RISK FACTORS AFFECTING THE INCIDENCE OF INFECTION AFTER ORTHOPAEDIC SURGERY: THE ROLE OF CHEMOPROPHYLAXIS

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SUMMARY

The incidence of surgical site infection and urinary tract infection following orthopaedic procedures has diminished in recent years due to modern antimicrobial prophylaxis.

We conducted a case-control study (100 cases, 100 controls) in order to evaluate the risk factors associated with infection after orthopaedic procedures. The following risk factors were defined: gender, age, comorbidities [rheumatoid arthritis, diabetes mellitus, obesity (>30 kg/m^2), peripheral vessel disease], pre- and post-operative glucose levels, pre-operative and post-operative length of stay (days), duration (days) of urinary catheterization, type of parenteral antibiotic prophylaxis (cefotaxime or vancomycin), time of surgery (elective or scheduled), American Society of Anesthesiologists (ASA) Score (0–3), type of surgery (fracture osteosynthesis, joint replacement, spinal surgery, other), and the type of anesthesia administered (general, epidural, spinal).

Urinary tract infection was the most frequent post-surgical infection (71 out of 100 cases) followed by surgical site infection (15 out of 100 cases). Using the multivariable logistic regression model, we found out that only the type of chemoprophylaxis was statistically significant risk factor ($p<0.001$) associated with post-surgical infection. More specifically, the use of vancomycin instead of cephalosporin is associated with a lower risk of infection.

Key words: infection, post-surgical, orthopaedic, risk factors

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INTRODUCTION

The incidence of deep and superficial surgical site infection (SSI) and urinary tract infection (UTI) following orthopaedic procedures has extremely decreased during recent decades due to modern antibiotic prophylaxis. Surgical site infection is the most serious complication occurring in 1% to 3% of orthopaedic surgical procedures (1). Most of these infections are the result of direct or airborne contamination at the time of surgery although approximately one-third of infections follow hematogenous seeding of the joint. Urinary tract infection is the second most common hospital-acquired infection reaching incidence of 25–28%. Mortality is tripled in patients having UTI and there is evidence of increased risk for metastatic infection around joint replacements although the latter finding remains controversial (2).

Risk factors associated with SSI include obesity, diabetes mellitus, rheumatoid arthritis, increased American Society of Anesthesiologists (ASA) risk index score (3), whereas female sex, number of days of urinary catheterization, and inappropriate catheter management seem to affect the risk of UTI (2).

In order to elucidate further the aetiology of any kind of infection in patients undergoing orthopaedic procedures, we conducted an observational study using a case-control design.

MATERIALS AND METHODS

A case-control study was performed in a tertiary care university teaching hospital aiming at the identification of risk factors for infection developing after an orthopaedic procedure. The study was approved by the institutional ethics committee.

The study group consisted of patients who experienced an infection following orthopaedic surgery while controls were randomly selected among patients who had undergone orthopaedic surgery without a subsequent infection. The definitions of infections investigated are given below: A superficial surgical site infection had a discharge, which yielded organisms from the culture of aseptically aspirated fluid or tissue from a swab; Deep infection was considered in case of strong clinical and radiological evidence of infection such as periosteal elevation, focal osteolysis, hot and swollen joint, draining sinus and/or positive intraoperative culture; A urinary tract infection was defined as urine culture with >100,000 colony-forming units/ml (CFU/ml) plus urinary symptoms (dysuria, frequency, urgency and/or suprapubic pain and/or fever); Pneumonia was defined as fever plus radiological findings on chest X-ray consistent with pneumonia.

Parenteral antibiotic prophylaxis was started pre-operatively and continued for a maximum of 48 hours after surgery and for

5–7 days for a potentially contaminated field. Broad spectrum antibiotics (cefotaxime or vancomycin if the patient had a penicillin allergy) were used. The prophylactic anticoagulation regimen consisted of administration of low molecular weight heparin at post-operative day 1 with continuing administration for 6 weeks.

All cases and controls had sterile urine culture pre-operatively. A urinary catheter was inserted perioperatively and was left in place from 12 hours up to 72 hours in several cases.

