JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Original Article

Risk factors for periprosthetic joint infection after primary artificial hip and knee joint replacements

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Abstract

Introduction: We aimed to explore the risk factors for periprosthetic joint infection (PJI) after primary artificial hip and knee joint replacements by performing a case-control study.

Methodology: The clinical data of patients receiving primary hip and knee joint replacements were retrospectively analyzed. The case group included 96 patients who suffered from PJI, comprising 42 cases of hip joint replacement and 54 cases of knee joint replacement. Another 192 patients who received joint replacement at the ratio of 1:2 in the same period and did not suffer from PJI were selected as the control group. Differences between the two groups were compared in regard to etiology, pathogen, blood type, urine culture, body mass index (BMI), surgical time, intraoperative blood loss, postoperative 1st day and total drainage volumes, length of hospitalization stay, and history of surgery at the affected sites.

Results: Gram-positive bacteria were the main pathogens for PJI. The most common infection after hip joint replacement was caused by *Staphylococcus epidermidis*, which accounted for 38.10%, while *Staphylococcus aureus* was mainly responsible for the infection of knee joint (40.74%). High BMI, long surgical time, large postoperative drainage volume, long hospitalization stay, history of surgery at incisions, previous use of immunosuppressants, preoperative hypoproteinemia and superficial infection were independent risk factors ($p < 0.05$).

Conclusions: PJI after primary replacement was mainly caused by gram-positive bacteria, and patients with high BMI, long surgical time, large postoperative drainage volume, long hospitalization stay, history of surgery at incisions, previous use of immunosuppressants, preoperative hypoproteinemia and superficial infection were more vulnerable.

Key words: Artificial joint; arthroplasty; periprosthetic joint infection; risk factor.

J Infect Dev Ctries 2020; 14(6):565-571. doi:10.3855/jidc.11013

(Received 06 November 2018 – Accepted 16 March 2019)

Introduction

Artificial joint replacement can be used to treat end-stage joint disorders, including severe osteoarthritis, rheumatoid arthritis, traumatic arthritis, ankylosing spondylitis, joint pain and motility dysfunction due to congenital malformations, Paget's disease, and tumors of bones and joints. It can replace the affected joint to function, thereby relieving pain and restoring joint function [1,2]. Currently, the 10-year success rates of hip and knee joint replacements have exceeded 90%, which, therefore, have been rapidly applied worldwide [3]. With population aging and social development, the number of cases receiving artificial hip and knee joint replacements have been increasing [4]. However, the accompanied postoperative complications are also on the rise. If not treated properly, they may lead to permanent disability.

Postoperative infections of artificial joint replacement can be classified into superficial and deep ones. Superficial infection refers to infection limited only to the skin and subcutaneous tissue, whereas deep infection refers to the invasion of inflammation from superficial tissue into joint cavity, causing intra-articular inflammatory response, i.e. prosthetic joint infection (PJI). PJI is one of the most serious complications of joint replacement. The incidence rates of PJI after primary total knee arthroplasty (TKA) range between 1% and 4% [5], and that after total hip arthroplasty (THA) is 1%. The incidence rates of PJI after revision knee and hip arthroplasties are 2- and 3.2-fold those of primary replacement respectively [6]. In China, the incidence rates of PJI after primary TKA and THA are 2% and 2.59% respectively [7,8], and those after revision arthroplasties are approximately 10.3% [9]. In the case of superficial inflammation and suppuration, the risk of infection in deep tissues increases by 35-fold [10].

PJI not only elevates treatment cost and causes joint dysfunction, but also significantly raises the rates of secondary surgery and mortality. Therefore, orthopedics should pay particular attention to the monitoring and effective prevention of postoperative

PJI. To reduce the risk of PJI, logistic regression analysis was performed for the risk factors related to primary artificial hip and knee joint replacements. The findings provide valuable evidence for the early prevention of PJI.

