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Original article

The impact of preoperative bacteriuria on the risk of periprosthetic joint infection after primary knee or hip replacement: a retrospective study with a 1-year follow up

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ABSTRACT

Objectives: Patients who undergo elective joint replacement are traditionally screened and treated for preoperative bacteriuria to prevent periprosthetic joint infection (PJI). More recently, this practice has been questioned. The purpose of this study was to determine whether preoperative bacteriuria is associated with an increased risk of PJI.
Methods: Patients who had undergone a primary hip or knee replacement in a tertiary care hospital between September 2002 and December 2013 were identified from the hospital database (23 171 joint replacements, 10 200 hips, and 12 971 knees). The results of urine cultures taken within 90 days before the operation were obtained. Patients with subsequent PJI or superficial wound infection in a 1-year follow-up period were identified based on prospective infection surveillance. The association between bacteriuria and PJI was examined using a multivariable logistic regression model that included information on the operated joint, age, gender and the patients' chronic diseases.
Results: The incidence of PJI was 0.68% (n = 158). Preoperative bacteriuria was not associated with an increased risk of PJI either in the univariate (0.51% versus 0.71%, OR 0.72, 95% CI 0.34–1.54) or in the multivariable (OR 0.82, 95% CI 0.38–1.77) analysis. There were no cases where PJI was caused by a pathogen identified in the preoperative urine culture. Results were similar for superficial infections.
Conclusions: There was no association between preoperative bacteriuria and postoperative surgical site infection. Based on these results, it seems that the preoperative screening and treatment of asymptomatic bacteriuria is not required. **M. Honkanen, Clin Microbiol Infect 2018;24:376**

Introduction

To prevent postoperative infections, patients undergoing elective joint replacement have traditionally been routinely screened for bacteriuria [1,2]. The risk for haematogenous seeding to a prosthetic joint from a postoperative urinary tract infection has been reported [3–5]. However, the association between preoperative asymptomatic bacteriuria (ASB) and periprosthetic joint infection (PJI) is less clear. Therefore, the efficacy of the practice of routine urine cultures has been questioned in recent studies [6,7].

The relationship between preoperative ASB and PJI has previously been examined in small retrospective studies [8,9] and in one large registry-based study [10]. However, only in the last decade have there been prospective studies carried out on the subject [7,11–15]. Some of these studies have shown an increased risk of postoperative infection complications in patients with preoperative ASB [11,14], but direct seeding to the prosthetic joint has not been reported. Furthermore, treating preoperative ASB with antibiotics has not been shown to be effective in preventing PJI [7,12,14,15].

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ASB is fairly common in the general population, especially in older women. In people in their 70s, the estimated prevalence of ASB is between 11% and 16% for women and between 4% and 19% for men [16]. For women and men aged ≥ 80 years, the estimated prevalence is 20% and 10%, respectively [17]. In patients undergoing elective joint replacement, the prevalence of ASB varies from 3.5% to 36% [8,12–15]. The unnecessary treatment of ASB with antibiotics has several drawbacks, such as the emergence of resistant bacterial strains, the occurrence of *Clostridium difficile* infection, and increased costs [18,19], and is therefore not currently recommended for the general population [16].

Guidelines concerning the screening of the preoperative urine samples of asymptomatic patients undergoing elective joint replacement surgery are conflicting. The British Orthopaedic Association recommends preoperative urine screening [6], whereas the consensus statement from the International Consensus Meeting on Periprosthetic Joint Infection opposes it [20]. The current Infectious Diseases Society of America guideline gives no recommendations on the matter [16], but lists urine screening before joint replacement surgery as an important topic for future research as does the International Consensus statement [20].

The purpose of this retrospective observational study with a 1-year follow up was therefore to determine whether preoperative bacteriuria before elective joint replacement increases the risk of PJI or surgical site infection in a 1-year follow up.

