

and despite the widespread use of THA, it is unknown whether the rate of complications after THA in patients with SLE is higher than in patients without SLE. Corticosteroids and other immunosuppressant medications have also been reported to increase the risk of postoperative infections⁵. Increased morbidity and mortality following total hip replacement have been reported in patients with SLE^{6,7}. However, these historical rates may not reflect improved SLE treatment or modern anesthetic and surgical techniques.

The purposes of our study were to determine whether patients with SLE have the same number of adverse events (AE) in the first 6 months after primary THA surgery compared with patients with osteoarthritis (OA), and to identify whether medication use or comorbidities contribute to the number of complications.

MATERIALS AND METHODS

Ours was a retrospective case-control study of patients with SLE aged ≥ 18 who underwent primary THA at a single high-volume institution from 2007 to 2011. Patients with SLE were identified by the International Classification of Diseases, 9th ed (ICD-9) code 710.0 and were validated by chart review using previously published algorithms^{8,9}. Each validated patient with SLE had ICD-9 codes for SLE on 2 or more visits, 3 of 11 American College of Rheumatology criteria for SLE, diagnosis of SLE by a rheumatologist, and/or use of immunosuppressant medications other than prednisone documented in their chart. Patients with ICD-9 codes for any other rheumatic disease, those undergoing revision hip replacement, those with an acute fracture necessitating hip replacement, and those who did not consent or enroll in the THA registry were excluded. Patients with 2 consecutive unilateral THA only contributed data from the first procedure. Patients selected as controls had operations listed within the same institutional registry and underwent primary THA between 2007 and 2011. For each SLE THA case, 2 OA controls were identified from the registry and matched to each SLE THA on age, sex, unilateral versus bilateral surgery (both hips replaced during the same operation), year of surgery, and THA versus hip resurfacing.

The hospital's Institutional Review Board approved this research study.

Adverse events. AE were identified from 3 sources: 6-month postoperative patient self-report questionnaires collected as part of the joint replacement institutional registry, inpatient hospital records, and surgeons' outpatient office charts. AE were categorized as either major or minor. Major AE included PE, deep vein thrombosis (DVT), deep surgical site infection, a major bleeding event, pneumonia, stroke, myocardial infarction (MI), fracture, dislocation, reoperation, acute renal failure (defined using the Responder Index for Lupus Erythematosus criteria), and death¹⁰. Minor AE included minor bleeding, superficial infection, ecchymosis, transient neuropathy, incision site drainage, poor wound healing, erythema, and atelectasis. Length of followup for all patients was recorded from surgeons' office charts. Charlson-Deyo comorbidity scores were calculated preoperatively excluding the diagnosis of SLE. Preoperative and 6-month postoperative Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores for pain and function, scored from 1 to 100 with 1 being the worst pain or function, were recorded for patients in both groups in the joint registry database.

Statistical analysis. Descriptive statistics and inferential statistics comparing SLE cases with OA controls were performed. Continuous variables were compared between groups using the 2-sample Student t test, and categorical variables were compared using the chi-square or Fisher's exact test when appropriate. Multiple logistic regressions were performed to identify variables independently associated with developing short-term AE. The multiple logistic regression included variables found to be significant in the

univariate analysis. All tests were 2-sided with significance level of 0.05, and all analyses were conducted using SAS for Windows 9.2 (SAS Institute Inc.).

RESULTS

Fifty-eight patients with SLE met the inclusion criteria and were matched with 116 OA controls. All cases and controls had hospital records and office charts available. Of the patients, 53% of the SLE group and 84% of the OA group returned the registry 6-month self-report questionnaires. The duration of recorded postoperative followup available for review did not differ between groups (23.24 weeks SLE vs 23.39 weeks OA, $p = 0.89$).

Mean age was 52 years for SLE versus 50 years for OA ($p = 0.57$). Of the patients, 89.6% were women in the SLE group versus 90.5% in the OA group. For both groups, 5.2% of patients underwent hip resurfacing. Of the patients, 94.8% of the SLE group and 97.1% of the OA group had unilateral procedures. WOMAC pain scores were significantly statistically but not clinically worse in the SLE group (40.5 vs 48.4, $p = 0.04$). WOMAC function scores were also worse in the SLE group (39.6 vs 46.9, $p = 0.06$), though this was not statistically significant (Table 1). Charlson-Deyo Comorbidity Index scores showed that patients with SLE had significantly more comorbidities than OA: 47.4% of SLE had scores ≥ 1 vs 13.1% of OA ($p < 0.0001$).

