



# Lupus and Perioperative Complications in Elective Primary Total Hip or Knee Arthroplasty

Keith T. Aziz, MD, Matthew J. Best, MD, Richard L. Skolasky, ScD, Karthik E. Ponnusamy, MD, Robert S. Sterling, MD, Harpal S. Khanuja, MD

Department of Orthopaedic Surgery, The Johns Hopkins Hospital, Baltimore, MD, USA

**Background:** The number of patients with systemic lupus erythematosus (herein, lupus) undergoing total hip arthroplasty (THA) or total knee arthroplasty (TKA) is increasing. There is disagreement about the effect of lupus on perioperative complication rates. We hypothesized that lupus would be associated with higher complication rates in patients who undergo elective primary THA or TKA.

**Methods:** Records of more than 6.2 million patients from the National Inpatient Sample who underwent elective primary THA or TKA from 2000 to 2009 were reviewed. Patients with lupus ( $n = 38,644$ ) were compared with those without lupus ( $n = 6,173,826$ ). Major complications were death, pulmonary embolism, myocardial infarction, stroke, pneumonia, and acute renal failure. Minor complications were wound infection, seroma, deep vein thrombosis, hip dislocation, wound dehiscence, and hematoma. Patient age, sex, duration of hospital stay, and number of Elixhauser comorbidities were assessed for both groups. Multivariate logistic regression models using comorbidities, age, and sex as covariates were used to assess the association of lupus with major and minor perioperative complications. The alpha level was set to 0.001.

**Results:** Among patients who underwent THA, those with lupus were younger (mean age, 56 vs. 65 years), were more likely to be women (87% vs. 56%), had longer hospital stays (mean, 4.0 vs. 3.8 days), and had more comorbidities (mean, 2.5 vs. 1.4) than those without lupus (all  $p < 0.001$ ). In patients with THA, lupus was independently associated with major complications (odds ratio [OR], 1.4; 95% confidence interval [CI], 1.1 to 1.7) and minor complications (OR, 1.2; 95% CI, 1.0 to 1.5). Similarly, among patients who underwent TKA, those with lupus were younger (mean, 62 vs. 67 years), were more likely to be women (93% vs. 64%), had longer hospital stays (mean, 3.8 vs. 3.7 days), and had more comorbidities (mean, 2.8 vs. 1.7) than those without lupus (all  $p < 0.001$ ). However, in TKA patients, lupus was not associated with greater odds of major complications (OR, 1.2; 95% CI, 0.9 to 1.4) or minor complications (OR, 1.1; 95% CI, 0.9 to 1.3).

**Conclusions:** Lupus is an independent risk factor for major and minor perioperative complications in elective primary THA but not TKA.

**Keywords:** Complications, Perioperative, Systemic lupus erythematosus, Arthroplasty, Total knee, Arthroplasty, Total hip

Systemic lupus erythematosus (herein, lupus) is a complex, chronic autoimmune inflammatory disease with many clinical and immunologic manifestations. It occurs dis-

proportionately among women and African Americans.<sup>1,2</sup> The musculoskeletal system is affected severely in patients with lupus, causing arthralgia and arthritis in as many as 95% of patients.<sup>3-5</sup>

Arthritic changes in patients with lupus are different from those in patients with inflammatory arthropathies. These arthritic changes may be related closely to vasculitic changes that also occur with lupus.<sup>6,7</sup> In some series, 4%–30% of patients with lupus develop osteonecrosis, with the femoral head being the most common site of involvement.<sup>8,9</sup> Lupus is often treated with glucocorticoids, which

Received March 27, 2019; Accepted August 30, 2019

Correspondence to: Harpal S. Khanuja, MD

Department of Orthopaedic Surgery, Johns Hopkins Bayview Medical Center, The Johns Hopkins University, 4940 Eastern Ave, Baltimore, MD 21224-2780, USA

