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Antibiotic Prophylaxis Decreases Surgical Site Infections after Radical Prostatectomy

*Chatenet M[1], Vincendeaua S[1], Bataillon-Buf S[2], Peyronneta B[1], Verhoesta G[1], Manuntaa A[1], Guille F[1], Shariat SF[3,4,5,6], Bensala K[1], Mathieu R[1]**

[1]Department of Urology, Rennes University Hospital, France

[2]Unité d'Hygiène Hospitalière, Pôle Microorganismes, CHU Pontchaillou, Rennes, France

[3]Department of Urology, Medical University Vienna, General Hospital, Vienna, Austria

[4]Department of Urology, University of Texas Southwestern Medical Center at Dallas, Dallas, Texas, USA

[5]Department of Urology, Weill Cornell Medical College, New York, USA

[6]Karl Landsteiner Institute, Vienna, Austria

Abstract

Background: Routine use of Antibiotic Prophylaxis (AP) in Radical Prostatectomy (RP) is still questionable since no comparative placebo-controlled study has been conducted. The aim of the study was to describe Surgical Site Infections (SSI), identify predictive factors of SSI, and determine the role of AP in a large cohort of patients treated with RP.

Methods: Laparoscopic or robot assisted RP was performed in 295 consecutive patients between January 2010 to December 2013 in a single academic institution. Patients and operative characteristics, post-operative complications and SSI were retrospectively collected. From July 2012, patients received systematic AP during the procedure. Qualitative and quantitative variables were compared by using chi2 and Student t tests. Relationships between SSI and patient or treatment parameters including use of AP were determined using univariable and multivariable regression logistic analyses.

Results: 292 patients were analyzed. Median age was 62 years. 107 patients (36.6%) received AP. SSI occurred in 52 patients (17.8%). SSI were superficial incisional SSI (n=28), and organ/space SSI (n=26). No deep incisional SSI was reported. In univariable analysis, SSI was associated with a pre-operative immunosuppressive therapy (HR=7.286; CI 95% = 1.185-44.761; p=0.035), post-operative complications (HR=2.545; CI 95% = 1.027-6.312; p=0.044), and use of AP (HR=0.458; CI 95% = 0.223-0.918; p=0.028). In multivariable analysis, only post-operative complications (HR=2.603; CI 95% = 1.014-6.680; p=0.047), and use of AP (HR=0.410; CI 95% = 0.198-0.847; p=0.016) remained independent predictors.

Conclusion: Use of AP in RP is associated with a decrease of SSI. The impact of AP on SSI incidence should be confirmed in a comparative, prospective, controlled study.

Keywords: Surgical wound infection; Antibiotic prophylaxis; Predictive factors; Radical prostatectomy; Prostate cancer

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Correspondence:
Romain Mathieu, Department of Urology, Rennes University Hospital, Rennes, France,
E-mail: romain.mathieu@chu-rennes.fr

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Introduction

Postoperative infection is a common complication after urological procedures [1]. These infections are associated with an increase in length of stay, cost of health care and patient anxiety. Antibiotic Prophylaxis (AP) has been proposed to prevent surgical site infections in many surgical procedures. However, its systematic use remains controversial due to a potential risk of allergic side effects, bacterial resistance emergence and cost increase. Surgical Site Infections (SSI) incidence and corresponding risk factors have been recently reviewed in urological surgery to identify high-risk procedures and propose prevention cares [1].

Radical Prostatectomy (RP) is classified as a clean-contaminated surgery according Altemeier classification [1-2]. Incidence of SSI after RP is approximately 6% [3]. Accordingly, EAU (European Association of Urology) guidelines recommend AP in RP. These recommendations are mainly based on a low level of evidence (grade C) [4]. Indeed, few studies assessed the role of AP in urological procedures and no comparative placebo-controlled study has been conducted in RP [5-6]. Routine

Table 1: Patients, operative and postoperative characteristics.