Preoperative immunosuppressant use was far more common in the SLE group than in the OA group (Table 2). Of the patients, 57% of the SLE group was taking hydroxychloroquine versus 0% of the OA group. Corticosteroid use and perioperative "stress-dose" steroids were more common in SLE than OA (44.8% vs 0.9%, $p < 0.0001$, and 53.4% vs 1.7%, $p < 0.0001$, respectively). Only 21% of the SLE group took no immunosuppressant medication versus 98% of the OA group.

Combined spinal/epidural anesthesia was more common in patients with OA (98.3% OA vs 82.5% SLE, $p < 0.0001$), while more patients with SLE received either spinal alone

Table 1. Preoperative patient characteristics. Values are mean (SD) or % unless otherwise specified.

Characteristics	SLE, n = 58	OA, n = 116	p
Age, yrs	52.0 (2.3)	50.3 (1.8)	0.57
Female	89.6	90.5	0.83
Hip resurfacing	5.2	5.2	0.17
Unilateral replacement	94.8	97.1	0.42
BMI	27.2 (0.8)	27.0 (0.6)	0.88
Diabetes	3.5	0.9	0.25
WOMAC pain, 1–100,			
1 is worst pain	40.5 (18.4)	48.4 (20.6)	0.04
WOMAC function, 1–100,			
1 is worst function	39.6 (19.8)	46.9 (20.0)	0.06

Significant data are in bold face. SLE: systemic lupus erythematosus; OA: osteoarthritis; BMI: body mass index; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.

Table 2. Preoperative immunosuppressant use. Values are %.

Medications	SLE	OA
Hydroxychloroquine	56.9	0.0
Prednisone	44.8	0.9
Methotrexate	17.2	0.0
Mycophenolate mofetil	17.2	0.0
Azathioprine	8.6	0.0
IV immunoglobulin	1.7	0.0
Cyclophosphamide	0.0	0.0
Perioperative "stress-dose" steroids	53.4	1.7
No immunosuppressant medication	20.6	98.3

SLE: systemic lupus erythematosus; OA: osteoarthritis; IV: intravenous.

(14% SLE vs 0.9% OA, $p < 0.0001$) or general anesthesia (3.5% vs 0.9%, $p < 0.001$). More patients with OA received aspirin for DVT prophylaxis in the first 6 weeks following discharge (74.1% vs 34.5%, $p < 0.0001$), while more patients with SLE received enoxaparin (13.8% vs 0%, $p < 0.0001$) or warfarin (65.5% vs 25.9%, $p < 0.0001$). There was no difference in the operative time between the groups (86.9 min SLE vs 84.4 min OA, $p = 0.65$). Length of stay was significantly longer in the SLE group (6.0 days vs 4.7 days, $p = 0.0008$).

Six months after surgery, patients with SLE had significantly more falls (10.3% vs 1.7%, $p = 0.017$), acute renal disease (8.6% vs 0%, $p = 0.004$), superficial wound infections (6.9% vs 0.9%, $p = 0.043$), and additional surgeries, including revision of prostheses and repair of fracture resulting from postoperative fall (6.9% vs 0%, $p = 0.012$; Table 3). No MI, PE, pneumonia, neuropathy, deep infection, or death were recorded within 6 months in either group. Overall, 50% of those with SLE had any AE versus 19.8% of those with OA ($p < 0.0001$), and 34.5% of patients with SLE had a major

Table 3. Adverse events. Values are n (%) unless otherwise specified.

