ORIGINAL ARTICLE

Risk factors for periprosthetic joint infection of the hip and knee

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ABSTRACT

Aim To investigate risk factors for the development of prosthetic joint infection.

Methods A group of 50 patients with periprosthetic infection was compared with a group of 100 randomly selected patients with total hip or knee arthroplasty without infectious complications. Twelve risk factors in both groups were analysed.

Results Five factors showed to be significant: body mass index higher than 40, diabetes mellitus on insulin therapy, kidney and liver disease, vascular disease of the lower extremities and positive drain tip culture.

Conclusion One of the ways to reduce the incidence of periprosthetic infection is the maximum possible elimination of risk factors in patients who have a high probability of endoprosthesis infection. If this elimination is not possible for a long time, it is advisable to consider abandoning the planned operation.

Key words: body mass index, diabetes mellitus, total joint replacement

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INTRODUCTION

Infection is the most serious complication of total joint arthroplasty. Its treatment is very complicated from surgical, psychological and economical perspectives (1,2). Repeated surgical interventions, prolonged antibiotics administration and difficult rehabilitation create psychological burden for the patient (2). Revision surgery often fails to deliver satisfactory functional outcomes even after successful treatment of infected primary implant (3). Hence orthopaedic surgeons are focused on reducing the incidence of infections.

The prevalence of infectious complications in endoprosthetic centres is rather constant and reported between 1%-3%, despite differences in antibiotic prophylaxis, operating theatre environment, surgical technique, duration of the procedure and surface and fixation modalities of an implant (3-5). Establishment of periprosthetic joint infection is determined by multiple factors related to host, surgical wound, operative technique, theatre environment and microbiological characteristics of infectious agent (6,7). It is generally accepted that joint implants per se represent important risk factor for developing infection (6,8).

Patient related risk factors can be divided in two groups: systemic (associated pathologies, past medical history) and local (previous surgeries or trauma of the joint) (9,10). In general, all systemic pathologies which affect host immune response to bacterial infection and facilitate establishment of infectious focus with possible haematogenic spread should be considered as risk factors (10,11). Local pathological states with influence over immune response of the organism, which facilitate bacterial colonisation (compromised blood flow in a limb, presence of scar or necrotic tissue) are also considered as risk factors (12).

The aim of this study was to determine risk factors for infection in the patients with periprosthetic joint infection, to examine their weight and role and to contribute to the general understanding of the establishment of periprosthetic infection.

PATIENTS AND METHODS

Patients and study design

Between 2013 and 2018 a total of 64 cases of periprosthetic infection of the hip and knee joints were surgically treated at the Banska Bystrica Orthopaedic Clinic. The time from the primary arthroplasty to the development of the first signs of infection was in each patient less than five years. All cases of periprosthetic infection were confirmed by laboratory, microbiological, local tissue changes and radiological findings. The basis for diagnostics was positive microbiological culture results. Samples were collected from abscess incisions, or swabs were taken from the prosthesis surface during a revision of the joint. During each surgery the infection was also confirmed macroscopically.

The type of primary prosthesis, site of infection and demographics were not considered as inclusion criteria for the study. Patients were excluded from the study if the primary arthroplasty was indicated due to malignancy, as in these cases the infection may be promoted by other factors (use of megaprosthesis, effects of chemotherapy). Patients in whom the primary arthroplasty was performed in another centre and patients who underwent revision surgery after five years from primary arthroplasty were also excluded.

The control group consisted of twice the number of randomly selected patients, who all underwent primary arthroplasty of the knee or hip joint in our Department during the same period of time and in whom no signs of infection have become apparent so far. In order to include a patient in the control group, their last follow up appointment must have taken place at least 5 years after the primary arthroplasty.

Methods

Factors considered as potentially increasing the risk of infection were determined according to the literature review (7) and to our own observations. From general attributes in the context of risk factors age and body mass index (BMI) were examined. Among systemic diseases diabetes mellitus (DM), rheumatoid arthritis (RA), nephropathies and hepatopathies, as well as the presence of malignancy in the past medical history were examined. With regards to the local findings the presence of lower limb venous pathology (varicosities, leg ulcers and phlebothrombosis), previous joint surgical interventions - revision arthroplasties, arthroscopies, osteosynthesis and osteotomies - and positive post-operative drain microbiology cultures result were analysed. Risk factors were divided according to the frequency of their distribution and respective statistical significance into important (prevalence three times more frequent in the infected group) and less im-

portant risk factors (prevalence in the infected group is less than three times).

