Incidence of infectious complications in hip and knee arthroplasties in rheumatoid arthritis and osteoarthritis patients

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ABSTRACT

Introduction: Rheumatoid arthritis (RA) is one of the major indications of total hip (THA) or knee (TKA) arthroplasty. International studies have suggested that RA is a risk factor for prosthesis infections. **Objectives:** To compare patients with RA and patients with osteoarthritis (OA) of other etiologies with regard to the incidence of prosthesis, incisional, and other systemic postoperative infections in THA and TKA. **Methods:** Retrospective, comparative cohort of patients followed up after undergoing THA or TKA at the Hospital SARAH-Brasília, from 1996 to 2007. **Results:** Seventy-five arthroplasties (28 TKA and 47 THA) were identified in RA patients. As controls, 131 surgeries (56 TKA and 75 THA) in OA patients were randomly selected and stratified by surgery and gender. No significant difference was observed between the RA and OA groups regarding the rates of prosthesis infections (TKA 7.1% vs. 0% and THA 2.1% vs. 0%, respectively, both with $P > 0.1$), incisional infections (TKA 14.3% vs. 3.3% and THA 4.3 vs. 1.3%, respectively, both with $P > 0.1$), and systemic infections (TKA 7.1% vs. 3.6%, $P = 0.92$ and THA 4.3% vs. 10.7%, $P > 0.1$, respectively). After multiple logistic regression, the results did not change. **Conclusions:** RA was not identified as a risk factor for perioperative infections in THA and TKA in this case series of the Hospital SARAH-Brasília, as compared with the group of patients with primary OA or OA secondary to non-inflammatory diseases. The low incidence of infections in both groups may explain our findings.

Keywords: rheumatoid arthritis, arthroplasty, infection, osteoarthritis.

INTRODUCTION

Rheumatoid arthritis (RA) affects 0.2% to 1% of the Brazilian population.[1] Its main characteristic is peripheral, symmetric polyarthritis, which leads to joint deformity and destruction by erosion of both bone and cartilage. Many patients progress to secondary osteoarthritis (OA), which, together with OA and traumatic lesions, represents one of the most frequent indications of total arthroplasty.

Patients affected by RA have a different profile from those with OA due to other etiologies. Osteoarthritis usually affects patients over the age of 50 years, while RA may affect younger patients.[2] Furthermore, they have chronic systemic inflammation, usually use immunomodulatory drugs and corticosteroids, and more often have other comorbidities, such as osteoporosis,[3] other autoimmune diseases,[4] and early atherosclerosis.[5] Such patients may be more susceptible to complications, such as surgical infections, suture dehiscence, periprosthetic fractures, and shorter prosthesis durability, which have a great impact on morbidity, mortality, and quality of life.

The first comparative studies have not evidenced shorter prosthesis durability in RA patients,[6,7] while others have shown that such patients have important benefits regarding pain and joint function with surgical treatment.[8,9] However, two studies, including a recently-published retrospective cohort, have evidenced a small increase in the number of revisions due to infection in RA patients.[10,11] Case-control studies conducted with a large number of patients undergoing arthroplasties have

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pointed out RA[12–17] and the use of corticosteroids[18] as risk factors for infections.

The objective of this study is to compare patients with RA and OA due to other etiologies with regard to the incidence of prosthesis infections, incisional infection and other postoperative systemic infections in total hip (THA) and total knee (TKA) arthroplasties.

MATERIALS AND METHODS

Study design

Retrospective, comparative study of patients with RA and OA due to other etiologies, undergoing THA and TKA.

Inclusion and exclusion criteria

The participants of the study were 18 years old or older. The study included patients followed up at the orthopedics program after undergoing THA or TKA, with the first joint arthroplasty performed at the Hospital SARAH-Brasília, from 1996 to 2007.

The group of RA patients had their diagnosis established based on the 1987 American College of Rheumatology (ACR) criteria.[19] The control-group comprised patients with primary OA or OA secondary to other etiologies, whose diagnosis was established based on the ACR clinical-radiographic criteria,[20–22] by using clinical, laboratory and radiological data, whose dates were as close as possible to that of the surgery. If possible, two OA patients for each RA patient would be included, randomly selected within the universe of patients undergoing surgery within the same period, even if they had already undergone other previous joint surgeries different from arthroplasty (e.g., osteotomy). The sample was balanced by gender and operated-upon joint.