Adverse Events	SLE	OA	p
Major events			
Acute renal insufficiency	5 (8.6)	0 (0)	0.004
Arrhythmia	1 (1.7)	0 (0)	0.33
Deep vein thrombosis	3 (5.2)	0 (0)	0.036
Falls	6 (10.3)	2 (1.7)	0.017
Postoperative fracture	2 (3.4)	0 (0)	0.11
Dislocation	5 (8.6)	3 (2.6)	0.12
Additional surgery*	4 (6.9)	0 (0)	0.012
Minor events			
Superficial surgical site infection	4 (6.9)	1 (0.9)	0.04
Excessive surgical site drainage	3 (5.2)	1 (0.9)	0.09
Surgical site ecchymosis	0 (0)	2 (1.7)	0.55
Surgical site erythema	3 (5.2)	2 (1.7)	0.33
Spinal headache	2 (3.4)	0 (0)	0.11
Delayed wound healing	0 (0)	2 (1.7)	0.55

* Additional surgeries include 3 revisions and 1 repair of fracture resulting from postoperative fall. Significant data are in bold face. SLE: systemic lupus erythematosus; OA: osteoarthritis.

AE versus 10.3% of patients with OA ($p = 0.0001$). Length of followup did not differ between groups (23.24 weeks SLE vs 23.39 weeks OA, $p = 0.89$).

In a multiple logistic regression analysis controlling for comorbidities and type of anesthesia, SLE was associated with an increased risk of total AE compared with OA (OR 3.77, 95% CI 1.74–8.16), as well an increased risk of minor AE (OR 3.54, 95% CI 1.41–8.91) and major AE (OR 3.70, 95% CI 1.52–8.89; Table 4A, Table 4B, and Table 4C). Interestingly, comorbidity scores with SLE excluded were not significantly associated with the risk of AE. Among patients with SLE, there was no increased risk of AE in those taking preoperative corticosteroids, those receiving periop-

Table 4A. Multivariate logistic regression*. Any adverse event.

Variables	OR	95% CI	p
SLE vs OA	3.77	1.74–8.16	0.0008
Charlson-Deyo Comorbidity Index**, ≥ 1 vs 0	1.69	0.76–3.76	0.20
Epidural block vs no	1.29	0.35–4.73	0.71

* All models control for disease (SLE vs OA), comorbidities, and type of anesthesia. ** The Charlson-Deyo Comorbidity Index was calculated by excluding SLE. Significant data are in bold face. SLE: systemic lupus erythematosus; OA: osteoarthritis.

Table 4B. Multivariate logistic regression*. Any major adverse event: DVT, PE, fall, fracture, additional surgery, acute renal disease, cardiac event, MI, dysrhythmia, deep surgical site infection, bleeding event requiring transfusion, pneumonia, neuropathy, and death.

Variables	OR	95% CI	p
SLE vs OA	3.70	1.52–8.89	0.004
Charlson-Deyo Comorbidity Index**, ≥ 1 vs 0	1.82	0.75–4.41	0.19
Epidural block vs no	0.87	0.22–3.35	0.84

* All models control for disease (SLE vs OA), comorbidities, and type of anesthesia. ** The Charlson-Deyo Comorbidity Index was calculated by excluding SLE. Significant data are in bold face. SLE: systemic lupus erythematosus; OA: osteoarthritis; DVT: deep vein thrombosis; PE: pulmonary embolus; MI: myocardial infarction.

Table 4C. Multivariate logistic regression*. Any minor adverse event: superficial infection, ecchymosis, erythema, incision site drainage, spinal headache, and poor wound healing.

Variables	OR	95% CI	p
SLE vs OA	3.54	1.41–8.91	0.007
Charlson-Deyo Comorbidity Index**, ≥ 1 vs 0	1.19	0.46–3.12	0.72
Epidural block vs no	1.91	0.37–9.86	0.44

* All models control for disease (SLE vs OA), comorbidities, and type of anesthesia. ** The Charlson-Deyo Comorbidity Index was calculated by excluding SLE. Significant data are in bold face. SLE: systemic lupus erythematosus; OA: osteoarthritis.

erative stress-dose steroids, or those taking any immunosuppressant medication.

DISCUSSION

Our study demonstrates that, despite improvements in SLE treatment and the use of modern anesthesia and surgical techniques, patients with SLE continue to be at high risk for complications following THA. In our cohort, patients with SLE had significantly higher rates of minor, major, and all AE when compared with matched OA controls, even after controlling for anesthesia type and non-SLE comorbidities. Rates of superficial surgical site infection, falls, acute renal insufficiency, and additional surgery were significantly higher than in patients with OA. In addition, the mean length of stay in the hospital was significantly longer in the SLE group. Despite prior studies indicating that immunosuppressant medications and corticosteroids in particular increase the risk of postoperative complications, in our cohort of patients with SLE there was no significant association between immunosuppressant medication used, if any, and the risk of postoperative infections or total AE.