CHARACTERISTICS	Total	no AP group	AP group	p values
Number of patients (n, %)	292	185	107	
Patient characteristics				
Median age (years) (IQR)	62 (57.5-66)	62 (58-66)	63 (57-66)	0.013
ASA>2 (n, %)	8 (2.8)	5 (2.7)	3 (2.8)	1
Obesity (n, %)	37 (12.7)	20 (10.8)	17 (15.9)	0.21
Diabetes mellitus (n, %)	13 (4.5)	7 (3.8)	6 (5.6)	0.47
Immunosuppressive therapy (n, %)	5 (1.7)	2 (1.1)	3 (2.8)	0.36
Urinary tract infection history (n, %)	12 (4.1)	8 (4.3)	4 (3.7)	1
Anticoagulant therapy (n, %)	4 (1.4)	2 (1.1)	2 (1.9)	0.63
Antiplatelet therapy (n, %)	25 (8.6)	16 (8.7)	9 (8.4)	0.94
Operative characteristics				
Transperitoneal laparoscopic approach (n, %)	41 (14.0)	38 (20.5)	2 (1.9)	<0.001
Robot-assisted transperitoneal laparoscopic approach (n, %)	251 (86.0)	146 (78.9)	105 (98.1)	<0.001
Lymph node dissection (n, %)	118 (40.4)	61 (33.0)	57 (53.3)	0.001
Median operative time (min) (IQR)	200 (170-240)	205 (180-250)	180 (160-240)	0.001
Median blood loss (mL) (IQR)	500 (400-800)	500 (400-800)	500 (400-600)	0.12
Postoperative characteristics				
Median length of urethral catheter (days) (IQR)	6.7 (6-6)	6.6 (6-6)	6.8 (6-7)	0.02
Median length of hospital stays (days) (IQR)	4.8 (4-5)	5 (4-7)	4.4 (4-4)	0.009

IQR: Inter Quartile Range; ASA: American Society of Anaesthesiologists

use of AP is still questionable and further studies in large cohorts are needed to determine its benefice in RP.

The aim of this study was to describe SSI, identify predictive factors of SSI and determine the role of AP in a large cohort of patients who underwent RP.

Material and Methods

Data collection

This study included 295 consecutive patients who underwent laparoscopic or robot assisted RP between January 2010 to December 2013 in a single academic institution. After institutional board approval, patient records were extracted and entered into a standardized database. The following items were queried: Age, American Society of Anesthesiologists score [7], Body Mass Index (BMI), nutritional status, diabetes mellitus, urinary tract infection history, abdominal and prostatic surgery history, immunosuppressive therapy, anticoagulant therapy, antiplatelet therapy, antibiotic treatment, surgical approach, lymph node dissection, extension of the lymph node dissection, neurovascular bundles preservation, operative time, estimated blood loss, length of urethral catheter, length of hospital stay. Tumors were staged according TNM classification [8]. Patient with pre-operative bacteriuria were excluded (n=3). Surgical Site Infections (SSI) were classified in superficial incisional SSI, deep incisional SSI or organ/space SSI according Centers for Disease Control (CDC) guidelines [10-11]. Postoperative complications were defined as any abnormal medical or surgical event that occurred within 30 days after surgery, classified according to the Clavien system [9]. Organ/Space SSI included Urinary Tract Infection (UTI) defined by clinical symptoms, bacteriuria on urine culture and a prescription of antibiotics by general practitioner or surgeon. All patients underwent a postoperative visit at 1 month. Occurrence of a post-operative complication was retrospectively determined according the physicians reports and a systematic phone call to patients using a specific questionnaire.

Antibiotic prophylaxis

No AP was performed before RP from January 2010 to July 2012. All patients received a systematic AP from July 2012. Systematic AP consisted in a single dose of Cephalosporin 30 min before the procedure and a new dose of cephalosporin after two hours of operative time.

Statistical analysis

Qualitative and quantitative variables were compared by using chi^2 and Kruskal Wallis tests, respectively. Relationships between SSI and patient, tumor or treatment parameters including use of AP were first analyzed using univariable regression logistic analysis. Multivariable analyses included covariates with a p value <0.2 in univariate analysis. All p values were two sided and a $p<0.05$ was considered significant. All data analysis were processed using Stata 11.0 statistical software (Stata Corp., College Station, TX, USA).

Results

Patients, operative and postoperative characteristics

A total of 292 RP procedures were analyzed. Patients, operative and post-operative characteristics according the use of AP are shown in Table 1. AP was administered in 107 patients (36.6%). No allergic reaction was reported. Use of AP was associated with none of the patient characteristics except age. Surgical approach, rates of lymph node dissection, median operative time and length of urethral catheterization and hospital stay were significantly different among the two groups.

Postoperative complications

Postoperative complications occurred in 68 cases (23.3%). Post-operative complications according Clavien classification are shown in Table 2. Complications were major (Clavien >2) in 8 patients

Table 2: Characteristics of postoperative complications.