The following patients were excluded from the study: RA patients with indication for arthroplasty due to avascular bone necrosis or femoral neck fracture; patients with OA secondary to other autoimmune diseases, such as ankylosing spondylitis; patients with juvenile idiopathic arthritis; and patients undergoing hemiarthroplasty.

Outcomes

The major variable assessed was prosthesis infection, defined as prosthesis malfunction, with pain and/or loss of joint function, beginning in the first postoperative year and causing the exchange or removal of prosthetic components, and meeting one of the following criteria based on the Centers for Diseases Control (CDC) criteria:[23] a) two or more cultures of bone biopsy or surgical material or synovial fluid growing the same microorganism; b) purulent synovial fluid seen by the surgeon; c) signs of inflammation in the histopathological examination of the periprosthetic tissue; d) presence of cutaneous fistula communicating directly with the prosthesis.

Superficial incisional infection was identified as the occurrence of superficial involvement of the surgical wound, in other words, of the skin and/or subcutaneous tissue, manifesting within 30 days of the surgery, meeting one of three criteria based on the CDC and the Brazilian Health Surveillance Agency (ANVISA) criteria:[24–27] a) superficial inflammatory alterations of the surgical wound, in other words, skin and subcutaneous tissue (heat, redness, pain, edema, discharge), for which the assistant surgeon considered drainage and/or systemic antibiotic treatment necessary, except in case of negative culture; b) purulent discharge from the surgical wound; c) positive culture from tissue from the surgical wound.

Deep incisional infection was identified as the occurrence of deep involvement of the surgical wound, in other words, fascia or muscle, manifesting within the first year of surgery and meeting one of the three criteria:[24–26] a) purulent drainage from the deep incision, but not from the organ/cavity; b) partial or total dehiscence of the surgical scar or wound opening by the surgeon, if the patient had at least one of the following signs or symptoms: axillary temperature ≥ 37.8ºC, pain or increased local sensitivity, except in case of negative culture; presence of an abscess or other evidence that the infection involved deeper layers of the wound, identified on reoperation, or clinical, histo/cytopathological or imaging examinations.

Systemic infection was defined as the occurrence of an infection in any organ or system, for which oral or venous antibiotic therapy was indicated by the assistant team, with or without microbiological evidence, during hospitalization.

Data collection

Data were collected from the electronic medical records of the SARAH network. Patients with RA and OA undergoing hip or knee arthroplasties were selected through automatic search. The cases were counted according to the procedures performed. The following data were recorded: a) regarding the surgical procedures: surgical procedure performed; date of the first arthroplasty; date of revision surgery or date of the last consultation or date of the patient's death; infection documentation, including site, date, type of positive culture and causing germ, when available; American Society of Anesthesiology (ASA) physical status classification and duration of surgery, which have been reported as factors related to prosthesis infection in at least three studies;[15,27,28] b) data of RA patients: age, gender, educational level; disease-modifying antirheumatic

drugs (DMARDs) and/or corticosteroids used, with dose on the occasion of surgery; rheumatoid factor: positivity and measurement; c) data of OA patients: age, gender, educational level, OA etiology.

Statistical analysis

Both descriptive and exploratory analyses of data were performed. Continuous variables were analyzed with mean comparison tests by use of analysis of variance (ANOVA). The qualitative variables were analyzed by use of Pearson's chi-square test and/or Fisher's exact test. Multiple logistic regression was used to exclude the influence of possible confounding variables. P values < 0.05 were considered statistically significant. The software used for statistical analysis was SPSS® 13 for Windows.

RESULTS

Case series

In the studied period, 160 surgeries were identified in patients classified as having RA. After excluding those that did not meet the above-mentioned criteria, 75 arthroplasties in patients with confirmed RA were identified as follows: 28 TKA and 47 THA (Figure 1). The controls were randomly selected, according to case availability: 131 surgeries in OA patients (56 TKA and 75 THA).

All TKAs were performed by only one senior orthopedic surgeon, while the THAs were performed by two senior surgeons. All senior surgeons had a great experience with the procedures, and two of them have worked in the institution for over 30 years.

