



# Assessment of Predictors of Infection in Primary Knee and Hip Arthroplasty: A Case-control Study

## *Avaliação de fatores preditores de infecção na artroplastia primária de joelho e quadril: Um estudo caso-controle*

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### Abstract

**Objective** This study assesses risk factors for periprosthetic joint infection after elective primary total knee or hip arthroplasty.

**Methods** The study included 706 medical records of patients undergoing elective primary total hip or knee arthroplasty from January to December 2018. We used a multivariate analysis of infection predictors through a logistic regression model. The R software performed all statistical analysis.

**Results** The prevalence of infection in the sample was 2.0% (14 cases). Most patients were women (79.6%), with an afflicted right side (50.6%), and underwent a total knee arthroplasty (61.3%). Significant risk factors ( $p < 0.05$ ) for infection included surgical time greater than 120 minutes ( $p = 0.009$ ) and a history of diabetes ( $p = 0.025$ ).

**Conclusion** The risk of infection after elective primary total knee or hip arthroplasty is higher when the surgical procedure is lengthy (over 120 minutes), or the patient has a history of diabetes mellitus.

**Level of Evidence** IIIB, retrospective, case-control study.

### Keywords

- ▶ infection
- ▶ arthroplasty
- ▶ predictor
- ▶ diagnosis

### Resumo

**Objetivo** Avaliar os fatores de risco para infecção articular periprotética após procedimento cirúrgico eletivo de artroplastia primária total de joelho ou quadril.

**Métodos** Incluem-se no estudo 706 prontuários de pacientes que foram submetidos a artroplastia total primária eletiva de quadril ou joelho entre os meses janeiro e dezembro de 2018. Utilizou-se a análise multivariada dos fatores preditores de infecção por meio de um modelo de regressão logística. Toda a análise estatística foi realizada no software R.

### Palavras-chave

- ▶ infecção
- ▶ artroplastia
- ▶ predição
- ▶ diagnóstico

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**Resultados** A prevalência de infecção de toda a amostra foi de 2,0% (14 casos). A amostra contou com a maioria do gênero feminino (79,6%), com o lado direito afetado (50,6%) e predomínio da artroplastia total de joelho (61,3%). Os fatores de risco significativos ( $p < 0,05$ ) para a infecção foram: tempo cirúrgico maior do que 120 minutos ( $p = 0,009$ ) e diagnóstico prévio de diabetes ( $p = 0,025$ ).

**Conclusão** Artroplastias totais primárias eletivas de joelho ou quadril possuem maior risco de infecção quando ocorre um tempo prolongado do procedimento cirúrgico (acima de 120 minutos) e quando o paciente possui diagnóstico prévio de diabetes mellitus.

**Nível de Evidência** IIIB, estudo retrospectivo caso-controle.

## Introduction

Total arthroplasties have a high success rate, improving pain and quality of life for virtually all patients.<sup>1</sup> However, their complications include periprosthetic joint infection (PJI), which is hard to diagnose and treat, generally requiring an additional surgical intervention and prolonged antibiotic therapy.<sup>2</sup>

Several protocols try to stratify the preoperative risk of infection and optimize the patient most appropriately before the procedure.<sup>3</sup> However, despite this care, PJI cases occur in all services.

According to the literature, the main avoidable factors associated with PJI are inadequate glycemic control, obesity, malnutrition, and smoking. Additionally, authors cite adequate antibiotic prophylaxis, asepsis with alcoholic chlorhexidine, reduced staff in the operating room, and proper postoperative anticoagulation (to avoid hematoma formation) as significant variables.<sup>4</sup>

As there are no Brazilian studies with a significant number of cases on this subject, our work aims to evaluate the risk factors for PJI after an elective primary total knee or hip arthroplasty.

## Methods

This is a retrospective case-control study with 706 medical records of patients undergoing elective primary total hip or knee arthroplasty from January to December 2018. The institutional ethics committee and the Brazil Platform (*Plataforma Brasil*, CAAE number 30995420.2.0000.8114) approved the study.

We used the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) initiative<sup>5</sup> that guides observational studies to outline the general methodology of our research. Additionally, we followed the good clinical practices and the Declaration of Helsinki.