Materials and methods

This retrospective study was performed at the Coxa Hospital for Joint Replacement, Tampere, Finland, a publicly funded tertiary orthopaedic hospital. Patients who had undergone primary hip or knee replacement between September 2002 and December 2013 were identified from the local prospective joint replacement database. According to the national legislation, patient consent is not required in retrospective studies like this. If more than one primary joint replacement was performed on a patient during the study period, each joint replacement was considered separately. With a few exceptions, the patients underwent surgery under spinal anaesthesia. Unless contraindicated, a single dose of cefuroxime was used as antibiotic prophylaxis. Cemented prostheses were fixed with gentamicin-impregnated bone cement.

Urine cultures were part of the routine preoperative laboratory testing for all patients. For this study, the results of urine cultures taken within 90 days before the joint replacement were obtained from the electronic records of a microbiology laboratory accredited by Tampere University Hospital. The species of bacteria found in the urine samples and their antibiotic susceptibility data were recorded. If more than one urine sample was taken, the one taken closest to the date of operation was used in the analyses. All bacterial growth in the urine was considered significant. If more than one bacterium was reported in the sample, they were all recorded. The outcomes with patients with missing urine samples are reported separately.

Information regarding chronic diseases was gathered from the drug reimbursement register of the Social Insurance Institution of Finland. All permanent residents of Finland are covered by national health insurance, which includes drug reimbursements. To receive reimbursements, patients require a certificate issued by the treating doctor and the right to reimbursement is granted based on the specific diagnostic criteria for each disease. Patients with a valid entitlement to reimbursement for certain chronic diseases (diabetes, rheumatic diseases, hypertension, chronic heart failure, chronic coronary disease, arrhythmias, chronic lung disease, Parkinson's disease, epilepsy, Alzheimer's disease, psychotic disorders, haematological and solid malignancies) at the time of the joint replacement were identified. For the analyses, chronic heart failure, chronic coronary disease and arrhythmias were grouped together, as were Parkinson's disease, epilepsy, Alzheimer's disease and psychotic disorders.

Information on the antibiotics (identified based on their ATC codes) purchased by the patients within 90 days before the joint replacement was gathered from the prescription register of the Social Insurance Institution of Finland. In Finland, antibiotics are not available without a prescription and all purchases are recorded in the national prescription register. The type of antibiotic and the date of purchase were also recorded. Antibiotics for preoperative bacteriuria were prescribed by orthopaedists at the operating hospital, but other antibiotics could have been prescribed elsewhere.

Cases of infection were identified from prospective post-discharge surveillance data gathered by an infection control nurse according to the Centers for Disease Control and Prevention criteria [21] and National Nosocomial Infection Surveillance system methodology adapted for Finland [22]. The primary outcome was the occurrence of PJI. The occurrence of any surgical site infection (superficial or deep incisional infection or PJI) was analysed as a secondary outcome. Microbiological data on the occurrence of PJI were collected from the electronic records of the microbiology laboratory. In order to have a 1-year follow-up period for all operated joints, cases of infection recorded between September 2002 and December 2014 were identified.

Statistical analysis

All data analyses and management were performed using the SPSS for Windows 23.0 statistical software package.

Categorical variables were compared with χ^2 test and continuous variables (age) with Student's independent-samples *t*-test. A p value <0.05 was considered statistically significant.

The association between potential risk factors for infection and the outcome (PJIs and all infections separately) was examined using logistic regression with univariate analysis. A multivariable model was developed that included all potential risk factors for infection that were examined in the univariate analysis.