Statistical Methods

The descriptive statistics of continuous characteristics are presented as mean ± standard deviation. The distribution of continuous variables within cases and controls was compared using the Student's t statistic. Categorical characteristics are displayed as frequencies. Potential association between categorical variables was examined by the chi-squared test. The multivariable analysis was conducted using the logistic regression approach. The estimates derived from regression models were in the form of odds ratios (OR), which are presented along with their 95% confidence intervals (CI).

The effect of the following factors was examined in multivariable analysis: gender, age, comorbidities [rheumatoid arthritis, diabetes mellitus, obesity (>30 kg/m^2), peripheral vessel disease], pre- and post-operative glucose levels, pre-operative and post-operative length of stay (days), duration (days) of urinary catheterization, type of parenteral antibiotic prophylaxis (cefotaxime or vancomycin), time of surgery (elective or scheduled), American Society of Anesthesiologists (ASA) Score (0–3) the ASA score (0–3), type of surgery (fracture osteosynthesis, joint replacement, spinal surgery, other), and the type of anesthesia administered (general, epidural, spinal). In the first step of the model selection strategy, we applied models containing each of the aforementioned variables one at a time. Variables that appeared significant from step one were incorporated concurrently in one model and, subsequently, those that did not remain important were dropped. Insignificant variables from step one were retested in the model derived from step two as they may become important in the presence of others.

All tests of significance were two-sided and a p-value less than 0.05 was indicative of statistical significance. In model selection, the p-value of 0.10 was used as a criterion for inclusion. All statistical analyses were performed using the package STATA 10.0.

RESULTS

The current study involved 100 cases and 100 controls treated in the orthopaedic department of a tertiary care hospital in Greece during a 4 year period (2005–2009). Among cases, 71 had UTI, 15 had SSI, 10 developed pneumonia, 1 patient had SSI plus UTI while the remaining 3 cases experienced other kind of infection (acute cholecystitis, bacteremia probably related to UTI, and acute sinusitis) (Table 1).

In UTIs, the most common pathogen detected was *Escherichia coli* (*E. coli*) (n=32, 45.1% of UTIs) followed by *Pseudomonas aeruginosa* (*Ps. aeruginosa*) (n=14, 19.7% of UTIs), *Enterococcus spp* (n=12, 16.9% of UTIs), *Klebsiella pneumoniae* (n=9, 12.7% of UTIs), and *Acinetobacter spp.* (n=4, 5.6% of UTIs). Among SSIs, 2 infections (13.3%) were deep and the rest were superficial. The most common microorganism isolated in SSIs was *Staphylococcus aureus* (*S. aureus*) (n=9, 60% of SSIs) and more than half of these isolates were methicillin resistant (MRSA)

Table 1. *Characteristics and clinical parameters of the study population*

	Cases (n=100)	Controls (n=100)	p-value
Age	76.51 (±16.76)	66.45 (±16.94)	<0.001
Gender (males)	23	25	0.74
Obesity	44	26	0.01
Diabetes mellitus	19	14	0.34
ASA score			
1	31	62	<0.001
2	56	35	
3	13	3	
Anatomical location of surgery			
Knee	33	40	0.004
Hip	15	10	
Fracture	45	28	
Other	7	22	
Chemoprophylaxis			
Cephalosporin	49	28	0.002
Vancomycin	51	72	
Type of anesthesia			
General	60	73	0.06
Epidural	6	8	
Spinal	34	19	
Emergency of surgical procedure			
Scheduled	59	72	0.05
Urgent	41	28	
Pre-operation glucose levels	103.94 (±22.16)	100.88 (±25.92)	0.37
Post-operation glucose levels	109.42 (±26.58)	110.19 (±31.35)	0.85
Pre-operation hospitalization days	3.31 (±1.68)	3.67 (±2.42)	0.22
Total duration of hospitalization	12.35 (±3.06)	13.61 (±10.09)	0.23
Days of use of a urinary catheter	1.26 (±1.00)	0.82 (±0.73)	<0.001
Site of infection			
Urinary	71		
Surgical field	15		
Lung	10		
SSI+UTI	1		
Acute cholecystitis	1		
Bacteremia	1		
Acute sinusitis	1		

(n=6, 66.6% of *S. aureus* infections). Other organisms observed were coagulase-negative staphylococci (n=3, 20% of SSIs), *E. coli* (n=1, 6.7% of SSIs), whereas in 2 infections the pathogenic organism remained unidentifiable (n=2, 13.3% of SSIs).