### Data collection

The TechSallus (Felipe e Menezes LTDA. Salvador, Bahia, Brazil) software for hospital medical records provided the required consecutive data. Variables included were gender, age, operated joint, previous comorbidities, surgical time, laterality, and culture-identified pathogen.

## Inclusion criteria

- Medical records from patients aged 40 to 90 years old.
- Previous diagnosis of hip or knee osteoarthritis, Kellgren 3 or 4.
- Incapacitating pain, diagnosed with the visual analog scale (VAS) for pain  $> 7$ , with bad response to analgesia/joint infiltrations/motor physical therapy.
- Patients undergoing primary total knee or hip arthroplasty in 2018.
- Infection diagnosis followed the Musculoskeletal Infection Society criteria updated in 2018:<sup>6</sup> presence of an active fistula and two positive cultures with the same etiologic agent or a minor criteria score of  $> 5$  points confirm an infection; a minor criteria score of  $< 2$  excludes an infection. In patients with scores ranging from 2 to 5, 3 months after the initial screening, we request erythrocyte sedimentation rate (ESR) and C-reactive protein levels. If these test findings are abnormal, we perform an ultrasound-guided joint puncture in the operating room for cytology and culture. A score  $> 5$  at this new staging confirms the infection.

## Exclusion criteria

- Conversion surgeries due to previous osteosynthesis failure at arthroplasty.
- Arthroplasty review surgeries.

## Patient preparation and surgical technique

Candidates for total arthroplasty went through a preparation program consisting of the following:

- Ten sessions of preoperative motor physical therapy during 5 consecutive weeks (2 sessions per week).
- An orientation lecture for the patient and their family/caregivers about the surgical procedure, risks, benefits, postoperative care, home adjustments, and routine medications.
- Oral supplementation with Whey Protein, 50 mg per day, for 7 days before surgery.

- Referral of morbidly obese patients to a specialized center before arthroplasty. If required, the patient underwent bariatric surgery before the orthopedic procedure.
- Referral of patients with hemoglobin A1C levels > 5.5% to the diabetes center for control before surgery.

Hospitalization occurred on the same day of surgery, and patients were under an abbreviated fasting protocol. Expected discharge was within 24 hours after the procedure, except in cases of orthopedic or clinical complications.

All surgeries occurred in the same conventional operating rooms with no laminar flow. Prophylactic antibiotic therapy consisted of cefuroxime sodium, 1.5 g, 1 hour before skin incision (patients allergic to cephalosporin, penicillin, or both received vancomycin, 2 g, 2 hours before incision). We administered tranexamic acid per our routine unless formally contraindicated due to a previous severe thromboembolic event; the dosage was 10 mg/kg of body weight applied during anesthetic induction. Spinal anesthesia with sedation was the choice whenever there was no contraindication. Skin asepsis used alcoholic chlorhexidine after previous local degermation. After placing the sterile drapes, the exposed area was again treated with alcoholic chlorhexidine, dried, and received an incise drape.

There was no routine urinary catheter placement. At the end of the procedure, we provided a 7/8 elastic stocking with medium compression and requested follow-up radiographs. The sterile dressing used, a hydrocolloid, remained occluded for the first 24 hours, as long as there was no significant bleeding. In case of surgical wound bleeding and issues with the dressing, we changed it using a sterile protocol at the hospital.

We resumed prophylactic anticoagulant (routine: enoxaparin, 0.5 mg/kg) administration within 6 to 12 hours per hemoglobin curve findings. Additionally, we requested follow-up tests at the end of the surgery, 6 hours after the procedure, and in the morning of the following day.

The motor physical therapy protocol consisted of sitting the patient up in bed during the immediate postoperative period and training gait with a walker and partial load on the first postoperative days. The perioperative antibiotic agent administered was sustained for up to 24 hours. At hospital discharge, patients got a prescription for a simple analgesic agent, an opioid analgesic agent, and an oral anticoagulant (rivaroxaban, 10 mg/day for 30 days).