Statistical analysis

Doubling the number of patients in the control group was necessary in order to achieve statistical validity when comparing with the group of infected patients. Statistical significance of differences in proportions of variables between groups was evaluated by Fisher's exact test. Data were also processed using z-test for two proportions /two - tailed test, Mann-Whitney test and $\chi 2$ test. Statistical significance was set as $p < 0.01$.

RESULTS

Calculated age mean value in the group of infected patients was 63 years, in the control group, 64 years. Proportions of hip to knee arthroplasties in each group were comparable (p=0.8615). Similarly, age distribution within both groups was homogeneous (p=0.9539).

The age distribution of the patients in both groups was not statistically significantly different (p=0.6245).

Mean value of BMI within the group of infected prosthesis was 31 and in the control group 30 (p=0.2149).

In accordance with the obtained prevalence of presumed risk factors in each group and respective statistical significance and proportions of relative prevalence and according to our criteria five important risk factors were identified: BMI above 40, insulin-dependent DM (DM-INS), hepatopathy and nephropathy, lower limb vascular disease (Table 1).

Table 1. The incidence of presumed risk factors in each group and respective statistical significance of differences and proportions of relative incidences

Risk factor	No (%) of patients		p	Relative risk
	Infected group (n 50)	Control group (n 100)		
BMI > 40	9 (18)	4 (4)	0.0064	4.5
DM-PAD	10 (20)	9 (9)	0.0522	2.2
DM- INS	7 (14)	4 (4)	0.0330	3.5
RA	6 (12)	5 (5)	0.1134	2.4
Nephropathy	5 (10)	3 (3)	0.0821	3.3
Hepathopathy	8 (16)	5 (5)	0.0285	3.2
Malignancy	4 (8)	8 (8)	1.0000	1.0
Vascular disease of the LE	9 (18)	6 (6)	0.0242	3.0
Previous surgery	6 (12)	5 (5)	0.1134	2.4
Revision arthroplasty	6 (12)	6 (6)	0.1684	2.0
Positive drain tip culture	8 (16)	11 (11)	0.2676	1.5

BMI, body mass index; DM-PAD, diabetes mellitus on per oral antidiabetic treatment; DM-INS, insulin-dependent diabetes mellitus;

Altogether 78 risk factors (RFs) were identified in the infected group, 38 of them were important. In the control group there were 66 RFs identified, of which 22 were important RFs. The number of patients with a risk factor in the infected group was high, 45 (90%), in the control group it was 41 (41%) (p<0.0001) (Table 2).

Table 2. Distribution of risk factors (RFs)

Risk factors distribution factors		Infected group (n=50)	Control group (n=100)
All RFs (No)		78	66
	Important RFs*	38	22
	Less important RFs†	40	44
Patients with RFs (No; %)		45 (90)	41 (41)
Patients without RFs (No; %)		5 (10)	59 (59)

*prevalence three times more frequent in the infected group; †prevalence in the infected group is less than three times

Subsequent analysis of risk factors according to their prevalence in both groups showed 18 (36%) patients with one RFs in the infected group and 30 (30%) in the control group; 15 (30%) patients in the infected group had two RFs and 12 (24%) had three RFs. In the control group eight (8%) patients had two and three patients (3%) had three RFs. The frequency of occurrence of a risk factor with a given number was statistically different in the groups (p=0.0056) (Table 3).

Table 3. Distribution of risk factors (RFs) in both groups

No of risk factors	No (%) of patients with RFs		Relative risk
	Infected group (n 50)	Control group (n 100)	
one	18 (36)	30 (30)	1.2
two	15 (30)	8 (8)	3.8
three	12 (24)	3 (3)	8.0
Total	45 (90)	41 (41)	

p=0.0056

Our results suggest, that if a patient had 2 or more important risk factors, probability of him/her suffering from periprosthetic infection increases 7 times (p=0.00037); if a patient presents with 2 or more less important risk factors then the probability of suffering from periprosthetic infection was 4 times higher (p=0.0957). Patients who present with one important and one less important risk factor face 5 times increased relative risk of infection (p=0.0163) (Table 4).

