Seminars in Arthritis and Rheumatism ▮ (2016) ▮▮▮–▮▮▮

Contents lists available at ScienceDirect

Seminars in Arthritis and Rheumatism

journal homepage: www.elsevier.com/locate/semarthrit

Moderating effects of immunosuppressive medications and risk factors for post-operative joint infection following total joint arthroplasty in patients with rheumatoid arthritis or osteoarthritis

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ARTICLE INFO

Keywords:
Total joint arthroplasty
Infections
Risk factors
Immunosuppressive medications
Perioperative management
Case–control study

ABSTRACT

Objective: Inconclusive findings about infection risks, importantly the use of immunosuppressive medications in patients who have undergone large-joint total joint arthroplasty, challenge efforts to provide evidence-based perioperative total joint arthroplasty recommendations to improve surgical outcomes. Thus, the aim of this study was to describe risk factors for developing a post-operative infection in patients undergoing TJA of a large joint (total hip arthroplasty, total knee arthroplasty, or total shoulder arthroplasty) by identifying clinical and demographic factors, including the use of high-risk medications (i.e., prednisone and immunosuppressive medications) and diagnoses [i.e., rheumatoid arthritis (RA), osteoarthritis (OA), gout, obesity, and diabetes mellitus] that are linked to infection status, controlling for length of follow-up.

Methods: A retrospective, case-control study ($N = 2212$) using de-identified patient health claims information from a commercially insured, U.S. dataset representing 15 million patients annually (from January 1, 2007 to December 31, 2009) was conducted. Descriptive statistics, *t*-test, chi-square test, Fisher's exact test, and multivariate logistic regression were used.

Results: Male gender (OR = 1.42, $p < 0.001$), diagnosis of RA (OR = 1.47, $p = 0.031$), diabetes mellitus (OR = 1.38, $p = 0.001$), obesity (OR = 1.66, $p < 0.001$) or gout (OR = 1.95, $p = 0.001$), and a prescription for prednisone (OR = 1.59, $p < 0.001$) predicted a post-operative infection following total joint arthroplasty. Persons with post-operative joint infections were significantly more likely to be prescribed allopurinol ($p = 0.002$) and colchicine ($p = 0.006$); no significant difference was found for the use of specific disease-modifying anti-rheumatic drugs and TNF-α inhibitors.

Conclusion: High-risk, post-operative joint infection groups were identified allowing for precautionary clinical measures to be taken.

Introduction

Due to the high number of persons undergoing total large-joint arthroplasty in the United States, a clear understanding of the risk of infection and related hospital readmissions and surgical revisions is important [1–8]. Specifically, in the United States, there were 719,000 total knee arthroplasties, 332,000 total hip arthroplasties, and 29,127 total shoulder arthroplasties carried out in 2010 with annual costs estimated to be $18.7 billion [1–3]. Infection is reported as a leading cause of hospital readmission following a total joint arthroplasty (post-operative joint infection rates: 0.3–0.7%) [4–6]. An estimated 14% of hospital readmissions following total joint arthroplasty are as a result of deep or superficial surgical site infection and 44% of joint revisions are as a result of infections [4–8].

In efforts to improve infection rates, prior research studies have identified high-risk groups which have included the

Abbreviations: RA, rheumatoid arthritis; OA, osteoarthritis; U.S., United States; OR, odds ratio; DM, diabetes mellitus; DMARDs, disease-modifying anti-rheumatic drugs; TNFα, tumor necrosis factor alpha; CPT, current procedural terminology; ICD-9, International Statistical Classification of Disease; HIV/AIDs, human immunodeficiency virus infection and acquired immune deficiency syndrome; SLE, systemic lupus erythematosus.

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http://dx.doi.org/10.1016/j.semarthrit.2016.08.011
0049-0172/

following: male gender [odds ratio (OR): total knee arthroplasty—1.89; total shoulder arthroplasty—2.59; total joint arthroplasty—1.79], age older or younger than 56–65 years (OR: total knee arthroplasty—1.42–2.59), diagnosis of diabetes mellitus (DM; OR: total knee arthroplasty—1.28; total hip arthroplasty—1.77), scoring at or higher than 2 on the American Society of Anesthesiologist Scale (OR: total knee arthroplasty—1.42–1.65; total hip arthroplasty—1.95–2.74; TSA—1.41), history of cancer (OR: total knee arthroplasty—11.73), higher Charlson Comorbidity Score [OR: total joint arthroplasty—2.29 (score $\geq$ 2), total knee arthroplasty—2 (score $>$ 3)], current smoker (OR: total knee arthroplasty or total hip arthroplasty—1.41), and body mass index $\geq$ 35 (OR: total knee arthroplasty—1.47; total hip arthroplasty—3.02; total shoulder arthroplasty—2.48). Yet, there are inconsistencies in the variables investigated and study findings [7–18]. Similarly, many of these risk factors are largely unmodifiable in the perioperative period.

Because of the potential for modification, an understanding of risks of immunosuppressive medications on rates of infection and readmission following total joint arthroplasty is needed. Prior research on this topic is largely based on studies of rheumatoid arthritis (RA) patients [8,19,20]. Research suggests the use of traditional disease-modifying anti-rheumatic drugs (DMARDs), a nonbiologic class of immunosuppressive medications used to treat RA, prior to surgery does not increase infection risk [20]. In contrast, steroid use has been found to increase risks of infection and hospital readmission [19,21]. There are conflicting findings on TNF inhibitor use (biologic medications used to treat RA) and infection risk [20–26].