Tel: +1-410-550-0101, Fax: +1-410-550-1375

E-mail: hkhanuj1@jhmi.edu

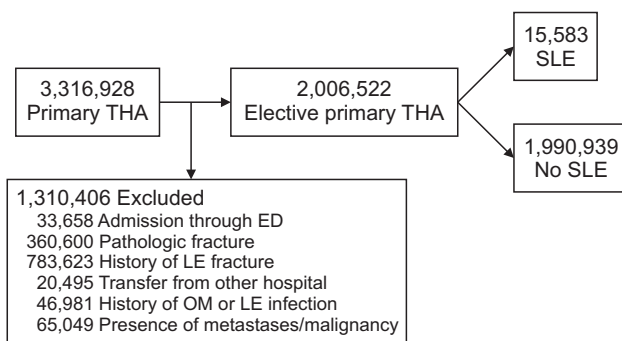
further increase the risk of osteonecrosis.<sup>10-12)</sup>

Lupus treatment has improved, and life expectancy for some patients with lupus has improved;<sup>7,13,14)</sup> however, the effects of lupus still cause major financial and societal burdens.<sup>15)</sup> Total joint arthroplasty is an excellent option for patients whose joints have been damaged by lupus-related arthritis. The numbers of total hip arthroplasties (THAs) and total knee arthroplasties (TKAs) being performed for patients with lupus are increasing.<sup>16)</sup> It is important to characterize the perioperative complications associated with lupus to optimize care and counsel patients about perioperative risks.

The aim of this study was to compare patients with and without lupus who underwent THA or TKA in terms of their characteristics and acute inpatient perioperative complications. We hypothesized that patients with lupus would have higher rates of major complications (including death) and minor complications compared with those of patients without lupus. We report on the risk of acute perioperative inpatient complications after THA or TKA in patients with lupus versus patients without lupus.

## METHODS

We searched the National Inpatient Sample (NIS) database for patients who underwent primary THA or TKA from 2000 through 2009. The NIS database includes discharge information from a 20% stratified sample of U.S. hospitals and patient information for all payers. The sampling method reportedly captures 97% of U.S. hospital discharges.<sup>11)</sup> Discharge weights were used to scale the NIS data to represent the general US population. Our institutional review board deemed this study exempt from approval.



**Fig. 1.** Patient selection flowchart for total hip arthroplasty (THA) group. SLE: systemic lupus erythematosus, ED: emergency department, LE: lower extremity, OM: osteomyelitis.

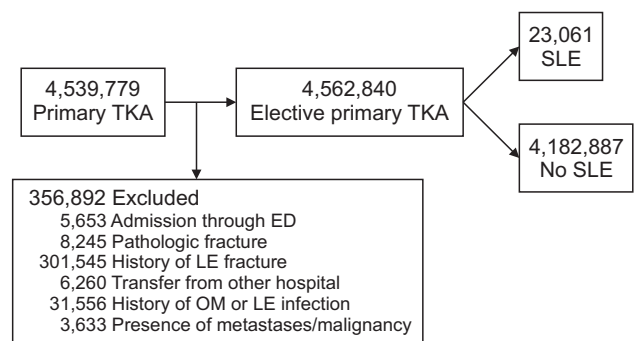
## Inclusion and Exclusion Criteria

All patients with an International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)<sup>17)</sup> procedure code for primary THA (code 81.51 or 81.52) or primary TKA (code 81.54) were candidates for inclusion.<sup>13)</sup> To select for an elective primary arthroplasty population, we excluded patients who had a hip or lower extremity fracture; were admitted through the emergency department; were transferred from another hospital; or had acute or chronic osteomyelitis, malignancy, or history of pathologic fracture. Patients were assigned to one of two subgroups: those with lupus (ICD-9-CM code 710.0), or those without lupus.

Of the 3,316,928 patients who underwent THA, 1,310,406 were excluded (Fig. 1). The remaining 2,006,522 patients formed the THA study group. Of this group, 0.78% (n = 15,583) were diagnosed with lupus. Of the 4,562,840 patients who underwent TKA, 356,892 were excluded (Fig. 2). The remaining 4,205,948 patients formed the TKA study group. Of this group, 0.055% (n = 23,061) were diagnosed as having lupus.