Methodology

Baseline clinical data

This study has been approved by the ethics committee of our hospital, and written consent has been obtained from all patients. A total of 96 patients with PJI after receiving primary artificial hip and knee joint replacements between February 2013 and February 2017 in our hospital were selected as a case group, irrespective of age, gender or type of disease. In the meantime, another 192 patients who received joint replacement at the ratio of 1:2 in the same period and did not suffer from PJI were selected as a control group.

Methods

The clinical data of all patients were completely recorded. All cases were retrospectively analyzed by reviewing each original medical record, and important information was followed up through telephone calls. In addition, gender, age, body mass index (BMI), type of disease, type of replacement, complications, use of hormones and immunosuppressants, hypoproteinemia, anemia, type of infection, postoperative drainage volume, preoperative and intraoperative articular fluid or incision secretion cultures, and drug susceptibility were investigated. The clinical data of all patients from admission were processed and input into SPSS software by experienced medical staffs to establish a database. To reduce information bias, two experienced staffs were required to compare, validate and correct the clinical data, and all the results were rechecked by a third staff to ensure the integrity and accuracy.

Quality control

All surgeries were performed in a laminar flow surgery room, and all patients were treated under general anesthesia. Antibiotics were prophylactically administered 30 minute before surgery and 24 hours after surgery. The use of antibiotics was prolonged for 3-5 days depending on the actual situation. Anterolateral incision and median incision were made for hip and knee joints respectively. Drainage tubes were placed in the joint capsule and removed generally 48 hoursafter surgery. PJI patients after joint replacement were treated with sensitive antibiotics according to culture and drug susceptibility results. The patients with superficial infections were first given the drug susceptibility test. Then they were intravenously injected with susceptible antibiotics and orally administered with rifampicin (300-450 mg, twice each day) for 2-6 weeks, followed by oral administration with rifampicin plus corresponding antibiotics (ciprofloxacin or levofloxacin) for 3 months. If the patients showed side reactions to quinolones, cotrimoxazole, minocycline, doxycycline, first-generation cephalosporins or penicillin were used instead. If the patients were allergic to rifampicin, susceptible antibiotics were intravenously administered for 4-6 weeks. For the patients with moderate infections, the prosthesis was retained while being incised for debridement and drainage, and those with severe infections were given revision arthroplasties.

Diagnostic criteria

PJI was definitely diagnosed when all the four criteria below were met. 1) The same pathogenic bacteria were cultured twice or more times continuously from joint fluid or periprosthetic tissues; 2) acute inflammation was found by pathological examination of periprosthetic tissues; 3) sinus tracts connected with the prosthesis appeared around the skin [11]; 4) synovial fluid or site where the prosthesis was placed underwent suppuration. PJI was diagnosed mainly based on criterion 1). Antibiotics should be discontinued two weeks before joint puncture, and local anesthesia should be avoided during puncture to prevent the spread of superficial infections to deep tissues. During surgery, periprosthetic tissues were taken for bacterial culture. The sample collection device must not touch the skin. As soon as it entered the surgical field, samples were immediately collected, and irrigation or electrosurgical operation should be avoided. The case group received consecutive culture from synovial fluid or intraoperative tissue at least twice to obtain pathogenic bacteria. In the meantime, drug susceptibility test was conducted to exclude other causes of infection. The criteria for investigated risk factors were as follows. Obesity: BMI $\leq$ 24; low hemoglobin level: preoperative level < 100 g/L; hypoproteinemia: preoperative serum albumin level < 35 g/L.

Statistical analysis

All data were analyzed by SPSS17.0 software (SPSS Inc., Chicago, USA). The categorical data were expressed as mean ± standard deviation (SD), and inter-group comparisons were conducted by the independent samples t-test. The numerical data were expressed as rates, and subjected to the χ^2 test and corrected χ^2 test.

The PJI-related factors in univariate analysis were included for multivariate unconditional logistic regression analysis. The odds ratio and 95% confidence interval were calculated. P<0.05 was considered statistically significant.