Studies investigating the role of immunosuppressive medications in RA patients have not clearly described the role of treatment vs. disease-related (inflammatory arthritis vs. non-inflammatory arthritis) effects on post-operative infection risks [9,10,27–29]. Two retrospective U.S. studies found no difference in infection rates between those diagnosed with RA vs. osteoarthritis (OA) in persons who had undergone a total hip arthroplasty or total knee arthroplasty [9,10]. Yet, a number of studies have reported increased risks of infection in patients with RA ranging from two to four-times that of patients with OA [5,15,19,27]. Singh et al. [4] (N = 34,311) recently reported that persons with RA are 1.29 times more likely to be readmitted to the hospital for post-surgical complications (infection leading cause), and that these rates are increasing yearly (0.85, 1.37, and 1.63 in 2009, 2010, and 2011, respectively). Interpretation of the literature is complicated by the inconsistent antibiotic protocols, definitions of infection, and sampling [28].

Evidence-based perioperative management for total joint arthroplasty is limited by the lack of conclusive research findings about risk factors, the role of immunosuppressive medications, and the role of type of arthritis (OA vs. RA) in the development of an infection following total joint arthroplasty [9,10,27,29]. The aim of this study was to describe risk factors for developing post-operative infections in patients undergoing total joint arthroplasty of a large joint (total hip arthroplasty, total knee arthroplasty, or total shoulder arthroplasty). To achieve this aim, initially we identified clinical and demographic factors, including the use of high-risk medications (i.e., prednisone and immunosuppressive medications) and diagnoses (i.e., gout, obesity, DM, RA, and OA), that are linked to infection status, controlling for length of follow-up by comparing cases and control, and using logistic regression modeling. During this iterative process, we further explored the potential for clinical and demographic factors that moderate the relationship between RA/OA diagnosis and infections post-operatively.

Materials and methods

Procedure and sample

De-identified patient health claims information was extracted retrospectively from a dataset representing a commercially insured, U.S. population of 15 million patients annually from January 1, 2007 to December 31, 2009. This dataset includes 1,284,681 prescribers and 3631 health care provider designations from all geographic regions in the United States. Patient-level data were extracted including administrative demographic data (e.g., gender and age), pharmacy claims data (e.g., national drug code), and physician and facility claims (e.g., procedure codes and diagnosis codes). Medical Institutional Review Board approval was obtained for the use of this dataset.

First, all patients with the diagnosis of OA (ICD-9: 715.0–715.9) and RA (ICD-9: 714.0, 714.2, and 714.4) who had a total joint arthroplasty (CPT codes: total knee arthroplasty—27447, total hip arthroplasty—27130, and total shoulder arthroplasty—23472) were extracted from the database which resulted in 55,861 unique persons. Patients who developed a post-operative joint infection following total joint arthroplasty surgery (ICD-9: 996.66—*Infection and inflammatory reaction due to internal joint prosthesis*) were identified as cases (Fig. 1). Of the 55,861 patients followed during this 2-year period, 1127 developed a post-operative infection following total joint arthroplasty surgery and therefore were defined as cases in this study. Only one operative event was included for a given patient. If a patient had more than one total joint arthroplasty, only the first surgery was retained in this analysis. The only exception to this was when a patient had a subsequent total joint arthroplasty surgery that resulted in infection; in this case, only the information from the first surgery associated with an infection was retained. Controls were randomly selected to frequency match cases based on age (within 10-year increments) with a 1:1 sampling ratio; therefore, only persons with complete data on matching criteria were eligible. Ten cases had missing data on year of birth and were excluded from the study; 11 cases were omitted because they did not have confirmation of OA or RA diagnosis, since the corresponding ICD-9 code was listed only once in their record; therefore, the final sample consisted of 2212 patients: 1106 cases and 1106 controls.

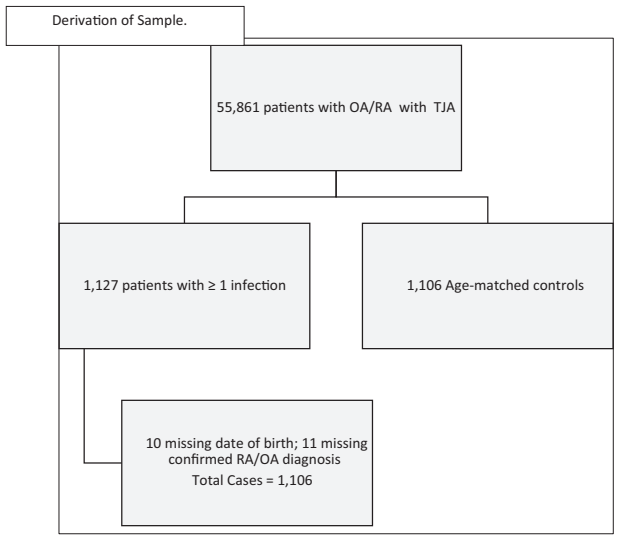

Fig. 1. Derivation of sample.