The patients received instructions on how to care for the surgical wound. They would clean the wound with a neutral soap daily during the shower. Next, dry it with a separate towel and a blow-dryer at a cool temperature. Keep the dressing up to suture removal in the specialized outpatient clinic in the second or third postoperative week.

## Total hip arthroplasty

Surgeons with a hip specialization and more than 5 years of experience performed all arthroplasties via the right lateral approach (Hardinge, Inc. Berwyn, PA, USA)<sup>7</sup>. All patients received a cementless prosthesis, with the potential addition

of acetabular screws according to the initial press fit. The femoral component was from a taper type.

We assign the tribological pair according to the following age distribution: patients younger than 75 years old receive a ceramic femoral head and a highly cross-linked polyethylene acetabular insert; those aged 75 or older receive a metallic femoral head with the same insert. Simple, monofilament sutures closed the wound. We did not use a suction drain or abduction triangle on a routine basis.

## Total knee arthroplasty

All arthroplasties were performed by surgeons with a knee specialization and more than 5 years of experience via the medial parapatellar approach.<sup>8</sup> All procedures were from the cemented type, with no addition of antibiotics to the polymethylmethacrylate. The tribological pair consisted of metal-polyethylene. Simple, monofilament sutures closed the wound. We did not use a suction drain on a routine basis.

## Statistical analysis

Statistical analysis used the descriptive method for nominal (proportion) and continuous (mean and standard deviation) variables. Additionally, the Shapiro test was used to classify the normality of continuous variables,<sup>9</sup> while the Pearson chi-square test or the Fisher exact test were used to analyze nominal variables.

Next, a univariate analysis assessed the influences of variables on the outcome using individual logistic regression. The multivariate analysis included variables with  $p < 0.20$ , based on a multiple logistic regression using the iteratively reweighted least squares method. Odds ratio (OD) and 95% confidence intervals (95% CI) estimated associations. Statistical significance was set at  $p < 0.05$ . The R software (R Foundation for Statistical Computing, Vienna, Austria) were used to perform the analyzes.<sup>10</sup>

## Results

Most patients were women (79.6%), with an afflicted right side (50.6%), and underwent a total knee arthroplasty (61.3%). A total of 706 patients underwent surgery in 2018, including 273 hip arthroplasties and 433 knee arthroplasties.

The prevalence of infection in the entire sample was 2.0% (14 cases). Infection rates were 2.93% within the hip surgery group and 1.38% within the knee surgery group. The number of periprosthetic infection cases was higher in females (2.31%) compared with males (0.69%). Additionally, the right side was affected (2.52%) more often than the left side (1.43%).

► **Table 1** shows the epidemiological features of the case and control groups, and highlights their homogeneity.

The most common pathogen in cultures was *Staphylococcus aureus*, corresponding to 66.6% of the identified organisms, followed by coagulase-negative *Staphylococcus* (11%) and *Escherichia coli* (11%). The multivariate analysis revealed that the factors associated with the development of infection

**Table 1** Epidemiological features of the patients include in the study

	Cases (n = 14)	Controls (n = 692)	p-value
Gender	13 female 1 male	549 female 143 male	0.21*
Side	9 at the right side 5 at the left side	348 at the right side 344 at the left side	0.29*
Prosthesis type	8 hip prostheses 6 knee prostheses	265 hip prostheses 427 knee prostheses	0.15*

Notes: \*Pearson chi-square test.

after hip or knee arthroplasty were a surgical time greater than 120 minutes (OR = 6.55 [1.33–25.58];  $p = 0.009$ ) and diabetes (OR = 3.46 [1.16–10.88];  $p = 0.025$ ). ► **Table 2** shows all tests, both for the univariate and multivariate analyzes.

## Discussion

The infection rate found in our study (2%) is consistent with the literature, ranging from 1 to 2.5%.<sup>6</sup> The main findings of our study were that a surgical time above 120 minutes and a history of diabetes, even if compensated before surgery, represented significant risk factors for PJI.