General characteristics of the patients

The general data of the patients are summarized in Tables 1 and 2. The significant difference in the distribution of the ASA classification may be explained by the fact that the presence of RA already increases the classification to at least ASA 2. In the group of RA patients, rheumatoid factor was available in 65 patients, being positive in 73.2% of the THA group and in 87.5% of the TKA group. The mean rheumatoid factor titer was 266.97 (± 378.3) U/mL in the THA group and 188.79 (± 164.1) U/mL in the TKA group. The DMARDs used by RA patients and their respective mean doses are shown in Table 3.

Infections

The comparison of the incidence of infections is shown in Figures 2 and 3. Due to the small number of infections,

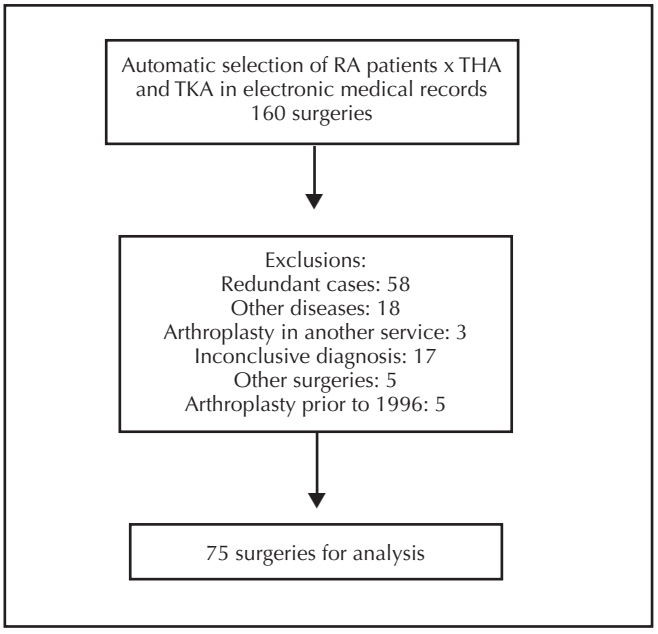

Figure 1
Selection of RA patients who underwent surgery.
RA: rheumatoid arthritis; THA: total hip arthroplasty; TKA: total knee arthroplasty.

Table 1
General characteristics of the patients of the THA group

THA group	RA	OA	P
Gender (%)			0.276
Female	41 (87.2)	61 (81.3)	
Male	8 (12.8)	14 (18.7)	
Mean age (± SD)	50.6 (11.7)	63.46 (11.3)	< 0.001
ASA (%)			< 0.001
1	0 (0)	23 (30.7)	
2	46 (97.9)	47 (62.7)	
3	1 (2.1)	5 (6.7)	
Mean surgical time in minutes (± SD)	142.09 (36.61)	136 (28.36)	0.307
Educational level (n = 113) (%)			0.001
Illiterate	1 (2.3)	3 (4.3)	
Elementary School	16 (36.4)	48 (69.6)	
High School	15 (34.1)	13 (18.8)	
Higher Education	12 (27.3)	5 (7.2)	

RA: rheumatoid arthritis; OA: osteoarthritis; ASA: American Society of Anesthesiology classification of physical status.

Table 2
General characteristics of the patients of the TKA group

TKA group	RA	OA	P
Gender (%)			0.46
Female	20 (71.4)	42 (75.0)	
Male	8 (28.6)	14 (25.0)	
Mean age (± SD)	54.91 (11.34)	70.97 (7.12)	< 0.001
ASA (%)			0.200
1	0 (0)	6 (10.7)	
2	27 (96.4)	48 (85.7)	
3	1 (3.6)	2 (3.6)	
Mean surgical time in minutes (± SD)	102.86 (39.62)	142.09 (25.84)	0.129
Educational level (n = 113) (%)			< 0.001
Illiterate	0 (0)	8 (17.0)	
Elementary School	8 (34.8)	34 (72.3)	
High School	12 (52.2)	4 (8.5)	
Higher Education	3 (13.0)	1 (2.1)	

RA: rheumatoid arthritis; OA: osteoarthritis; ASA: American Society of Anesthesiology classification of physical status.