Post-operative complications	Total	no AP group	AP group	p values
Global complications (n, %)	68	50 (27.0)	18 (16.8)	0.047
Clavien I (n)	31			
Clavien II (n)	29			
Clavien III (n)	7			
Clavien IV (n)	1			
Clavien V (n)	0			
Global SSI (n, %)	52	40 (21.6)	12 (11.2)	0.025
Superficial incisional SSI (n, %)	28	24 (13.0)	4 (3.7)	0.01
Organ/space SSI (n, %)	26	18 (9.7)	8 (7.5)	0.51
Deep incisional SSI (n, %)	0	-	-	-

SSI: Surgical Site Infections

Table 3: Predictors of SSI in univariable analysis.

	Univariable analysis		
	HR	CI 95%	p value
Age	0.99	0.94-1.04	0.61
ASA score >2	2.87	0.66-12.39	0.16
Diabetes mellitus	2.14	0.63-7.23	0.22
Obesity	1.59	0.70-3.60	0.27
Immunosuppressive therapy	7.29	1.19-44.76	0.035
Urinary tract infection history	1.57	0.41-6.02	0.51
Antiplatelet therapy	1.17	0.42-3.28	0.77
Anticoagulant therapy	1.55	0.16-15.20	0.71
Robot-assited tranperitoneal laparoscopic approach	1.66	0.62-4.45	0.32
Lymph node dissection	0.91	0.49-1.68	0.75
Operative time	1	0.99-1.00	0.78
Blood loss	1	0.99-1.00	0.66
Length of urethral catheter	1	0.94-1.07	0.9
Length of hospital stay	1.06	0.88-1.27	0.56
Global complications (excluding SSI)	2.55	1.03-6.31	0.044
Antibiotic prophylaxis	0.46	0.22-0.92	0.028

SSI: Surgical Site Infections; ASA: American Society of Anesthesiologists

and included hemorrhagic events (pelvic hematoma in 2 patients), inguinal hernia with occlusion (in 2 patients), covered evisceration on umbilical incision with occlusion (2 patients), anastomotic fistula (1 patient), and compartment syndrome (1 patient). Patients who received AP had a lower rate of post-operative complications (16.8% *vs.* 27%, p=0.047).

Surgical site infections characteristics

SSI occurred in 52 patients (17.8%). SSI characteristics are shown in Table 2. SSI included superficial incisional SSI in 28 patients and organ/space SSI in 26 patients (Both type of SSI was reported in two patients). No deep incisional SSI was reported. Superficial incisional SSI only included superficial abscess of the umbilical incision while all organ/space SSI were UTI. There was a lower rate of SSI in patients that received AP (11.2% *vs.* 21.6%, p=0.025). In subgroups analysis, there was a lower rate of superficial incisional SSI with AP (3.7% *vs.* 13%, p=0.01) but no significant difference was observed regarding Organ/space SSI (7.5% *vs.* 9.7%, p=0.51).

Predictors of SSI

In univariable analysis, the predictors of SSI were a pre-operative immunosuppressive therapy (HR=7.286; CI 95% = 1.185-44.761; p=0.035), post-operative complications (excluding SSI) (HR=2.545; CI 95% = 1.027-6.312; p=0.044), and use of AP (HR=0.458; CI 95% = 0.223-0.918; p=0.028) (Table 3). In multivariable analysis, the predictors of SSI were post-operative complications (excluding SSI) (HR=2.603; CI 95% = 1.014-6.680; p=0.047), and use of AP (HR=0.410; CI 95% = 0.198-0.847; p=0.016) (Table 4).

Table 4: Predictors of SSI in multivariable analysis.

	Multivariable analysis		
	HR	CI 95%	p value
ASA score >2	1.75	0.31-9.77	0.53
Immunosuppressive therapy	7.33	0.99-54.37	0.051
Global complications (excluding SSI)	2.6	1.01-6.68	0.047
Antibiotic prophylaxis	0.41	0.20-0.85	0.016

SSI: surgical Site Infections; ASA: American Society of Anesthesiologists

Discussion

Few studies have investigated the role of AP in RP and its recommendation in this procedure is still questionable. The potential side effects, microbial resistance development and cost health increase associated with any AP need to assess its benefice before its introduction in clinical practice. In this study, we demonstrated the independent role of AP to decrease SSI after laparoscopic and robot assisted RP.