Results

In total, 23 171 primary joint replacements were performed in 17 562 people between September 2002 and December 2013. Of these, 10 200 (44%) were primary hip and 12 971 (56%) primary knee replacements, respectively. In addition, 1805 (8%) operations

Table 1
Bacteria found in the preoperative urine samples (some samples contained more than one bacterium, these are recorded separately)

Bacterium species	*n* (*N*=1378)	%
Gram-negative		
Escherichia coli	822	59.7
Klebsiella	114	8.3
Proteus	36	2.6
Citrobacter	10	0.7
Morganella	4	0.3
Pseudomonas	23	1.7
Acinetobacter	8	0.6
Other	39	2.8
Gram-positive		
Coagulase-negative staphylococci	63	4.6
Staphylococcus aureus	11	0.8
Streptococcus agalactiae	136	9.9
Enterococcus spp.	149	10.8
Other	8	0.6

were simultaneous bilateral hip or knee replacements. From the total number of operations, 14 361 (62%) were performed for women and 8810 (38%) for men. The mean age at the time of operation was 67 years (range 14 years to 109 years).

A preoperative urine sample was available in 20 226 operations (87%), and 1378 (6.8%) of the urine cultures were positive. Most of the samples were collected within 30 days before the surgery (see Supplementary material, Fig. S1). The bacteria found in the urine are listed in Table 1. Of the positive urine samples, 1237 (90%) were in women. Patients with positive urine cultures were also older and had more chronic diseases than patients with a negative urine culture (see Supplementary material, Table S1). Positive urine cultures were more frequent in patients undergoing knee replacement than hip replacement. A preoperative urine sample was missing in 2945 (12.7%) operations. There were more missing samples in men than in women (16% versus 11%) and more before hip replacements than before knee replacements (16% versus 10%). The mean age of the patients with a missing urine sample was also lower (64 years versus 68 years) and there were fewer patients suffering from diabetes (7.1% versus 8.2%).

During the 1-year follow up, 490 surgical site infections (2.11% of the study population) were identified. Of these, 158 were PJIs, giving an incidence of 0.68% in the whole study population. The incidence of PJI was 0.57% (58/10 200) for hip replacements and 0.77% (100/12 971) for knee replacements. In seven (4%) of the PJI cases, the preoperative urine culture was positive, and in 133 (84%) cases the culture was negative. In 18 (11%) PJI cases, the urine sample was missing. In the PJI cases with a positive urine culture, the pathogens found in the urine cultures and those identified from the joint were not the same in any of the cases (Table 2). Furthermore, no evidence to link preoperative urine cultures to superficial or deep wound infections could be found (data not shown).

In patients with a positive urine culture, the incidence of PJI was 0.51% (7/1378), and 0.71% (133/18 848) in patients with a negative culture. The incidence of all surgical site infections was 1.89% (26/1378) in patients with a positive urine culture and 2.18% (411/18 848) in those patients with a negative urine culture. No statistically significant association was found in univariate or multivariable analysis between positive urine culture and PJI or all surgical site infections (Table 3). The impact of other risk factors on the risk of PJI is presented in Table 3.

Of the patients with preoperative bacteriuria, 344 (25%) received antibiotics after the urine sample was taken. In 51 patients, the prescribed antibiotic was not effective against the pathogen found in the urine, mostly because of the acquired or natural resistance properties of the pathogen. Of the 293 patients with effective antibiotic treatment, one (0.34%) had a subsequent PJI, whereas of the 1085 patients with bacteriuria and no or no effective antibiotics, six (0.55%) had a PJI. Treating the bacteriuria with effective antibiotics did not affect the risk of PJI (OR 0.62, 95% CI 0.07–5.14).

There were 18 PJI cases (incidence 0.61%) and 35 superficial or deep wound infections (incidence 1.19%) among the 2945 patients without preoperative urine samples. These incidences were similar to the overall incidence. In 11 PJI cases, the pathogens causing the infection could be identified (*Staphylococcus aureus*, *Corynebacterium* species and coagulase-negative staphylococci) and none were typical urinary tract pathogens.

Discussion

The findings of this large retrospective study show that there is no association between preoperative bacteriuria and subsequent postoperative PJI after primary joint replacement when possible confounding factors, such as chronic diseases, are taken into account. Furthermore, there were no postoperative infections caused by the pathogens found in the preoperative urine samples and treating the bacteriuria with effective antibiotics did not decrease the incidence of PJI.