Table 3
DMARDs used by RA patients

	THA	TKA
DMARD (%)	37.0 (78.7)	24.0 (85.7)
MTX	28.0 (78.7)	16.0 (85.7)
LFN	9.0 (19.1)	5.0 (17.9)
SSZ	4.0 (8.5)	5.0 (17.9)
Antimalarial	13.0 (28.0)	7.0 (25.0)
Anti-TNF	1.0 (2.1)	2.0 (7.1)
Corticosteroid	30.0 (63.8)	18.0 (64.3)
Mean dose of DMARDs in mg (± SD)		
MTX	10.7 (4.0)	9.3 (2.9)
LFN	20.0 (0.0)	20.0 (0.0)
SSZ	1000.0 (0.0)	1200.0 (273.9)
CQN	250.0 (0.0)	204.6 (65.6)
HCQN	200.0 (0.0)	400.0 (0.0)
Equivalent prednisone	6.9 (4.0)	10.2 (6.5)

THA: total hip arthroplasty; TKA: total knee arthroplasty; DMARD: disease-modifying antirheumatic drug; MTX: methotrexate; LFN: leflunomide; SSZ: sulfasalazine; CQN: chloroquine; HCQN: hydroxychloroquine.

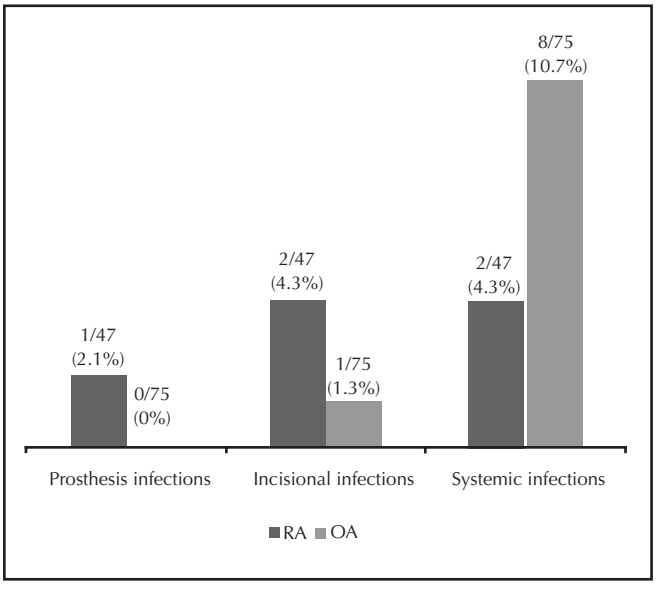

Figure 2
Incidence of prosthesis infections in the subsequent year of surgery, incisional infections in the subsequent month of surgery, and systemic infections during hospitalization of the total hip arthroplasty group (fraction and percentage).
RA: rheumatoid arthritis; OA: osteoarthritis.

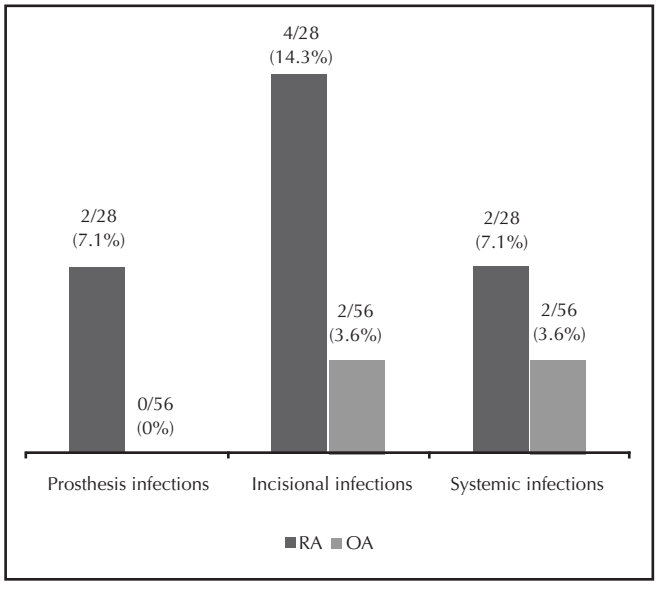

Figure 3
Incidence of prosthesis infections in the subsequent year of surgery, incisional infections in the subsequent month of surgery, and systemic infections during hospitalization of the total knee arthroplasty group.
RA: rheumatoid arthritis; OA: osteoarthritis.

superficial and deep incisional infections were grouped as incisional infection.