The detailed demographic and clinical characteristics of the participants are presented in Table 1. Participants had a higher mean age at enrollment (76.51 vs. 66.45), were more obese (44 vs. 26), they were assigned higher ASA score, experienced mostly a knee (15 vs. 10) or a fracture surgery (45 vs. 28), and they had received mainly cefotaxime as prophylaxis (49 vs. 28).

The univariable logistic regression model revealed the following significant predictors ($p<0.10$) of post-operative infection: age, obesity, ASA score, the duration of urinary catheterization, the anatomical location of the surgical procedure, the type of anesthesia and the kind of the chemoprophylactic regimen. However, in multivariable modeling only the type of chemoprophylaxis retained the statistical significance (Table 2). More specifically, cases were almost 60% less likely (OR: 0.41; 95% CI: 0.19–0.89) to have received vancomycin as prophylaxis rather than cephalosporin compared with the control population.

DISCUSSION

Surgical site infection is a rare but true complication in orthopaedic surgery and is the most common compared to others. Although advances in surgical techniques, improvements in operating room ventilation, and the use of prophylactic chemoprophylaxis have all contributed to the decline of SSIs, it still remains the most serious infection following orthopaedic surgery, especially after arhthroplasty.

In our study, SSI represented the second most frequent infection after orthopaedic procedure, a finding not consistent with the results of previous studies where SSI represented the most prevalent post-surgical infection (4, 5). Several risk factors have been related to the incidence of SSI following joint arthroplasty including rheumatoid arthritis (5, 6), urinary tract infection (4, 7), the timing of prophylactic administration of antibiotics (8, 9), the use of surgical drainage (10), increased INR (3), admission from a health care facility (1), diabetes mellitus and morbid obesity (>40 kg/m^2) (5, 10, 11). In the univariable analysis of our study, age, obesity, ASA score, type of surgical procedure, and the kind of chemoprophylactic regimen were significant predictors for infection after orthopaedic surgery and, therefore, for SSI, which was the second most prevalent post-surgical complication in the cases' group.

Urinary infection is the most frequent infective complication in orthopaedic surgery after SSI and represents 28% of hospital acquired infections. The reported incidence of urinary infection after joint arthroplasty is from 28% up to 32.6% (12, 13) and approximately 10% after multilevel spinal instrumentation (14). UTI represented the most frequent of post-operative infections in the most cases included in our study. The use of an indwelling catheter is a well-recognized risk factor for developing UTI. In orthopaedic surgery, urinary retention is common and is attributed to anesthesia, to neural dysfunction of the bladder and, in males, to prostatic hypertrophy (15, 16). Thus, an indwelling Foley catheter or intermittent catheterization is often required. Intermittent catheterization has been found to cause less bacteriuria compared with an indwelling catheter for 48 hours (17). On the other hand, short-term use (less than 24 h) of an indwelling catheter after joint replacement reduces the incidence of urinary retention without

Table 2. *Results of univariable and multivariable logistic regression analysis*

Variable[1]	Univariable analysis			Multivariable analysis[4]		
	OR[2]	(95% CI[3])	P-value	OR	(95% CI)	p-value
Age	1.04	(1.02, 1.06)	<0.001	1.03	(0.99, 1.06)	0.11
Obesity (Rc[5]: no)	2.24	(1.23, 4.06)	0.01	2.07	(0.90, 4.76)	0.09
ASA (Rc:1)			<0.001			0.55
2	3.20	(1.75, 5.85)	<0.001	1.56	(0.68, 3.58)	0.30
3	8.70	(2.30, 32.68)	<0.001	2.34	(0.22, 24.56)	0.48
Days of use of a urinary catheter	2.07	(1.29, 3.32)	0.003	1.08	(0.52, 2.23)	0.84
Anatomical location of surgery (Rc: knee)			0.006			0.22
Hip	1.82	(0.72, 4.58)	0.20	1.96	(0.71, 5.42)	0.19
Fracture	1.95	(1.01, 3.77)	0.05	3.71	(0.59, 23.53)	0.16
Other	0.39	(0.15, 1.01)	0.05	0.68	(0.20, 2.27)	0.53
Chemoprophylaxis (Rc: cephalosporin)	0.40	(0.23, 0.73)	0.003	0.41	(0.19, 0.89)	0.03
Type of anesthesia (Rc: general)			0.006			0.60
Epidural	0.91	(0.30, 2.78)	0.87	0.79	(0.24, 2.57)	0.69
Spinal (rax)	2.18	(1.13, 4.20)	0.02	1.39	(0.64, 3.03)	0.41
Type of surgery (Rc: scheduled)	1.79	(0.99, 3.23)	0.05	0.26	(0.04, 1.74)	0.16