While type of DVT prophylaxis differed between the SLE and OA groups as a whole, this difference did not explain the disparity in complication rates. Of the 2 SLE cases with DVT, 1 was taking acetylsalicylic acid (ASA) for DVT prophylaxis and 1 was taking warfarin. All of the 5 patients who had increased wound drainage while in the hospital (3 SLE cases and 2 OA controls) were receiving ASA and warfarin. Of the 4 SLE cases with superficial wound infection, all developed the complication while in the hospital. At the time the infection developed, 2 were taking warfarin alone, 1 was taking ASA alone, and 1 was taking enoxaparin and warfarin. The 1 OA control with a superficial wound infection developed the infection after discharge and was taking ASA for DVT prophylaxis.

There is little literature on the rate and timing of superficial wound and prosthetic joint infection in patients with SLE. One early case series of patients with SLE undergoing THA reported a superficial wound infection rate of 16% (5/31 patients) and a prosthetic joint infection rate of 3% (1/31 patients), but did not give information on timing after surgery⁶. A systematic review of outcomes in SLE THA showed an overall superficial wound infection rate of 3.3% across 9 study cohorts, but also did not report timing after surgery¹¹. However, in a cohort analysis of patients with and without rheumatoid arthritis (RA) who developed prosthetic joint infection after undergoing total knee and hip arthroplasty, the RA group presented sooner following surgery compared with the control group (median joint age 72 days vs 128 days, $p = 0.001$), suggesting that most cases of prosthetic joint infection in a similarly immunosuppressed population would have been identified with a 6-month followup¹². Further, because prosthetic joint infections are

an extremely rare complication, we would not have expected to see any in our relatively small cohort.

It is unclear why the SLE cohort experienced a higher rate of falls than the OA controls. The literature on falls after THA identifies several risk factors for falls, including polypharmacy, which may be applicable to our patient population because the majority of the SLE group were taking immunosuppressant medications compared with < 1% of the patients with OA¹³. Patients with SLE have also been shown to have an increased incidence of Vitamin D deficiency, which has been associated with higher rates of falls¹⁴. Finally, functional status and strength are also well-known protective factors against falls, including in postoperative total joint arthroplasty patients and in those with rheumatic disease^{15,16}. Patients with SLE may be weaker than patients with OA because of their underlying disease or treatment with corticosteroids, thus putting them at higher risk of falls. It is unclear to what extent each of these factors contributes to the increased rate of falls after THA, and further research is needed to better understand the causes of falls in the SLE population.

Limitations of our study include that it was underpowered to find differences in very rare events such as death. Our study was performed at a single high-volume center performing over 4300 total hip replacements per year; therefore the results may not be generalizable because most hip replacements are performed at lower-volume centers¹⁷. Since our study was retrospective, AE were not systematically looked for, so bias in ascertainment might have been introduced. We also did not have information regarding the serologies, antiphospholipid syndrome status, or disease activity of patients with SLE, which may be useful in identifying higher risk patients. Moreover, as many of our surgical patients receive their rheumatology care elsewhere, our validation methodology was limited by our lack of specific SLE data in patients' records. However, the use of ICD-9 codes on multiple visits, specialist diagnosis, and the use of specific therapy have all been shown to improve diagnostic specificity and would decrease the risk of bias introduced through misclassification^{8,9}. The 6-month self-report surveys from patients with SLE were returned at a lower rate than those from the OA control group. Patients with greater preoperative disease severity and those with poorer surgical outcomes have been shown to have lower response rates to surveys^{18,19}, introducing a possible source of bias when comparing complication rates in groups with differing illness severity. However, in addition to the patient self-reported surveys, hospital charts and surgeon's outpatient office charts from postoperative appointments were reviewed for complications. Hospital and office charts were available for all patients, and the duration of followup visits was not different between patients with SLE and patients with OA, making it less likely that complications were missed because of the disparity in survey completion rates.

Strengths of our work included ours being the largest study of AE in a validated sample of patients with SLE undergoing total hip replacement, to our knowledge. Our study used contemporary data, with all procedures performed between 2007 and 2011. Access to hospital and outpatient records, as well as self-reported patient questionnaires, allowed for more sensitive identification of AE than previous studies based on ICD-9 codes alone.

