SYSTEMIC LUPUS ERYTHEMATOSUS IS A RISK FACTOR FOR COMPLICATIONS IN TOTAL JOINT ARTHROPLASTY

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ABSTRACT

Introduction: Systemic Lupus Erythematosus (SLE) has been associated with increased complications following hip and knee arthroplasty. The Purpose of this study was to determine the extent to which SLE is a risk factor in outcomes following total joint arthroplasty (TJA)

Methods: The nationwide inpatient sample was used to identify a cohort of 505,841 patients who had a total hip arthroplasty (THA) or total knee arthroplasty (TKA) between 2009-2011. Of these patients, 2,284 patients (0.45%) had been previously diagnosed with SLE. The impact of SLE on short-term TJA outcomes was determined using multivariate logistic regression. Differences in discharge destination and length of stay were also evaluated.

Results: SLE patients were more likely to have an all-cause medical complication, (OR 1.9, p<0.0001) and more likely to have an all-cause surgical complication (OR 1.3, p<0.0001). SLE patients were four times more likely to become septic in the post-operative period (OR 3.8, p<0.0487). SLE patients were more likely to have a genitourinary complication (OR 1.7, p<0.0001) and bleeding complications requiring transfusion (OR 2.1, p<0.0001). Patients with SLE also had an increased length of stay (0.38 days, p<0.0001) and increased probability of discharging to a facility (OR 2.1, p<0.0001).

Discussion: Patients with SLE had an increased rate of both medical and surgical all-cause complications. Patients were specifically found to be at higher risk for sepsis, genitourinary complications, and blood transfusions. Future risk adjustment models should include SLE as a contributor to medical and surgical complications in the post-operative period.

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INTRODUCTION

Systemic Lupus Erythematosus (SLE) is a complex autoimmune disease with wide variation in clinical manifestations and an incidence of 3.2-10.6 per 100,000 in the United States.[1–3] SLE manifestations include skin, joint, serological, hematological, immunological and renal disorders[4] with most common associated causes of death being organ failure, infection, and cardiovascular disease.[5] Ninety-five percent of patients develop arthritis[6] and 4.6-40% develop osteonecrosis during their lifetimes.[7–9] Prior to 1950, SLE had a five-year survival of 50%[10], but with modern medical treatment the 5-year survival rate now surpasses 95%.[11]

Traditionally, patients with SLE had arthroplasty for osteonecrosis, but as patients with SLE have increased lifespan and different medication regimens, many patients with SLE are having arthroplasty for osteoarthritis.[12] Arthroplasty rates in patients with SLE doubled from 1991 to 2005, and in 2005 osteoarthritis was the indication for arthroplasty in 61% of patients compared with osteonecrosis being the indication in 24% of patients.[13] Historically, SLE has been implicated as a risk factor for poor surgical outcomes including increased rates of postoperative mortality.[14–16] The literature is mixed, however, with multiple studies suggesting increased complications, adverse postoperative events and mortality in SLE patients,[17–20] while other studies have not found increased rates of complications.[21–23] These previous studies have been limited to small patient populations and frequently did not distinguish between other types of inflammatory arthropathies.

Therefore, the purpose of this study was to evaluate short-term complications of total hip and total knee arthroplasty in patients with a known diagnosis of SLE compared to a matched cohort of similar patients without SLE using a large inpatient database. We specifically investigated individual complications as well as composite medical complications and composite surgical complications utilizing the National Inpatient Sample (NIS) database. We further evaluated for potential dif-

Table I. Un-matched patient factors and demographic information

Variables	Controls	SLE	p-value
Number of surgeries	503,557	2,284	
Age, years, mean (sd)	65.73(10.94)	58.85(12.94)	<0.0001
Sex, %(N)			<0.0001
Male	39.53(198,715)	9.64(220)	
Female	60.47(303,947)	90.36(2,063)	
Race, %(N)			<0.0001
White	84.68(367,999)	68.70(1,385)	
Black	7.27(31,589)	21.83(440)	
Hispanic	4.47(19,419)	5.26(106)	
Other	3.58(15,579)	4.22(85)	
Corticosteroid, %(N)	0.72(3,612)	12.00(274)	<0.0001
Osteonecrosis of the hip, %(N)	2.93(14,769)	15.81(361)	<0.0001
Spasm of muscle, %(N)	0.18(888)	0.44(10)	0.0031
Gait abnormality, %(N)	0.58(2,928)	0.66(15)	0.6369
Contracture of joint, pelvic region and thigh, %(N)	0.14(726)	0.09(2)	0.7782
Hospital region, %(N)			<0.0001
South	35.60(179,277)	44.22(1,010)	
Northeast	18.16(91,427)	15.89(363)	
Midwest	26.36(132,746)	22.42(512)	
West	19.88(100,107)	17.47(399)	
Vitamin D deficiency, %(N)	0.88(4,410)	1.66(38)	<0.0001
Surgery Type, %(N)			<0.0001
THA	31.70(159,624)	36.56(835)	
TKA	68.30(343,933)	63.44(1,449)	
Charlson comorbidity index, mean(sd)	0.63(0.95)	1.61(0.91)	<0.0001

ferences in length of stay and facility discharge rates for patients with SLE.

MATERIALS AND METHODS

The Nationwide Inpatient Sample was utilized to identify a cohort of patients undergoing total joint arthroplasty (TJA) between January 1st, 2009 and December 31st, 2012, utilizing ICD-9 codes 81.51 and 81.54 for total hip arthroplasty and total knee arthroplasty respectively. SLE patients were identified using ICD-9 code 710.0. The NIS is part of a family of tools designed for the Healthcare Cost and Utilization Project (HCUP) and contains weighted data from more than 35-million hospitalizations nationally and is the largest public all-payer inpatient health care database in the United States. NIS data includes patient outcomes of procedures performed including demographics, length of stay, complications, facility discharges among other measures. Patients were excluded from the study if they had an emergency procedure, fracture, revision procedure, surgery for infection, or surgery for fracture. Additionally, patients with other inflammatory conditions including rheumatoid arthritis, psoriatic arthritis, inflammatory bowel disease, juvenile idiopathic arthritis, and septic arthritis were excluded from the study. The current project was granted exemption by the institutional review board at our institution.