During the study, the influence of possible confounding factors, especially chronic diseases, was taken into account extensively. Furthermore, the data were based on prospective systematic surveillance, which strengthens the reliability of this retrospective study. It has been estimated that to conduct a reliable prospective randomized controlled trial that compares the screening and treatment of bacteriuria with no screening and treatment, it would require a study population of 50 000 patients in each study arm, which is not feasible [13]. Previous prospective studies [11,12,14,15] have had small sample sizes, and so have been insufficiently powered.

The incidence of PJI in this study (0.68%; 0.57% for hip and 0.77% for knee replacements) is similar to the findings of previous studies: 0.3%–0.6% for hip replacements [23,24] and 0.8%–1.1% for knee replacements [23–25], with the exception of a study by Lamb *et al.* [7], where the overall incidence of PJI was very low (0.02%). The cases of infection in the present study were identified by postoperative infection surveillance that has been shown to miss some infections [22]. This should not, however, be seen to bias the findings of this study. Male gender, age, knee replacement and diabetes were all associated with an increased risk of PJI, which is in line with previous studies [25,26]. Obesity has also been shown to be a risk factor for PJI [26]; however, body mass index data were not available for this study population.

The prevalence of preoperative bacteriuria was 6.8%, which is similar to two earlier Spanish studies [12,15] and slightly lower than in other studies [8,13,14]. There was no association between preoperative bacteriuria and postoperative surgical site infection or PJI. Furthermore, in the cases with preoperative bacteriuria and

Table 2
Comparison between pathogens found in the preoperative urine sample and postoperative prosthetic joint infection (PJI)

Case number	Age	Gender	Operated joint	Time between urine sample and surgery (days)	Time between surgery and infection (days)	Pathogen found in urine	Pathogen causing PJI
1	81	Female	Hip	36	16	*Enterococcus faecalis*	*Staphylococcus aureus*
2	76	Female	Knee	9	16	*Escherichia coli*	NA[a]
3	76	Male	Knee	31	18	*Enterococcus faecalis*	Coagulase-negative staphylococcus
4	63	Female	Knee	11	36	*Klebsiella pneumoniae*	*Staphylococcus aureus*
5	81	Female	Knee	64	85	*Escherichia coli*	Coagulase-negative staphylococcus
6	75	Female	Knee	0	142	*Escherichia coli*	NA[a]
7	79	Male	Knee	29	258	Coagulase-negative staphylococcus	*Staphylococcus epidermidis*[b]

[a] Culture-negative PJI.
[b] Different antibiotic resistance pattern from the strain found in the urine.

Table 3
Potential factors affecting the risk of periprosthetic joint infection and any surgical site infection in primary joint replacements

Factor	Periprosthetic joint infection				Any surgical site infection			
	Univariate analysis		Multivariable analysis[a]		Univariate analysis		Multivariable analysis[a]	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Positive urine culture	0.72	0.34–1.54	0.82	0.38–1.77	0.86	0.58–1.29	0.92	0.61–1.39
Male gender	1.96	1.43–2.68	2.21	1.56–3.11	1.31	1.10–1.57	1.45	1.19–1.77
Knee replacement	1.36	0.98–1.88	1.43	1.01–2.04	1.53	1.27–1.85	1.58	1.29–1.94
Age	1.01	1.00–1.03	1.03	1.01–1.05	1.00	0.99–1.01	1.01	1.00–1.02
Chronic diseases								
Chronic heart disease[b]	0.78	0.55–1.10	0.58	0.28–1.21	0.97	0.80–1.17	0.73	0.48–1.12
Chronic lung disease	1.07	0.58–1.98	1.04	0.53–2.05	1.46	1.07–1.99	1.39	0.99–1.95
Diabetes	1.65	1.03–2.65	1.64	0.99–2.73	1.30	0.96–1.75	1.09	0.78–1.52
Hypertension	0.76	0.52–1.11	1.09	0.50–2.38	1.02	0.83–1.24	1.25	0.80–1.96
Malignancy	0.54	0.17–1.68	0.55	0.17–1.72	0.51	0.26–1.00	0.58	0.30–1.14
Neurological or psychiatric disorder[c]	1.02	0.45–2.30	1.15	0.51–2.63	1.04	0.65–1.65	1.21	0.76–1.92
Rheumatic disease	0.59	0.24–1.44	0.61	0.23–1.67	1.06	0.71–1.57	1.09	0.72–1.66