Although our findings corroborate data from the international literature, we demonstrated that even patients with compensated blood sugar levels present an increased infection rate. The literature reports serum glucose concentrations ranging from 6.1 to 10 mmol/L and hemoglobin A1C levels of 7.0% as critical values.<sup>3</sup> Diabetes remained a risk factor even when we were more rigorous regarding the cut-off point of hemoglobin A1C (< 5.6%). This fact evidences a

potential immunological compromise associated with the disease despite normal test results.<sup>11</sup>

Furthermore, the literature is controversial regarding a cut-off surgical time associated with a higher infection rate.<sup>12</sup> In our study, with an adequate sample for the Brazilian population, a surgical time higher than 2 hours resulted in higher infection rates. This fact implies that a lengthier exposure of the surgical wound increases the risk of infection. Additionally, the surgical time is usually longer in complex orthopedic cases that may require higher surgical exposures, along with greater intra- and postoperative bleeding.

Advanced age patients are more susceptible to prosthetic infections, mainly due to comorbidities that lower the body's immune response.<sup>13</sup> However, we did not detect an increase in the infection rate when stratifying patients into three age groups (< 65, 65 to 80, and > 80 years old). Since most of the subjects were aged 65 to 80, the other age groups potentially had a lower statistical power in the comparative analysis.

There was no statistical difference in the infection rate after hip or knee arthroplasties. Although there were more

**Table 2** Results of univariate and multivariate analysis using logistic regression

Outcome	Univariate	Multivariate	
	p-value	OR (95% CI)	p-value
Gender	0.24	–	–
Prosthesis type	0.16	0.34 (0.10–1.09)	0.07
Side	0.30	–	–
Systemic arterial hypertension	0.67	–	–
Diabetes mellitus	0.02	3.46 (1.16–10.88)	< 0.05
Dyslipidemia	0.99	–	–
Hypothyroidism	0.80	–	–
Osteopenia	0.99	–	–
Osteoporosis	0.14	4.24 (0.21–27.10)	0.19
Age ≤ 65 years old	0.98	–	–
Age > 65 years old	0.50	–	–
Age ≥ 80 years old	0.59	–	–
Surgical time ≤ 60 minutes	0.56	–	–
Surgical time > 60 minutes	0.55	–	–
Surgical time ≥ 120 minutes	0.03	6.55 (1.33–25.58)	< 0.001

Abbreviations: CI, confidence interval; OR, odds ratio.

infection cases in females (13 females and 1 male), gender did not represent an isolated risk factor for PJI in the statistical analysis. This finding is not consistent with the literature, that shows a higher risk in males.<sup>14</sup> The most isolated pathogen was *Staphylococcus aureus*, agreeing with the literature.<sup>15</sup>

It is worth mentioning that the preoperative investigation of methicillin-resistant *Staphylococcus aureus* (MRSA) is not part of our protocol. Populational strategies guide antibiotic prophylaxis, and we routinely use cefuroxime sodium at a 1.5 g dosage. However, if the patient is a healthcare professional or an institutionalized subject (with a higher probability of MRSA colonization), prophylaxis changes to vancomycin, 2 g, administered 2 hours before skin incision.<sup>11</sup> In both scenarios, antibiotic therapy continues for 24 hours with the same drug given before surgery.

Factors such as smoking and obesity are related to a higher PJI rate.<sup>3</sup> However, since our study seeks a quantitative assessment of these variables—especially the body mass index (BMI) and smoking time and intensity—the data are incomplete, not allowing statistical analysis.

Thus, the main limitation of our research is information bias, as it is a retrospective study with data from medical records, lacking complete, quantitative information on smoking and obesity. On the other hand, our work has two strengths. The first strength is its robust sample (706 cases) within the Brazilian scenario. The second strength is the definition of a cut-off point of 2 hours of surgical time and diabetes (even if controlled from a laboratory point of view) as risk factors for PJI in primary elective total hip and knee arthroplasty procedures.

For future studies, our group aims to prospectively follow up and catalog all elective arthroplasties in the service. We also plan a new study on the rate of complications, including infection, in partial and total hip arthroplasties performed due to trauma (femoral neck fractures).

## Conclusion

Primary total knee or hip arthroplasties have a higher risk of infection when the surgical procedure is protracted (over 120 minutes) and the patient presents diabetes mellitus.

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## Conflict of Interests

The authors have no conflict of interests to declare.

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