SSI is the most common cause of infections after surgery. In our study, SSI complication rate reached 17.8%. This rate is higher than expected. SSI rates reported in the literature ranged from 4% to 7.5% [3,12]. In our study, SSI were superficial incisional and organ/space infection while no deep incisional SSI was reported. Superficial incisional SSI only included superficial abscess of the umbilical incision while all organ/space SSI were UTI (bacteriuria associated with clinical symptoms). The high rate of SSI we observed in our study can be explained by the definition of organ/space SSI according CDC. This definition identifies the combination of bacteriuria and clinical symptoms (urinary irritative symptomatology) as UTI and, consequently, as organ/space SSI. After RP, this definition may include urinary symptoms that are not related to bacteriuria but consistent with other surgical complications or healing. Indeed, asymptomatic bacteriuria is common after urological procedures. Bacteriuria develops in up to 25% of patients who require a urinary catheter for one week or more, with a daily risk of 5% to 7% [13]. Therefore, in recent studies that reported infectious complications outcomes after transurethral resection of the prostate, photo vaporization of the prostate and radical prostatectomy, UTI were defined as the presence of bacteriuria associated with fever [14].

We demonstrated AP significantly decreased SSI. Other predictive factors of SSI were immunosuppressive therapy and surgical complication. Risk factors of SSI described in the literature [1] are ASA score, age, diabetes mellitus, obesity, immune disorders, urogenital infection history, urinary catheter and length of preoperative hospital stay. However, these risk factors have been mainly studied in cardiac and orthopedic surgery but not in urology. In our experience, diabetes mellitus was not associated with SSI. Diabetic patients have more asymptomatic bacteriuria and urinary infections [15]. In our institution, any asymptomatic pre- operative bacteriuria is searched and treated by antibiotics at least 48 h before surgery. However, patients with pre-operative bacteriuria were excluded from the analysis. It could explain that diabetes mellitus was

not found as a risk factor of SSI in our study. A recent study that assessed the role of AP in RP reported a duration of AP for more than 2 days, duration of urethral catheter and duration of surgical drain placement were independently associated with postoperative SSI [16]. In our study, AP was only use during the short-term pre-operative and operative time and duration of Foley catheter was not associated with SSI. In our experience, the surgical approach (laparoscopy *vs.* robot assistance) has not been found as a predictive factor. However, we did not compare laparoscopic or robot assisted RP to retropubic RP. Indeed, only 5 patients were treated with retropubic RP within the period of the study in our institution. Nevertheless, a recent study comparing 1084 robot-assisted laparoscopic RP and 4284 retropubic RP demonstrated that SSI incidence was lower in the robotic surgery group [17]. In another study comparing 4036 laparoscopic RP (robot-assisted or not) and 1283 retropubic RP, SSI rate was significantly lower in the laparoscopic group (p=0.001) [18].

Despite our results, the systematic use of an AP is still questionable in RP. Risk and benefice of the routine use of an AP in RP should be discussed. In our study, we demonstrated AP significantly decreased SSI. However, SSIs were only composed of superficial abscesses of umbilical incision and lower UTI. These infectious complications had no criterion of severity, and none required readmission. These SSIs could be classified as minor complications according EAU guidelines. The emergence of microbial resistance is a potential side effect of any antibiotic use in urology and a source of major concern [19]. A recent Japanese study showed that the improvement of hospital infection control strategies over 10 years, including a lower use of antibiotic prophylaxis, reduces the incidence of hospital-acquired Methicillin-Resistant *Staphylococcus aureus* [20]. Further studies on the impact of AP in terms of public health including evaluation of bacteriologic repercussion and cost effectiveness are needed.

Our study has limitations. The main limits are inherent to the non-controlled before-after study and retrospective design. Groups are not comparable for several characteristics. We tried to limit biases regarding this point by using multivariable regression approach. However, other issues regarding the impact of team and surgeon's experience remain and are not addressed in this study. Data were first collected retrospectively by reviewing physicians' report. However, to limit missing data's, all patients were interviewed during follow up with a systematic questionnaire to identify any SSI. Finally, as previously discussed, definitions of CDC may have overestimated UTI and organ/space SSI. Therefore, there is still a critical need for randomized study to confirm the use of AP in RP.

Conclusion

Our results warrant and strengthen the role of AP to decrease post-operative SSI after RP. However, further prospective, randomized and controlled trials comparing AP *vs.* placebo, cost analysis studies and public health considerations as well, are needed to state on its beneficial impact and its recommendation in routine use.

Ethical Standards

Research involving Human Participants. This study has been approved by the appropriate ethics committee.

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