The Journal of Arthroplasty xxx (2016) 1–5

Contents lists available at ScienceDirect

The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

Original Article

Incidence, Risk Factors, and Sources of Sepsis Following Total Joint Arthroplasty

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ARTICLE INFO

Article history:
Received 6 February 2016
Received in revised form
25 April 2016
Accepted 11 May 2016
Available online xxx

Keywords:
sepsis
total joint arthroplasty
urinary tract infection
surgical site infection
pneumonia

ABSTRACT

Background: Sepsis is a rare but serious complication following total joint arthroplasty (TJA). Common sources include urinary tract infection (UTI), surgical site infection (SSI), and pneumonia. The purpose of this study is to characterize the incidence, risk factors, and sources of sepsis following TJA.

Methods: Patients undergoing primary total hip arthroplasty or total knee arthroplasty during 2005-2013 were identified in the American College of Surgeons National Surgical Quality Improvement Program database. Independent associations were tested for using multivariate regression adjusting for baseline characteristics.

Results: A total of 117,935 patients were identified (45,612 undergoing total hip arthroplasty and 72,323 undergoing total knee arthroplasty). Of these, 402 (0.34%) developed sepsis following surgery. Patients who developed sepsis had an elevated mortality rate (3.7% vs 0.1%, $P < .001$). Among the 402 patients who developed sepsis, 124 (31%) had concomitant UTI, 110 (27%) SSI, and 60 (15%) pneumonia. Twenty-one patients (5%) had multiple infectious sources and 129 patients (32%) had no identifiable source. Independent risk factors for sepsis included greater age, male sex, functional dependence, insulin-dependent diabetes, hypertension, chronic obstructive pulmonary disease, current smoker, and greater operative time.

Conclusion: These findings suggest that the rate of sepsis following TJA is about 1 in 300, and that sepsis is associated with a high risk of mortality. The most common sources of sepsis are UTI, SSI, and pneumonia, potentially accounting for at least two-thirds of cases. The information provided here can be used to guide the diagnostic workup of sepsis in patients following TJA.

Sepsis is a clinical syndrome defined by the presence of both infection and systemic inflammatory response [1] and is a rare but serious complication following total joint arthroplasty (TJA). It is currently estimated that between 0.15% and 0.90% of patients who have undergone primary total hip arthroplasty (THA) or total knee arthroplasty (TKA) will experience sepsis in the perioperative period [2-6], and there has been an increase over the past decade in the diagnosis of sepsis following these procedures [4].

Sepsis following elective surgical procedures can prove devastating. For example, across an array of surgical procedures, sepsis was associated with an increase in mortality up to 32 times the normal incidence [2,6,7]. Perioperative sepsis not only represents a significant health burden to patients but also an economic burden to providers and payers [8-10]. As we shift toward systems of bundled payments and public reporting of physician and hospital metrics [11], it becomes increasingly important to understand the causes and risk factors for the adverse events for which providers will be penalized.

In order for sepsis to develop, there must be an infectious source. Common infectious sources include urinary tract infection (UTI), surgical site infection (SSI), and pneumonia. However, coincidence of sepsis and these potential sources following TJA has not been characterized. The purpose of this study is to characterize the

Institutional review board approval: Our institutional review board approved this study.

One or more of the authors of this paper have disclosed potential or pertinent conflicts of interest, which may include receipt of payment, either direct or indirect, institutional support, or association with an entity in the biomedical field which may be perceived to have potential conflict of interest with this work. For full disclosure statements refer to http://dx.doi.org/10.1016/j.arth.2016.05.031.

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http://dx.doi.org/10.1016/j.arth.2016.05.031
0883-5403/

(1) incidence, (2) risk factors, (3) coincident potential sources, and (4) mortality associated with sepsis following TJA. The study will also characterize risk factors for each of the potential infectious sources.

Methods

Data Set

The American College of Surgeons National Surgical Quality Improvement Program (NSQIP) is a prospective surgical registry that follows patients during the 30-day postoperative period following an array of common orthopedic procedures for purposes of quality improvement and clinical research. At each of several hundred voluntarily participating community and academic centers nationwide, patients are prospectively identified using a randomized selection process. Baseline demographic and comorbidity information is collected. At the end of the 30-day follow-up period, inpatient and outpatient charts are reviewed, and in cases where necessary, either patients or providers are contacted to identify the occurrence of 23 postoperative adverse events. A complete data set including all voluntarily participating institutions is made available to members of those institutions for purposes of clinical research. Now in existence for nearly a decade, the program has been widely used for both general [12-14] and orthopedic [15-18] surgical research.