[a] All variables analysed in the univariate analysis were included in the multivariable analysis.
[b] Includes chronic heart failure, chronic coronary disease and arrhythmias.
[c] Includes Parkinson's disease, epilepsy, Alzheimer's disease and psychotic disorders.

subsequent PJI, the pathogens were not the same. In addition, treating the bacteriuria with antibiotics did not decrease the risk of PJI. Previous studies have yielded variable results. Several studies, such as the classic study by Glynn and Sheehan [8], have found no association between preoperative bacteriuria and PJI. However, the study by Glynn and Sheehan had a small sample size and a follow-up period of only 3 months. In a more recent study, Cordero-Ampuero *et al.* [12] found no association between preoperative bacteriuria and postoperative infection following hip replacement, and treating the bacteriuria with antibiotics had no effect on the incidence of infection. The same research group reported similar results for knee replacements [15]. Unlike earlier studies, the current study takes into account the effect of both chronic diseases and outpatient antibiotic use. Even so, the results are still in line with those of the above-mentioned studies.

On the other hand, Sousa *et al.* [14] found that patients with preoperative ASB had a statistically significantly increased risk of PJI, but the micro-organisms found in the urine and those causing the PJI were different. Furthermore, there was no difference in the incidence of PJI when comparing those patients who had received antibiotics for the bacteriuria and those who had not. This suggests that in patients with ASB there are some other factors that could contribute to the risk of PJI. In fact, the current study shows that patients with preoperative bacteriuria have more chronic diseases than patients with negative urine cultures.

There were some limitations in this study. First, this was a retrospective study, and therefore it was not possible to differentiate between asymptomatic bacteriuria and symptomatic urinary tract infection due to a lack of clinical data, and unfortunately the concentration of bacterial growth in the urine samples could not be retrieved from the laboratory data. Furthermore, the timing of urine samples taken before the operation could not be influenced. Most samples were, however, collected close to the surgery. Second, a urine sample was not available in 13% of the operations. However, none of the PJIs in patients with a missing urine sample were caused by pathogens that typically cause urinary tract infections. The incidence of PJI was not higher among patients with a missing urine sample than in the overall study population. Third, it was not possible to take into account all possible confounding factors. The drug reimbursement data gives a fairly accurate estimate of the prevalence of certain chronic diseases. However, due to the nature of the reimbursement criteria, in certain diseases (such as hypertension) patients who only have a mild form of the disease receive no reimbursements, and so their prevalence may be underestimated. These mild forms of diseases probably have less effect on the risk of bacteriuria and should therefore not affect the results. Furthermore, information on body mass index, serum creatinine level or urinary tract diseases could not be obtained.

This study adds to the growing body of evidence that supports the view that asymptomatic preoperative bacteriuria does not cause PJI, and hence it should not be screened or treated. This finding should be taken into account in future guidelines regarding the screening and treatment of preoperative ASB before joint replacement surgery.

Transparency declaration

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Authors' contribution

MH, EJ, MK, RH and JS designed the study and MH collected the data and wrote the first draft of the article. All authors participated in the interpretation of the data and revising the article. All authors have seen and approved the final version of the article.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.cmi.2017.07.022.

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