Results

Baseline clinical data

The case group included 40 males and 56 females aged (66 ± 10) years old. There were 42 cases of hip joint replacement (30 cases of THA and 12 cases of hemiarthroplasty) and 54 cases of knee joint replacement (10 bilateral cases). The longest follow-up period was 12 months after surgery, which was terminated after the occurrence of PJI. The control group consisted of 82 males and 110 females aged (68 ± 11) years old.

Pathogenesis of PJI

The pathogenesis of hip joint PJI included femoral head necrosis, femoral neck fracture, osteoarthritis, rheumatoid arthritis and developmental hip dysplasia (16, 13, 7, 3 and 3 cases respectively) in the case group, and there were 36, 29, 10, 1 and 8 cases respectively in the control group, without statistically significant differences (P > 0.05) (Table 1). The pathogenesis of knee joint PJI included osteoarthritis, rheumatoid arthritis and traumatic arthritis (32, 14 and 8 cases

Table 1. Pathogenesis of hip joint PJI [n (%)].

Hip joint replacement	Case No.	Femoral head necrosis	Femoral neck fracture	Osteoarthritis	Rheumatoid arthritis	Developmental hip dysplasia
Case group	42	16 (38.10)	13 (30.95)	7 (16.67)	3 (7.14)	3 (7.14)
Control group	84	36 (42.86)	29 (34.52)	10 (11.90)	1 (1.19)	8 (9.52)
χ^2		0.2620	0.1607	0.5440	3.2275	0.1992
p		0.6088	0.6885	0.4608	0.0724	0.6554

Table 2. Pathogenesis of knee joint PJI [n (%)].

Knee joint replacement	Case No.	Osteoarthritis	Rheumatoid arthritis	Traumatic arthritis
Case group	54	32 (59.26)	14 (25.93)	8 (14.81)
Control group	108	72 (66.67)	22 (20.37)	14 (12.96)
χ^2		0.8594	0.6429	0.1052
P		0.3539	0.4227	0.7457

Table 3. Univariate analysis results of risk factors for hip joint PJI (x ± SD).

Hip joint replacement	Age (year)	BMI (kg/m^2)	Surgical time (minute)	Intraoperative blood loss	Postoperative 1st day drainage volume (mL)	Postoperative total drainage volume (mL)	Retention time of drainage tube (h)	Retention time of urethral catheter (h)	Postoperative use time of antibiotics (d)	Hospitalization stay length (d)
Case group (n=42)	66.2 ± 9.8	23.2 ± 2.0	134.6 ± 20.9	296.7 ± 39.5	245.2 ± 33.9	471.9 ± 50.8	50.4 ± 8.4	18.6 ± 3.1	2.8 ± 0.5	12.4 ± 2.5
Control group (n=84)	66.7 ± 10.2	21.5 ± 2.1	95.6 ± 19.7	292.8 ± 40.2	95.1 ± 32.8	239.4 ± 47.8	49.6 ± 7.9	18.7 ± 2.9	2.8 ± 0.4	9.1 ± 2.1
t	0.2627	4.3510	10.2647	0.5163	23.9466	25.2042	0.5246	0.1783	0.0000	7.7949
P	0.7932	< 0.001	< 0.001	0.6066	< 0.001	< 0.001	0.6008	0.8588	1.0000	< 0.001

BMI: Body mass index.

Table 4. Univariate analysis results of risk factors for knee joint PJI (x ± SD).

Knee joint replacement	Age (year)	BMI (kg/m^2)	Surgical time (minute)	Intraoperative blood loss	Postoperative 1st day drainage volume (mL)	Postoperative total drainage volume (mL)	Retention time of drainage tube (h)	Retention time of urethral catheter (h)	Postoperative use time of antibiotics (d)	Hospitalization stay length (d)
Case group (n=54)	66.8 ± 10.9	27.2 ± 4.3	135.7 ± 17.2	289.8 ± 43.9	287.9 ± 50.9	515.6 ± 60.7	57.1 ± 5.9	18.2 ± 3.2	2.9 ± 0.6	17.1 ± 2.5
Control group (n=108)	67.2 ± 9.8	24.2 ± 3.9	118.4 ± 14.9	285.7 ± 41.8	164.3 ± 30.8	307.9 ± 45.3	44.9 ± 6.1	17.9 ± 3.1	2.9 ± 0.5	8.8 ± 2.1
t	0.2358	4.4589	6.6118	0.5787	19.1954	24.4738	12.1303	0/5744	0.0000	22.2279
P	0.8139	< 0.001	< 0.001	0.5636	< 0.001	< 0.001	< 0.001	0.5665	1.0000	< 0.001

BMI: Body mass index.

respectively) in the case group, and there were 72, 22 and 14 cases respectively in the control group, without statistically significant differences ($p > 0.05$) (Table 2).