## Patient Characteristics and Complications

Using the National Inpatient Survey database, we collected data on patient age, sex, race, and comorbidities (Table 1). Race was categorized as black, white, other (Hispanic, Asian, or Native American), or missing. Comorbidities were classified according to the Elixhauser coding schematic described by Quan et al.<sup>18)</sup> Duration of hospitalization and total charges were evaluated as continuous variables. We searched the database for major complications (acute renal failure, death, myocardial infarction, pneumonia, pulmonary embolism, and stroke) and minor complications (deep vein thrombosis, hip dislocation, general complications, hematoma, seroma, and wound infection)



**Fig. 2.** Patient selection flowchart for total knee arthroplasty (TKA) group. SLE: systemic lupus erythematosus, ED: emergency department, LE: lower extremity, OM: osteomyelitis.

**Table 1.** Characteristics of Patients Who Underwent Elective Primary THA or TKA by Systemic Lupus Erythematosus Status, National Inpatient Sample, 2000–2009

Variable	THA			TKA		
	No lupus (n = 1,990,939)	Lupus (n = 15,583)	<i>p</i> -value	No lupus (n = 4,182,887)	Lupus (n = 23,061)	<i>p</i> -value
Age (yr)	65 ± 0.09	56 ± 0.4	< 0.001	67 ± 0.06	62 ± 0.2	< 0.001
Female sex	1,123,652 (56)	13,557 (87)	< 0.001	2,635,218 (63)	21,445 (93)	< 0.001
Race						
Black	86,482 (4.3)	2,240 (14)		197,415 (4.7)	1,905 (8.3)	
White	1,272,552 (64)	8,030 (52)		2,588,534 (62)	14,152 (61)	
Other	77,740 (3.9)	1,299 (8.3)		287,763 (6.9)	1,334 (5.8)	
Missing	544,165 (28)	4,014 (26)		1,109,175 (27)	5,670 (25)	
Hospital stay (day)	3.8 ± 0.02	4.0 ± 0.05	< 0.001	3.7 ± 0.02	3.8 ± 0.03	< 0.001
No. of Elixhauser comorbidities	1.4 ± 0.01	2.5 ± 0.02	< 0.001	1.7 ± 0.01	2.8 ± 0.02	< 0.001

Values are presented as mean ± standard deviation or number (%).  
THA: total hip arthroplasty, TKA: total knee arthroplasty.

by ICD-9-CM code. Complications in the National Inpatient Survey database are acute perioperative complications that occur during the same admission as the surgery.

### Statistical Analysis

Descriptive statistics with standard errors for continuous variables were used for analyzing complications, patient characteristics, hospital charges, and duration of hospitalization. Student *t*-tests were used for continuous variables, and chi-square tests were used for categorical variables. Significance was set at  $p < 0.01$ . Univariate and multivariate logistic regression models were constructed to assess the association of lupus with major and minor perioperative complications. Associations between major Elixhauser comorbidities (i.e., cardiac arrhythmia, chronic pulmonary disease, congestive heart failure, liver disease, obesity, excess weight loss, and peripheral vascular disease) and death and complications in patients with or without lupus were assessed as multivariate odds ratios (ORs) with 95% confidence intervals (CIs). Statistical analysis was performed using Stata ver. 10 (StataCorp., College Station, TX, USA).

## RESULTS

### Total Hip Arthroplasty

Among patients who underwent elective primary THA, those with lupus were younger (mean age, 56 ± 0.4 vs. 65 ±

0.09 years;  $p < 0.001$ ), were more likely to be women (87% vs. 56%,  $p < 0.001$ ), had longer hospital stays (mean, 4.0 ± 0.02 vs. 3.8 ± 0.03 days;  $p < 0.001$ ), and had more comorbidities (mean, 2.5 ± 0.02 vs. 1.4 ± 0.01;  $p < 0.001$ ) than those without lupus ( $p < 0.001$ ) (Table 1). Lupus was independently associated with major complications (OR, 1.4; 95% CI, 1.1 to 1.7) and minor complications (OR, 1.2; 95% CI, 1.0 to 1.5) (Table 2). Deep vein thrombosis, general complications, and pneumonia were associated with lupus on univariate analysis and independently on multivariate analysis (Table 2).

