision was mainly based on the result of the preoperative urine culture. Thus, we can note that those patients are treated with two antibiotic courses based on their preoperative UC.

Concerning our secondary end point, the only predictive factor that showed a significant association with postoperative urinary infection is the presence of postoperative non-infectious complication with an OR = 12 and a p-value < 0.001. This association should be analyzed with caution since the chronology of these two postoperative complications (infectious and non-infectious) is difficult to determine.

In our study, 14.9% presented a postoperative non-infectious complication, mainly hematuria, acute urinary retention, acute renal failure, and urine fistula. The presence of one of these complications could have led to a surgical revision, prolonged urinary system stenting (ureteral stent or bladder stent), or repeated bladder irrigation maneuverers, which would increase the risk of UTI [16, 17]. It is also probable that these non-infectious complications would have prolonged the hospital stay, thus increasing the risk of nosocomial infection [18]. However, a non-infectious complication could also be the consequence of a UTI, such as acute urinary retention after prostatitis [19].

In our daily practice, most medical centers screen for ABU before urological surgery. Treatment of such ABU depends usually on the systematic attitude of the center, but in the absence of clear guidelines, most of them are treated with a preoperative antibiotic. The choice of the molecule and the duration are usually decided by the surgeon [5, 20].

With about 11,000 nephrectomies performed in 2018 in France and about 30% of preoperative ABU, this represents about 3300 potential unnecessary antibiotic prescriptions that could increase bacterial resistance [21].

The TOCUS study was conceived as a multicentric retrospective study. Its main end point is to detect a potential relationship between preoperative urine culture and postoperative urinary tract infection in a wide range of urological surgery. This study focuses on radical and partial nephrectomies, for which the French and the European guidelines state that the management of preoperative urine culture is still controversial [7, 9].

We could not find any significant data in the literature about the association of preoperative urine culture and postoperative infectious complications in patients operated for partial or radical nephrectomy.

Our study seems to be a preliminary work to reveal the lack of an obvious link between preoperative ABU and postoperative infectious complications. This evidence, long awaited, would decrease the unnecessary prescription of preoperative and intra-operative antibiotics prior to nephrectomy. In light of our results, screening of ABU prior to partial or radical nephrectomy should be abandoned.

Our study has several limitations; thus, the results should be interpreted with caution. The data were retrospectively collected in the different hospitals included in the TOCUS database. Moreover, the diagnosis of UTI could have been occurred on an outpatient basis that could have been treated by the general practitioner without informing the urology department, causing measurement bias.

The other limiting factor in our study was the presence of a great number of unmeasured factors that may bias our results. The presence or absence of a mucosal breach during the operation and the exposure of urine would hypothetically be an important cofactor. However, this information

was not mentioned by most surgeons. Other cofactors such as medical history (diabetes and hypertension) would have been interesting to analyze.

We also noticed a heterogeneity in the management of urine culture among different hospitals, and it would have been interesting to consider the center effect as a covariate but it was not possible due to the low number of patients.

On the contrary, this study remains one of the largest multicentric cohort studies on this subject.

We have not encountered a high rate of missing data with few exclusion criteria to provide a "real-life" overview. Nevertheless, a prospective randomized trial would be the best strategy to confirm our results.

Conclusion

Our study shows that screening for ABU prior to radical or partial nephrectomy seems to be unnecessary to prevent postoperative urinary infection. In addition, treating such ABU could be a predictive factor for an increased risk of postoperative UTI. The only risk factor that showed a significant statistical association was the presence of postoperative complication.

These results could be interesting from an ecological and economic perspective owing to a significant decrease in antibiotic prescription, highly needed in our days to control microorganisms' resistance.

Appendix 1: The TOCUS database

The hospitals that participated in the TOCUS database were as follows: *Poitiers University hospital, Angers University hospital, Nantes University Hospital, La Rochelle Hospital, Limoges University Hospital, Marseille University Hospital, Saint Joseph Hospital–Paris, Strasbourg University Hospital, Saintes Hospital, Pointe à Pitre University Hospital,* and *Pontoise Hospital.*

The TOCUS database included all kinds of urological surgeries. Therefore, in this study, we extracted data concerning nephrectomy (partial or radical) exclusively.