Distribution of pathogenic bacteria

Gram-positive bacteria were the main pathogens for PJI. The infection rates of gram-positive bacteria of hip and knee joints were 76.19% (32/42) and 92.59% (50/54) respectively. The most common infection after hip joint replacement was caused by *Staphylococcus epidermidis*, which accounted for 38.10% (16/42), followed by *Staphylococcus aureus* and *Staphylococcus haemolyticus* (14.29%, 6/42) as well as *Staphylococcus capitis* (7.14%, 3/42). The main gram-negative bacterium for hip joint PJI was *Escherichia coli* (23.81%, 10/42).

In contrast, *S. aureus* was mainly responsible for the infection of knee joint (40.74%, 22/54), followed by *S. epidermidis* (20.37%, 11/54) and *S. haemolyticus* (12.96%, 7/54). In addition, knee joint PJI was also caused by *Staphylococcus lugdunensis*, *Streptococcus anginosus*, *Streptococcus agalactiae*, *Enterococcus faecalis* and *Enterobacter cloacae* (7.41% in total, 4/54).

Univariate analysis of risk factors for PJI after primary replacement

Univariate analysis showed that high BMI, long surgical time, large postoperative 1st day and total drainage volumes, long hospitalization stays, history of surgery at incisions, previous use of immunosuppressant, preoperative hypoproteinemia and superficial infection were the risk factors for hip joint PJI after primary replacement ($p < 0.05$) (Table 3). Long-term retention of drainage tube and anemia also evidently increased the risk of postoperative knee joint PJI (Table 4). The univariate analysis results of risk factors for hip and knee joint PJIs after primary replacement are summarized in Table 5.

Multivariate analysis of risk factors for PJI after primary replacement

Multivariate logistic regression analysis revealed that high BMI, long surgical time, large postoperative drainage volume, long hospitalization stays, history of surgery at incisions, previous use of immunosuppressant, preoperative hypoproteinemia and superficial infection were all independent risk factors ($p < 0.05$) (Table 6).

Discussion

Arthroplasty is an effective surgical technique for correcting joint deformity and restoring joint function to relieve pain and improve quality of life, which is a revolutionary progress in the field of orthopedics in the early 20th century. With the increasing number of young people with aging population and high-energy injuries, the number of joint replacement patients is on the rise, and the issue of surgical complications also receives much attention. PJI is one of the most important complications after joint replacement. The incidence of primary hip and knee joint replacement is high, which seriously affects joint function and reduces the quality of life of patients [12]. The results of this

Table 5. Univariate analysis results of risk factors for hip and knee joint PJIs (x ± SD).