### Total Knee Arthroplasty

Among patients who underwent elective primary TKA, those with lupus were younger (mean, 62 ± 0.2 vs. 67 ± 0.06 years), were more likely to be women (93% vs. 64%), had longer hospital stays (mean, 3.8 ± 0.03 vs. 3.7 ± 0.02 days), and had more comorbidities (mean, 2.8 ± 0.02 vs. 1.7 ± 0.01) than those without lupus (all  $p < 0.001$ ) (Table 1). Lupus was not associated with increased odds of major complications (OR, 1.2; 95% CI, 0.9 to 1.4) or minor complications (OR, 1.1; 95% CI, 0.9 to 1.3) (Table 2). Patients with lupus were no more likely than those without lupus to have major or minor perioperative complications according to a pooled analysis (Table 2).

**Table 2.** In-Hospital Complications after Elective Primary THA or TKA by Systemic Lupus Erythematosus Status, National Inpatient Sample, 2000–2009

Complication	THA			TKA		
	Lupus (n = 15,583)	No lupus (n = 1,990,939)	OR (95% CI)*	Lupus (n = 23,061)	No lupus (n = 4,182,887)	OR (95% CI)*
<b>Major</b>						
Acute renal failure	196 (1.3)	30,380 (1.5)	1.4 (0.9–2.0)	290 (1.3)	61,286 (1.5)	1.3 (0.9–1.7)
Death	28 (0.2)	2,648 (0.1)	2.5 (0.9–6.5)	NA <sup>†</sup>	NA <sup>†</sup>	NA <sup>†</sup>
Myocardial infarction	0	1,644 (0.1)	NA <sup>†</sup>	19 (0.1)	2,946 (0.1)	0.9 (0.3–2.7)
Pneumonia	178 (1.1)	18,036 (0.9)	1.5 (1.0–2.1)	276 (1.2)	42,220 (1.0)	1.4 (1.1–1.9)
Pulmonary embolism	34 (0.2)	3,961 (0.2)	1.2 (0.5–2.9)	90 (0.4)	18,742 (0.4)	1.1 (0.6–1.8)
Stroke	13 (0.1)	1,498 (0.1)	4.0 (0.9–18)	19 (0.1)	1,398 (0.03)	0.9 (0.3–3.3)
Any major complication <sup>§,  </sup>	496 (3.2)	56,218 (2.8)	1.4 (1.1–1.7)	748 (3.2)	123,965 (3.0)	1.2 (0.9–1.4)
<b>Minor</b>						
Deep vein thrombosis	39 (0.2)	2,825 (0.14)	2.4 (1.1–5.5)	70 (0.3)	13,088 (0.3)	1.2 (0.7–2.1)
Hip dislocation	42 (0.3)	2,938 (0.1)	1.9 (0.8–4.5)	NA	NA	NA
General complication	813 (5.2)	99,025 (5.0)	1.2 (1.0–1.4)	1,111 (4.8)	200,353 (4.8)	1.1 (0.9–1.3)
Seroma or hematoma	213 (1.4)	23,749 (1.2)	1.0 (0.7–1.4)	177 (0.8)	36,294 (0.9)	0.7 (0.5–1.1)
Wound infection	64 (0.4)	5,434 (0.3)	0.9 (0.5–1.7)	72 (0.3)	11,111 (0.3)	1.4 (0.8–2.4)
Any minor complication <sup>§</sup>	842 (5.3)	101,025 (5.1)	1.2 (1.0–1.5)	1,111 (4.8)	205,613 (4.9)	1.1 (0.9–1.3)

Values are presented as number (%).

THA: total hip arthroplasty, TKA: total knee arthroplasty, OR: odds ratio, CI: confidence interval, NA: not applicable.

\*From multivariate analysis using patient age, sex, and number of Elixhauser comorbidities as covariates. <sup>†</sup>The National Inpatient Sample agreement prohibits reporting on variables with cell sizes  $\leq 10$ . <sup>‡</sup>Insufficient patient number to generate OR for THA group. <sup>§</sup>Patients with more than one complication are counted only once in the aggregate complication categories. <sup>||</sup>Includes death in pooled analysis for TKA group.