In the THA group, one RA patient presented prosthesis infection, but no OA patient did. In the TKA group, two RA patients had prosthesis infection, but no OA patient had it. In two cases, the infectious agent was the oxacillin-sensitive *Staphylococcus aureus*, and, in the third case, no culture was available.

In the THA group, two RA patients and one OA patient had incisional infections. In the TKA group, four RA patients and two OA patients had incisional infections. No microbiological information on infection was available in any of those cases.

Regarding systemic infections, in the THA group, two RA patients were identified as follows: one upper airway infection and one cellulitis in the same operated-upon limb, but distant from the surgical site. Among OA patients, the following were identified: two pneumonias; four urinary tract infections (UTI); one sepsis secondary to catheter infection; and one cellulitis. In the TKA group, among RA patients, the following were identified: one sepsis secondary to septic arthritis of the contralateral knee, caused by oxacillin-sensitive *S. aureus;* and one cellulitis. Among OA patients, two UTIs were identified. In four cases of UTI, the etiologic agent was *Escherichia coli*, and no culture was available in the fifth case. No germ was isolated in the pneumonia cases, and, in the catheter infection, *Klebsiella pneumoniae* was isolated from the blood culture.

In univariate analysis, no significant difference was observed among the groups regarding the rates of prosthesis infection (both with $P > 0.1$), incisional infection (both with $P > 0.1$), and systemic infection (TKA, $P = 0.92$; and THA, $P > 0.1$).

Multiple logistic regression was carried out, including the following variables: gender; age; educational level; ASA classification; and surgery duration. The stepwise backward automatic selection method was used with selection criterion $P < 0.10$. To assess the educational levels, the "illiterate" classification was used as reference to compare with other educational levels. Regarding the ASA physical status classification, the "ASA 1" classification was adopted as reference. Because of the reduced number of cases of infection observed, the variables "educational level" and "ASA physical status" had extreme coefficients and P values, with no statistical significance. The other variables were also non-significant in the adjusted model ($P > 0.10$), in other words, showed no significant association in the groups regarding prosthesis, incisional and systemic infections.

DISCUSSION

Hip or knee arthroplasties in RA patients are relatively safe regarding the incidence of infections one year after the procedure, despite the use of corticosteroids and other immunomodulatory drugs, because no evidence of increased prosthesis, incisional and systemic infections was observed in this study. At first, there is no reason not to provide such therapeutic modality for RA patients to relieve pain secondary to joint sequelae of the disease, which can be extremely severe.

The groups assessed differed regarding age, because RA patients are usually younger. In addition, there were significant differences regarding the educational level of the patients, which may be explained by the progressive improvement in the socioeconomic status of the Brazilian population during the twentieth century. Such differences may have reduced the effect of the RA presence as a risk factor, in accordance with the findings of two large retrospective studies that have reported the low socioeconomic status as a risk factor for prosthesis infections.[28,29]

In this study, it is worth emphasizing the quality of data collection, which was obtained from electronic medical records. In addition, well-defined criteria were used for diagnosing OA and RA, avoiding the inclusion of patients with other correlated diseases. To our knowledge, Brazilian studies that have comparatively evaluated the incidence of incisional and systemic infections in this context in a more specific way still lack.

Regarding the limitations of this study, we point out that our case series, although using all cases available, may not have been large enough to successfully demonstrate differences among the groups: the statistical power calculated *post hoc* was 52% for the THA group, and 24% for the TKA group. One of the previously mentioned studies[10] has shown a 0.4% difference in survival of TKA and no difference in survival of THA in five years. This difference is very small and could only be evidenced because the study was multicenter and retrospective, assessing a whole country and including 108,786 surgeries. Analyzing the incidences of prosthesis and incisional infections in TKA, for instance, we observed a tendency towards a greater number of events in RA patients, but with no statistical significance. On the other hand, the general rate of nosocomial infections in our hospital is very low, being 0.63% in 2010. This may have been a bias to determine differences among groups. Another point is that the control group was very heterogeneous, with OA patients of many etiologies, including some rare causes

secondary to systemic diseases, which may have different postoperative prognosis.

In conclusion, RA was not identified as a risk factor for perioperative infections in THA and TKA in this case series of the Hospital SARAH-Brasília as compared with the group of patients with primary OA or OA secondary to non-inflammatory diseases. The low incidence of infections in both groups may explain our findings. A Brazilian multicenter study could clarify the matter more definitively.

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