Risk factor	Hip joint replacement				Knee joint replacement			
	Case group (n = 42)	Control group (n = 84)	χ^2	*P*	Case group (n = 54)	Control group (n = 108)	χ^2	*P*
Diabetes	13 (30.95)	30 (35.71)	0.2824	0.5951	18 (33.33)	31(28.70)	0.3657	0.5453
History of surgery at incisions	32 (76.19)	6 (7.14)	63.3768	< 0.001	29 (53.70)	7 (6.73)	44.4464	< 0.001
Use of hormones	16 (38.10)	28(33.33)	0.2794	0.5971	18 (33.33)	31(28.70)	0.3657	0.5453
Use of immunosuppressants	16 (38.10)	6 (7.14)	18.6136	< 0.001	18 (33.33)	7 (6.73)	19.8893	<0.001
Bilateral at the same time	0 (0.00)	0 (0.00)	Fisher's exact test	1.0000	0 (0.00)	0 (0.00)	Fisher's exact test	1.0000
Consecutive surgery	26 (61.90)	48 (57.14)	2.6845	0.1013	29 (53.70)	62 (57.41)	0.2006	0.6542
Renal dysfunction	10 (23.81)	16 (19.05)	0.3877	0.5335	11(20.37)	25 (23.15)	0.1607	0.6885
Elevation of alanine aminotransferase level	13 (30.95)	22 (26.19)	0.3165	0.5737	14 (25.93)	24 (22.22)	0.2750	0.6000
Hypoproteinemia	29 (69.05)	23 (27.38)	20.0559	<0.001	36 (66.67)	22 (20.37)	33.5710	<0.001
Anemia	29 (69.05)	54 (64.29)	0.2824	0.5951	32 (59.26)	18 (16.67)	30.6064	<0.001
Homologous transfusion	13 (30.95)	22 (26.19)	0.3165	0.5737	22(40.74)	39 (3611)	0.3287	0.5664
Superficial infection	16 (38.10)	10 (11.90)	11.7277	<0.001	32(40.74)	11 (10.18)	44.4653	<0.001
Addition to smoking and alcohol drinking	19 (45.24)	35 (41.67)	0.1458	0.7025	18 (33.33)	31(28.70)	0.3667	0.5453

Table 6. Multivariate analysis results of risk factors for PJI after primary replacement.

Risk factor	β	$s\bar{x}$	χ^2	OR	95%CI	*P*
BMI (kg/m^2)	2.153	0.121	5.221	0.090	0.1-0.9	0.04
Surgical time (min)	1.530	0.965	4.792	6.120	1.1-30.5	0.04
Postoperative 1st day drainage volume (ml)	1.018	0.921	4.500	4.101	0.7-0.9	0.03
Postoperative total drainage volume (ml)	6.922	0.835	5.232	1.009	1.3-2.1	0.04
Hospitalization stay length (d)	9.025	0.896	4.413	5.772	1.2-26.9	0.03
History of surgery at incisions	1.163	0.320	4.332	0.089	0.1-0.8	0.02
Use of immunosuppressants	1.547	0.976	3.852	6.200	1.1-25.3	0.04
Hypoproteinemia	1.017	0.901	4.501	5.200	1.2-3.8	0.04
Superficial infection	8.613	0.675	4.255	3.826	2.0-7.3	0.03

BMI: Body mass index; CI: confidence interval; OR: odds ratio.

study indicate that the risk factors for PJI after primary hip and knee joint replacement are not the same. Analysis of risk factors in the uniform category of hip and knee joint replacement may overlook some of the relevant factors. The results showed that there was a certain relationship between the patient's body mass and PJI, and a large BMI could significantly increase the chance of infection after joint replacement. Studies have shown that high BMI can not only increase the preoperative risks in many aspects such as anesthesia, but also greatly increase the complexity of surgical procedures such as exposed limbs and placement of implants. For patients with pathological obesity in particular, it is necessary to fully exfoliate soft tissue, which caused the soft tissue covered by the prosthesis surface was reduced and prone to postoperative infection [13]. Foster et al. followed up 2,106 patients undergoing hip replacement for up to 8 years, and found that the probability of having PJI for patients with BMI > 50 kg/m^2 was 18 times higher than that for those with normal BMI [14].