## DISCUSSION

Using 2000–2009 data from the NIS, we found associations between lupus and major and minor perioperative complications associated with elective primary THA, but not TKA. Patients with lupus who underwent THA or TKA were younger, were more likely to be women, had longer hospitalizations, and had more comorbidities than patients without lupus. As the life expectancy of patients with lupus continues to improve, their rates of osteonecrosis and joint replacement are likely to increase as well.<sup>12,19,20</sup>

Studies that have investigated the association between lupus and outcomes after THA have produced conflicting results, suggesting that lupus is and is not associated with negative outcomes. However, these studies were retrospective and used data from single centers or small patient cohorts.<sup>16,21</sup> The patient characteristics reported by Shah et al.<sup>21</sup> and Roberts et al.<sup>16</sup> have similarities to

the current findings, including female predominance and more comorbidities in patients with lupus.

In the current study, no association was found between lupus and major or minor perioperative complications after elective primary TKA. Patients with lupus were younger than those without lupus in both the THA and TKA groups. However, the age difference between the TKA groups (with vs. without lupus) was not as great as that between the THA groups. In patients with lupus, the pathophysiology of knee arthritis may be slightly different from that of hip arthritis. There may be more osteonecrosis because lupus has a vasculitic component, and perfusion to the periarticular regions in the hip is more tenuous than that in the knee.<sup>6,7</sup> The rate and nature of the development of severe hip pain necessitating THA may be an indirect way of identifying the severity of lupus.

Another possible explanation for differences in outcomes after THA versus TKA is the difference in blood

loss typically experienced during these procedures. THA frequently involves more blood loss than TKA and is associated with a 2–3 times higher transfusion rate.<sup>22,23</sup> In this and other studies, patients with lupus who undergo arthroplasty have more comorbidities than those without lupus, and blood loss may predispose these patients to perioperative complications.<sup>16,21</sup>

The limitations of our study are related to the use of the NIS database, which records administrative data for the duration of the initial hospitalization only. Administrative databases have various levels of reliability depending on the comorbidity.<sup>24</sup> Long-term outcomes after discharge, which are an important metric for arthroplasty, cannot be evaluated using the NIS. Another limitation is the completeness of the NIS data. The information coded in the NIS is reasonably accurate, with a specificity of more than 92%, but it may be incomplete.<sup>25</sup> The NIS has the major advantage of being the largest administrative database available that includes all payers. For patient subsets, such as those with lupus, in which there are few cases at a single institution or even multiple institutions, the NIS

database is an excellent tool for providing a large sample size to determine incidence of relatively rare outcomes, such as inpatient death.

Compared with those without lupus, patients with lupus are at substantially higher risk of acute perioperative inpatient complications after THA but not after TKA. Elective THA should be approached with caution after careful consideration of comorbidities and risk factors.

## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

## ACKNOWLEDGEMENTS

Karthik E. Ponnusamy, MD, received an Orthopaedic Research and Education Foundation (OREF) Resident Research Grant in support of research for or preparation of this work.