The data were collected retrospectively through patients' urology medical files in the 11 centers and reported anonymously using Excel software®.

This study is part of the TOCUS study that was validated by the CNIL (Commission Nationale de l'Informatique et des Libertés) in accordance with methodology MR004 and registered under number 2211250V0. It is also approved by the Ethics Committee of the French Urology Association (CERU) under number CERU_2022009.

Appendix 2

See Table 2.

Table 2 Results of the univariate analysis

Variables	No UTI in the post-operative 30-days' period n (%)	UTI in the postoperative 30-days' period n (%)	*p*-value
Sex			
Male	164 (66.9)	13 (54.2)	0.15
Female	81 (33.1)	11 (45.8)	
Age (years) (IC 95%)	63.8 (62.4–65.2)	61.92 (60.2–63.6)	0.18
BMI (Kg/m$^{2)}$ (CI 95%)	28.2 (27.5–28.9)	30.6 (29.6–31.6)	0.13
History of UTI			
Yes	27 (11)	5 (20.8)	0.09
No	218 (89)	19 (79.2)	
Preoperative urological stents			
Yes	23 (9.4)	23 (95.8)	0.19
No	222 (90.6)	1 (4.2)	
Type of surgery			
Radical	61 (24.9)	8 (33.3)	0.15
Partial	184 (75.1)	16 (66.7)	
Surgical approach			
Open	24 (9.8)	4 (16.7)	0.08
Laparoscopic	68 (27.8)	7 (29.1)	
Robotic	153 (62.4)	13 (54.2)	
Preoperative urine culture			
Positive	79 (32.2)	11 (45.8)	0.01
Negative	166 (67.8)	13 (54.2)	
Preoperative leukocyturia			
Positive	87 (35.5)	9 (37.5)	0.14
Negative	158 (64.5)	15 (62.5)	
Preoperative antibiotic therapy			
Yes	51 (20.8)	9 (37.5)	0.19
No	194 (79.2)	15 (62.5)	
Intra-operative antibiotic prophylaxis			
Yes	54 (22)	4 (16.7)	0.07
No	191 (78)	20 (83.3)	
Skin antiseptic			
Alcoholic betadine (5%)	169 (69)	15 (62.5)	0.18
Dermal betadine (10%)	42 (17.1)	6 (25)	
Other	34 (13.9)	3 (12.5)	
Intra-operative urinary stent			
Yes	207 (84.5)	21 (87.5)	0.18
No	38 (15.5)	3 (12.5)	
Postoperative complications			
Yes	28 (11.4)	12 (50)	< 0.001
No	217 (88.6)	12 (50)	
Operating time (min) (CI 95%)	175.24 (166.9–183.6)	183.6 (175.7–191,5)	0.08

Appendix 3

See Table 3.

Table 3 Subgroup multivariate analysis

	Preoperative UC/postoperative UTI OR	*p*-value
Partial nephrectomy subgroup	1.1 (0.7–2)	$p=0.5$
Radical nephrectomy subgroup	3 (0.3–4)	$p=0.3$

Author contributions Protocol/project development: MV. Data collection or management of local database: SK, HR, PB, MF, MC, CJ, OK, FTK, HJA, MG, BP, MB, BG-T, SDV, JR, LB, SB, AD, TT, ÉL, and MV were involved in data collection or management of local database. Data analysis: EA and MV performed data analysis. Manuscript writing/editing/critical revision: EA/MV/all authors performed manuscript writing/editing/critical revision, respectively.

Availability of data and materials On demand.

Declarations

Conflicts of interest The authors have nothing to disclose.

Ethical approval This study is part of the TOCUS study that was validated by the CNIL (Commission Nationale de l'Informatique et des Libertés) in accordance with methodology MR004 and registered under number 2211250V0. It is also approved by the Ethics Committee of the French Urology Association (CERU) under No. CERU_2022009.

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