This study showed that large postoperative incision drainage, surgical and long hospital stay were independent risk factors for PJI after initial hip and knee joint replacement. Severe intraoperative invasive operation, large soft tissue dissection, and incomplete hemostasis are the direct reasons for delayed extubation caused by postoperative injury bleeding and large drainage. Drainage fluid is a good medium for the growth and reproduction of bacteria. Excessive drainage can cause patients to lose part of the nutrients, reduce local immunity, and increase the susceptibility of the body. The studies of American physicians have shown that when there is more drainage after surgery, poor local environment, degraded defensive function of tissue, reduced immunity, and slow postoperative repair ability may increase the possibility of postoperative surgical site infection [15]. The longer the operation time, the more likely it was to infect postoperative infection, which is consistent with the study results of Dicks et al. [16]. The longer the operation time, the heavier the degree of soft tissue injury during dissection and traction, and the longer the tissue surrounding the incision is exposed to air, the greater the probability of bacterial colonization and of getting an infection. In the environment with poor condition of the wards, disorganized arrangement of beds, and infected and non-infected patients sharing the same ward, the longer the hospital stay, the more likely it is to cause nosocomial and cross-infection. The analysis results of this study showed that surgical history of affected joints is one of the risk factors for the occurrence of periprosthetic infections. A large number of scar tissues are produced after obsolete surgery, resulting in blood flow disorder of peripheral articular soft tissue and even ischemia, increasing the possibility of tissue necrosis and intra-articular bacterial infection. In addition, reconstruction of intra-articular anatomy, hyperplasia and residual foreign bodies are prone to bacterial colonization, resulting in increased incidence of PJI [17]. Immunosuppressive agents can inhibit the proliferation and function of T and B lymphocytes related to immune response by affecting the body's immune response and immunopathological response, thereby reducing the immune response of antibody and increasing the body's susceptibility. Zwartelé and Pöll observed 292 patients with hip replacement who took long-term oral immunosuppressants in 36-year follow-up, and found that the incidence of PJI in users of immunosuppressive agents was significantly higher than that of non-users [18]. Hypoalbuminemia not only shows fiber proliferation and the lack of raw materials for collagen synthesis, delayed injury healing, decreased plasma colloid osmotic pressure, edema formed by osmotic retention of tissue, but also results in reduction of antibody synthetase, leading to decreased body immunity and increased chance of infection. Low hemoglobin content indicates that the body's function of oxygen and carbon dioxide transfer decline, so that multiple organs are in anoxic state,

resulting in organ metabolic dysfunction, impaired function and increased infection rate. In the United States, a clinical trial selected 173 patients undergoing initial total hip or total knee replacement to study the relationship between nutritional status and surgical incision complications, and 46 patients in a state of malnutrition all had corresponding injury complications. The results showed that the risk of injury complications in joint replacement patients with malnutrition is over three times higher than that in normal patients [19].

The genitourinary system's infectious lesions are prone to spread into the bloodstream and are the most important source of bloodstream spread for infections, and are also one of the important factors in inducing PJI. The patients were followed up regularly and the study terminated until the occurrence of PJI. A total of 43 patients with PJI 1 year after surgery had an infection rate of 1.7%, mainly Gram-negative bacterial infection. Superficial infections often have tissue congestion, oozing, and neutrophil accumulation, followed by cell damage and tissue destruction, which results in loss of barrier capacity in superficial tissues. Combined with micro-environmental disturbances, hypoxia, and inadequate infiltration of antibiotics, it may further lead to microbial growth. Patients with superficial infections around the joints, who also have inconvenient mobility of joint diseases, long bed rest, decreased immune function, delayed inflammatory response from peripheral blood vessels, will experience weakened leukocytosis, neutrophil chemoattractant, and decreased phagocytosis after inflammation, which is easy to cause the growth of pathogens and postoperative infections [20].

Conclusion

In summary, the occurrence of PJI after the first postoperative hip and knee joint replacement is closely related to BMI, operation time, postoperative drainage, length of hospital stay, history of surgical incision, use of immunosuppressive agents, preoperative hypoproteinemia, presence and superficial infections. Therefore, it is necessary for such high-risk patients to strengthen the treatment of basic diseases, correct anemia, hypoalbuminemia, and disuse immunosuppressive agents, with rational use of antibiotics. Although PJI is a catastrophic complication after joint replacement, it can only reduce its incidence through comprehensive measures and multiple ways. However, it is not completely indispensable. As long as the above-mentioned risk factors appear in clinical work are given high vigilance, with corresponding measures, we will be able to minimize the incidence of PJI.

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Conflict of interests: No conflict of interests is declared.