We found that patients with SLE have higher rates of complications following total hip replacement compared with patients with OA, even when controlling for comorbidities and type of anesthesia used. AE in patients with SLE were not significantly associated with immunosuppressant medication use in our cohort. Despite the improvements in disease management, patients with SLE undergoing total hip replacement should be recognized as a high-risk population. Further research is needed to better understand the causes of increased postoperative risk in patients with SLE.

REFERENCES

1. Mourão AF, Amaral M, Caetano-Lopes J, Isenberg D. An analysis of joint replacement in patients with systemic lupus erythematosus. *Lupus* 2009;18:1298-302.
2. Trager J, Ward MM. Mortality and causes of death in systemic lupus erythematosus. *Curr Opin Rheumatol* 2001;13:345-51.
3. 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;41:867-74.
4. Lin JA, Liao CC, Lee YJ, Wu CH, Huang WQ, Chen TL. Adverse outcomes after major surgery in patients with systemic lupus erythematosus: a nationwide population-based study. *Ann Rheum Dis* 2014;73:1646-51.
5. Kang I, Park SH. Infectious complications in SLE after immunosuppressive therapies. *Curr Opin Rheumatol* 2003;15:528-34.
6. Hanssen AD, Cabanela ME, Michet CJ Jr. Hip arthroplasty in patients with systemic lupus erythematosus. *J Bone Joint Surg Am* 1987;69:807-14.
7. Domsic RT, Lingala B, Krishnan E. Systemic lupus erythematosus, rheumatoid arthritis, and postarthroplasty mortality: a cross-sectional analysis from the nationwide inpatient sample. *J Rheumatol* 2010;37:1467-72.
8. Moores KG, Sathe NA. A systematic review of validated methods for identifying systemic lupus erythematosus (SLE) using administrative or claims data. *Vaccine* 2013;31 Suppl 10:K62-73.
9. Ng B, Aslam F, Petersen NJ, Yu HJ, Suarez-Almazor ME. Identification of rheumatoid arthritis patients using an administrative database: a Veterans Affairs study. *Arthritis Care Res* 2012;64:1490-6.
10. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P; Acute Dialysis Quality Initiative workgroup. Acute renal failure - definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. *Crit Care* 2004;8:R204-12.
11. Kennedy JW, Khan W. Total hip arthroplasty in systemic lupus erythematosus: a systematic review. *Int J Rheumatol* 2015;2015:475489.
12. Hsieh PH, Huang KC, Shih HN. Prosthetic joint infection in patients with rheumatoid arthritis: an outcome analysis compared with controls. *PLoS One* 2013;8:e71666.
13. Ikutomo H, Nagai K, Nakagawa N, Masuhara K. Falls in patients after total hip arthroplasty in Japan. *J Orthop Sci* 2015;20:663-8.
14. Lane NE. Vitamin D and systemic lupus erythematosus: bones, muscles, and joints. *Curr Rheumatol Rep* 2010;12:259-63.
15. Matsumoto H, Okuno M, Nakamura T, Yamamoto K, Osaki M, Hagino H. Incidence and risk factors for falling in patients after total knee arthroplasty compared to healthy elderly individuals. *Yonago Acta Med* 2014;57:137-45.
16. Marques WV, Cruz VA, Rego J, da Silva NA. [The influence of physical function on the risk of falls among adults with rheumatoid arthritis]. [Article in Portuguese] *Rev Bras Reumatol* 2014;54:404-8.
17. Manley M, Ong K, Lau E, Kurtz SM. Effect of volume on total hip arthroplasty revision rates in the United States Medicare population. *J Bone Joint Surg Am* 2008;90:2446-51.
18. Hutchings A, Grosse Frie K, Neuberger J, van der Meulen J, Black N. Late response to patient-reported outcome questionnaires after surgery was associated with worse outcome. *J Clin Epidemiol* 2013;66:218-25.
19. Hutchings A, Neuberger J, Grosse Frie K, Black N, van der Meulen J. Factors associated with non-response in routine use of patient reported outcome measures after elective surgery in England. *Health Qual Life Outcomes* 2012;10:34.