Table 4. Clustering of risk factors (RFs) in infected and control group and their comparison

Risk factor cluster	No (%) of patients		p	Relative risk
	Infected group (n 50)	Control group (n 100)		
Patients with 2 or more important RFs	11 (22)	3 (3)	0.00037	7.3
Patients with 2 or more less important RFs	4 (8)	2 (2)	0.0957	4.0
Patients with one important and one less important RF	7 (14)	3 (3)	0.0163	4.7

DISCUSSION

Risk factors for periprosthetic infection were repeatedly studied in the past, some of them are generally accepted, while the interpretation of some others remains uncertain. Several scoring systems were published, evaluating risk factors according to their influence on the infection establishment, from those with minimal to those with maximal impact (13,14).

Among systemic diseases, rheumatoid arthritis is considered as an important risk factor. Various studies have reported 2-4 times higher risk of periprosthetic infection in patients who suffer from this disease (15,16). However, Berbari et al. did not prove rheumatoid arthritis to be the risk factor (9). In our study RA prevalence within the group of the infected patients was more than two times higher, which implies we could consider it as a less important risk factor.

In diabetic patients prevalence of prosthetic joint infection was reported 3-6 times more frequently than in non-diabetic patients (17). Again, there exist studies which did not prove higher prevalence of infection among diabetic patients (18). Our paper seems to have proved that diabetes, and in particular DM with insulin treatment, has considerable influence on the infection establishment. Among insulin-dependent patients the prevalence of periprosthetic infection was four times higher when compared to two-fold increase in the prevalence among patients on per oral antidiabetic treatment (DM-PAD).

The view on the role of obesity and its role as a risk factor for periprosthetic infection is not unified. Some authors report higher prevalence of infection among obese patients, others do not consider it as a risk factor (17,19,20). For us it seems that obesity is a definite risk factor with almost 2-fold higher prevalence among obese patients and 4.5-fold among patients who suffer from morbid obesity (BMI above 40).

Nephropathy, hepatopathy and malignancy in the past medical history are among other risk factors that could influence the establishment of periprosthetic infection (8,21). Our results are similar to those of others, with an exception of malignancy where its significance was not proven. No statistical difference was noted in the distribution of age between both groups.

Previous surgery (previous arthroplasty on native joint or other intraarcticular surgical interventions) is one of the local risk factors that impacts periprosthetic infection (8,23). According to Suzuki et al. (22) and Rand et al. (23) previous surgery increases the incidence of infection twofold in case of total knee arthroplasty, and threefold in hip arthroplasty (22,23). Berbari does not consider previous joint surgery as a risk factor. Our results suggest higher relative risk of infection, however, we agree with Gallo et al. that not all types of previous surgeries could be considered as definite risk factors. When evaluating the risk it is necessary to take into account type and length of surgery, time since primary arthroplasty and a number of previous surgical interventions prior to arthroplasty (6,23).

Poss et al. reported in his paper 8-fold increase in the incidence of infection in a group of patients with revision arthroplasty when comparing with patients with primary arthroplasty (24). Results of Berbari et al. (9) showed 2.2 times more revision arthroplasties in the infected group, which correlates with our results.

The staging system of Hanssen et al. contains vascular complications of lower limbs and algoneurodystrophy syndrome (25). We agree with this opinion and believe that vascular supply in the operated limb has crucial impact on adequate immune response and our paper considers vascular pathology to be an important risk factor with triple difference. Unlike other authors, in our paper we considered as a risk factor the post-operative complication of positive drain microbiology cultures results. Nevertheless we agree that any scoring system should help to decrease the prevalence of infectious complications by eliminating patients with clustered risk factors before the surgery takes place and its role is not to provide risk

assessment for infection post-operatively. In this context we were rather surprised that none of the cited papers mention positive drain microbiology results as a risk factor, whilst in our group of infected patients we report 2-fold increase.

The aim of our paper was to contribute to the reduction of prevalence of periprosthetic infections. A possible way to achieve this seems to involve the elimination of risk factors as much as possible in patients with high probability of periprosthetic infection. If such elimination is not achievable in long-term, it is fair to consider not to operate.

The likelihood of developing periprosthetic infection increases as risk factors cluster.

According to the criteria mentioned above, our paper considers important risk factors as follows: BMI above 40, insulin-dependent DM, hepatopathy and nephropathy, lower limb vascular disease.

It is necessary to weight risks and benefits of surgical intervention before indicating the procedure in patients, who present with these risk factors, and particularly in patients who present with multiple risk factors. We advise to assess each patient individually with regards to the risk factors as listed above.

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TRANSPARENCY DECLARATION

Competing interests: None to declare

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