[1]Odds ratios for continuous variables (age and duration of urinary catheterization) correspond to one unit increase
[2]OR: Odds ratio
[3]CI: Confidence interval
[4]The multivariable analysis includes all variables found statistically significant ($p<0.10$) in univariable modeling
[5]Rc: reference category

increasing the rate of urinary tract infection (16, 18). Herruzo-Cabrera et al. showed that the use of a catheter for a period of 1–4 days is associated with a four-fold increase in the incidence of infection while its use for more than 4 days increases the incidence by a factor of 26 (2). UTI might also be connected with other factors. In a previous study, a higher proportion of infected knees was observed in patients who had UTI during the post-operative period although this finding failed to reach statistical significance (7). In a study conducted by Thomas et al. UTI from *Ps. aeruginosa* in patients who had undergone total hip arthroplasty was attributed to chemoprophylaxis with cephalosporin for more than three days (19). Finally, a high incidence of asymptomatic bacteriuria has been found in patients admitted to the hospital for joint replacement. However, no correlation has been confirmed between bacteriuria and surgical infection in these patients (20, 21). In the univariate regression model of our analysis, the duration of urinary catheterization (1.26 days for cases vs. 0.82 days for controls) along with the type of anesthesia and the kind of chemoprophylactic regimen were significant predictors of infection and, therefore, of UTI. The above-mentioned results are in accord with findings derived from previous studies (2, 14, 19).

Pneumonia was the third most frequent infection in the cases' group of our study. Pulmonary hypertension (right ventricular systolic pressure ≥35 mm Hg on transthoracic echocardiography) has been reported as a risk factor for pulmonary complications including pneumonia in orthopaedic surgery (22). Furthermore, earlier surgery has been correlated with low incidence of pneumonia in a study conducted by Simunovic et al. (23). Although none of our patients reported a history of pulmonary hypertension and none had been intubated, 10 out of the 100 cases developed pneumonia. This may be relevant to the advanced age of the cases compared with controls (76.5 years vs. 66.45 years) and to the higher ASA score (56 of the cases have ASA score 2 vs. only 35 controls with ASA score 2), which raises the possibility of aspiration pneumonia.

In multivariable modeling, the type of chemoprophylaxis was the only parameter that retained its statistical significance. In particular, we found that the use of vancomycin is related to significant lower risk of acquiring infection after an orthopaedic procedure. Other studies have also revealed the role of chemoprophylaxis in the development of post-surgical infections. Herruzo-Cabrera et al. have showed that antibiotic prophylaxis decreases the incidence of urinary infection by a factor of 1.91 considering that cefazolin or vancomycin are effective not only for wound infection (24) but also against the habitual contaminants of the urinary tract (2). Suboptimal timing of prophylactic antibiotics was associated with a 3–4 fold increased risk of SSI in a study conducted by Olsen et al. (9). This is similar to the results presented by Classen et al., Kang et al. as well by Takahashi et al., in which postoperative administration chemoprophylaxis had the strongest association with infection (8, 25). Finally, a single dose teicoplanin was proved more effective as prophylaxis for total hip or knee arthroplasty compared with multiple doses of broad spectrum antimicrobials (26), a finding which enhances the results of our study.

All observational studies including case-control designs suffer from limitations. In particular, this research considered totally 200 individuals and might lacked power to identify more predictors of post-surgical infections apart from chemoprophylaxis. Second, this study was conducted in one orthopaedic clinic of a tertiary hospital in Athens and thus its results may not be generalized. Finally, all observational studies can be biased or confounded by unmeasured covariates although we tried to take into account all potential risk factors for post surgical infections.

CONCLUSION

UTI was the most frequent hospital cross infection after orthopaedic procedure in our study followed by SSI. Although many factors were significantly associated with post-operative infection in univariate analysis, only the kind of chemoprophylaxis remained a statistically significant predictor in multivariable modeling. More specifically, the use of vancomycin instead of cephalosporin is associated with a lower risk of infection.

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