## REFERENCES

- Borchers AT, Naguwa SM, Shoenfeld Y, Gershwin ME. The geoepidemiology of systemic lupus erythematosus. *Autoimmun Rev.* 2010;9(5):A277-87.
- Kamen DL. Environmental influences on systemic lupus erythematosus expression. *Rheum Dis Clin North Am.* 2014;40(3):401-12, vii.
- Esdale JM, Danoff D, Rosenthal L, Gutkowski A. Deforming arthritis in systemic lupus erythematosus. *Ann Rheum Dis.* 1981;40(2):124-6.
- Issa K, Pierce TP, Scillia AJ, Festa A, Harwin SF, Mont MA. Midterm outcomes following total knee arthroplasty in lupus patients. *J Arthroplasty.* 2016;31(3):655-7.
- Mourao AF, Amaral M, Caetano-Lopes J, Isenberg D. An analysis of joint replacement in patients with systemic lupus erythematosus. *Lupus.* 2009;18(14):1298-302.
- Stratta P, Marcuccio C, Campo A, et al. Improvement in relative survival of patients with vasculitis: study of 101 cases compared to the general population. *Int J Immunopathol Pharmacol.* 2008;21(3):631-42.
- Stratta P, Mesiano P, Campo A, et al. Life expectancy of women with lupus nephritis now approaches that of the general population. *Int J Immunopathol Pharmacol.* 2009;22(4):1135-41.
- Mont MA, Glueck CJ, Pacheco IH, Wang P, Hungerford DS, Petri M. Risk factors for osteonecrosis in systemic lupus erythematosus. *J Rheumatol.* 1997;24(4):654-62.
- Mok MY, Farewell VT, Isenberg DA. Risk factors for avascular necrosis of bone in patients with systemic lupus erythematosus: is there a role for antiphospholipid antibodies? *Ann Rheum Dis.* 2000;59(6):462-7.
- Apostolopoulos D, Morand EF. It hasn't gone away: the problem of glucocorticoid use in lupus remains. *Rheumatology (Oxford).* 2017;56(suppl\_1):i114-22.
- Di Franco M, Bazzichi L, Casale R, Sarzi-Puttini P, Atzeni F. Pain in systemic connective tissue diseases. *Best Pract Res Clin Rheumatol.* 2015;29(1):53-62.
- Mertelsmann-Voss C, Lyman S, Pan TJ, Goodman SM, Figgie MP, Mandl LA. US trends in rates of arthroplasty for inflammatory arthritis including rheumatoid arthritis, juvenile idiopathic arthritis, and spondyloarthritis. *Arthritis Rheumatol.* 2014;66(6):1432-9.
- Bernatsky S, Boivin JF, Joseph L, et al. Mortality in systemic lupus erythematosus. *Arthritis Rheum.* 2006;54(8):2550-7.
- Trager J, Ward MM. Mortality and causes of death in systemic lupus erythematosus. *Curr Opin Rheumatol.* 2001;13(5):345-51.
- Meacock R, Dale N, Harrison MJ. The humanistic and economic burden of systemic lupus erythematosus: a systematic

- review. *Pharmacoeconomics*. 2013;31(1):49-61.
16. Roberts JE, Mandl LA, Su EP, et al. Patients with systemic lupus erythematosus have increased risk of short-term adverse events after total hip arthroplasty. *J Rheumatol*. 2016;43(8):1498-502.
  17. Centers for Disease control and Prevention. ICD-9-CM: International Classification of Diseases, ninth revision, clinical modification. Washington, DC: Department of Health and Human Services; 2011.
  18. Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care*. 2005;43(11):1130-9.
  19. Mertelsmann-Voss C, Lyman S, Pan TJ, Goodman S, Figgie MP, Mandl LA. Arthroplasty rates are increased among US patients with systemic lupus erythematosus: 1991-2005. *J Rheumatol*. 2014;41(5):867-74.
  20. Abu-Shakra M, Buskila D, Shoenfeld Y. Osteonecrosis in patients with SLE. *Clin Rev Allergy Immunol*. 2003;25(1):13-24.
  21. Shah UH, Mandl LA, Mertelsmann-Voss C, et al. Systemic lupus erythematosus is not a risk factor for poor outcomes after total hip and total knee arthroplasty. *Lupus*. 2015;24(9):900-8.
  22. Ponnusamy KE, Kim TJ, Khanuja HS. Perioperative blood transfusions in orthopaedic surgery. *J Bone Joint Surg Am*. 2014;96(21):1836-44.
  23. Chen Y, Chen Z, Cui S, Li Z, Yuan Z. Topical versus systemic tranexamic acid after total knee and hip arthroplasty: a meta-analysis of randomized controlled trials. *Medicine (Baltimore)*. 2016;95(41):e4656.
  24. Al Kazzi ES, Lau B, Li T, Schneider EB, Makary MA, Hutfless S. Differences in the prevalence of obesity, smoking and alcohol in the United States Nationwide Inpatient Sample and the Behavioral Risk Factor Surveillance System. *PLoS One*. 2015;10(11):e0140165.
  25. Bozic KJ, Bashyal RK, Anthony SG, Chiu V, Shulman B, Rubash HE. Is administratively coded comorbidity and complication data in total joint arthroplasty valid? *Clin Orthop Relat Res*. 2013;471(1):201-5.