Patients, Baseline Characteristics, and Adverse Events

Institutional review board approval was obtained. Patients undergoing primary THA or TKA during 2005-2013 as part of the NSQIP were initially identified using Current Procedural Terminology codes (27,130 and 27,447, respectively). Cases were further reviewed to exclude any cases involving revision, preoperative infection, additional unrelated procedures, acute trauma, major ligament reconstruction, or hardware removal.

The NSQIP collects baseline demographic and comorbidity information on all patients. Demographic and comorbidity information that was extracted and analyzed in the present study consisted of age, sex, body mass index (BMI), functional status, current smoking status, and the presence/absence of hypoalbuminemia, chronic obstructive pulmonary disease (COPD), hypertension, dyspnea on exertion, and diabetes. Operative time was also collected.

Sepsis is defined by NSQIP using specific, detailed criteria outlined in their materials [19] and in Appendix 1. In brief, patients must have both vital sign or laboratory derangements and clinical evidence of infection. Notably, NSQIP differentiates between sepsis and severe sepsis [19]; however, for purposes of analysis, these two categories were analyzed together simply as the development of sepsis. Other adverse events captured by NSQIP and analyzed in this study include SSI, pneumonia, UTI, and death. NSQIP definitions of SSI, pneumonia, and UTI are outlined in NSQIP materials [19] and in Appendix 1.

Analysis

Stata version 13.1 (StataCorp, LLP, College Station, TX) was used for all analyses. The level of significance was set at $P < .05$.

First, the incidence and 95% confidence interval (CI) for development of sepsis was determined. Second, among patients who developed sepsis, coincident potential sources were tabulated. Third, the association between sepsis and coincident potential sources was characterized using multivariate Poisson regression with robust error variance with adjustment for demographic and comorbidity factors. Fourth, independent demographic and comorbidity risk factors for the development of sepsis, SSI, UTI, and pneumonia were determined using multivariate Poisson regression with robust error variance. Backward-stepwise selection was used to arrive at the final multivariate models. Finally, the development of sepsis was tested for association with mortality with adjustment for all baseline demographic and comorbidity characteristics.

Results

A total of 117,935 patients were identified (45,612 undergoing THA and 72,323 undergoing TKA). Demographic and comorbidity characteristics of the study population are described in Table 1.

A total of 402 patients developed sepsis following surgery, yielding an estimated 30-day incidence of 0.34% (95% CI = 0.31%-0.37%). Among these patients, 124 (31%) had coincident UTI, 110 (27%) coincident SSI, and 60 (15%) coincident pneumonia (Table 2). Twenty-one patients (5%) had multiple infectious sources, and 129 patients (32%) had no identifiable source. The rate of sepsis was increased in patients who developed UTI (9.2% vs 0.2%, adjusted relative risk [RR] = 33.7, 95% CI = 27.1-41.9, $P < .001$), SSI (9.5% vs 0.3%, adjusted RR = 30.5, 95% CI = 24.4-38.1, $P < .001$), or pneumonia (14.7% vs 0.3%, RR = 34.3, 95% CI = 25.8-45.6, $P < .001$; Table 3).

Independent risk factors for sepsis included greater age, male sex, functional dependence, insulin-dependent diabetes, hypertension, COPD, current smoker, and greater operative time

Table 1
Patient Population.

Characteristic	Number	Percent
Overall	117,935	100.0
Age		
18-59 y	30,153	25.6
60-69 y	41,286	35.0
70-79 y	32,839	27.8
≥80 y	13,657	11.6
Sex		
Female	46,814	39.7
Male	71,121	60.3
Body mass index		
<25.0 kg/m^2	17,077	14.5
25.0-29.9 kg/m^2	36,198	30.7
≥30 kg/m^2	64,660	54.8
Functional dependence		
No	115,180	97.7
Yes	2755	2.3
Current smoker		
No	105,881	89.8
Yes	12,054	10.2
Diabetic status		
No diabetes	101,340	85.9
Noninsulin-dependent diabetes mellitus	12,297	10.4
Insulin-dependent diabetes mellitus	4298	3.6
Hypertension		
No	43,128	36.6
Yes	74,807	63.4
Chronic obstructive pulmonary disease		
No	113,450	96.2
Yes	4485	3.8
Hypoalbuminemia		
No	115,498	97.9
Yes	2437	2.1
Dyspnea on exertion		
No	109,983	93.3
Yes	7952	6.7
Operative time		
<75 min	38,097	32.3
75-99 min	38,603	32.7
≥100 min	41,235	35.0