ICD-9 coding was utilized in the NIS to identify individual perioperative complications as well as combine complications grouped into medial or surgical complications. Surgical complications were comprised of: acute postoperative hemorrhagic anemia (285.1), Hematoma/seroma (998.11- 998.13, 729.92, 719.15, 719.16), wound infection (998.5x, 682.6, 682.9, 998.83, 890.0- 890.2, 894.0- 894.2), wound dehiscence (998.3x), mechanical

Table II. Logistic regression analysis of SLE-related perioperative complications (Un-matched cohort)

Variables	Odds ratio (95% Confidence interval)	P-value
Any complication	1.505(1.386,1.635)	<0.0001
Surgical complications	1.349(1.233,1.476)	<0.0001
Medical complications	1.664(1.521,1.820)	<0.0001
Individual Complications		
Acute postoperative hemorrhagic anemia	1.346(1.229,1.474)	<0.0001
Hematoma/seroma	1.420(0.932,2.163)	0.1025
Wound infection	0.849(0.352,2.045)	0.7152
Mechanical complication of implant	1.175(0.747,1.848)	0.4852
Periprosthetic infection	1.000(0.140,7.149)	1
Dislocation of prosthetic joint	1.480(0.368,5.949)	0.5806
Fever	1.555(1.244,1.946)	<0.0001
Altered mental status	1.898(0.983,3.662)	0.0561
Thrombocytopenia	1.796(1.419,2.274)	<0.0001
Central nervous system	0.551(0.077,3.923)	0.5517
Cardiac	1.316(0.837,2.069)	0.2345
Peripheral vascular	0.394(0.055,2.799)	0.3517
Gastrointestinal	0.374(0.121,1.161)	0.089
Genitourinary	1.565(1.322,1.853)	<0.0001
Sepsis	2.937(1.214,7.103)	0.0168
Pulmonary embolism	0.670(0.279,1.612)	0.3716
Deep venous thrombosis	1.659(0.939,2.932)	0.0814
Transfusion	1.658(1.498,1.836)	<0.0001

complication of implant (996.40, 996.41, 996.43- 996.49, 996.76- 996.79), periprosthetic infection (996.66, 996.67, 996.69), dislocation of prosthetic joint (996.42), peripheral nerve injury (956.0- 956.9), fall (E885, E886, E888). Medical complications included: Fever (780.60, 780.62), altered mental status (780.97), thrombocytopenia (287.4, 287.5), central nervous system (349.9x), cardiac (997.1), acute myocardial infarction (410), peripheral vascular (997.2), pulmonary insufficiency following surgery (518.51, 518.52, 518.53) pulmonary (997.3, 997.31, 997.32), pulmonary embolism (415.11, 415.13, 415.19), deep venous thrombosis (451.11, 451.19, 451.2, 451.81, 453.40-453.42), gastrointestinal (997.4), genitourinary (584.x , 599.0, 997.5), sepsis (995.91-2), postoperative shock (998.0), transfusion (procedure codes 99.03- 99.05, 99.07). Furthermore, discharge to home versus facility and length of stay calculated by date of admission and date of discharge. SLE patients undergoing TJA were compared with matched controls.

Statistical Analysis

Medical complications, surgical complications, and individual complications were first compared to the overall cohort of patients not having SLE through linear regression analysis. To control for demographic differences in the SLE patient population, a 3:1 propensity score matched cohort was then created to prevent confounding based on demographic differences. Logistic regression was then utilized to determine the odds ratio of having a medical complication, surgical complication, any complication, or an individual complication such as sepsis or blood transfusion. Length of stay differences for SLE patients compared to non-SLE patients was determined using the paired t-test.

RESULTS

After application of our exclusion criteria, 2,284 patients with SLE and 503,557 patients without (controls) totaling 505,841 patients were identified as undergoing TJA during our study period. The prevalence of SLE in the cohort was 0.45%. There were 160,459 THAs (835 SLE) and 345,382 TKAs (1,449 SLE) performed. Average age, sex, and ethnic majority for SLE patients were 58.9 years, 90% female, and 69% Caucasian. Patients with SLE had higher percentages of both steroid use and diagnosis of osteonecrosis of the hip compared to non-SLE patients. A complete list of demographics is provided in Table 1. Patients with SLE were also noted to have higher

Table III. Length of stay and discharge destination

Variable: LOS (Length of stay in days)				
	Number (n)	**Mean (days)**	**Std Dev**	**P-value**
Non-SLE	503,556	3.22	1.54	
SLE	2,284	3.5	1.62	p<0.001
Discharge Destination	**Odds ratio (95% Confidence interval)**	**P-value**		
Not home vs. Home	1.219(1.104,1.346)	<0.0001		

Table IV. Matched cohort patient factors and demographic information

	3:1 Matched Cohort		
Variables	**Controls**	**SLE**	**P-value**
Number of surgeries	6,852	2,284	
Age, years, mean(sd)	65.41(11.09)	58.85(12.94)	<0.0001
Sex, %(N)			<0.0001
Male	39.78(2696)	9.64(220)	
Female	60.22(4082)	90.36(2,063)	
Race, %(N)			<0.0001
White	82.96(667)	68.70(1,385)	
Black	8.71(70)	21.83(440)	
Hispanic	4.48(36)	5.26(106)	
Other	3.86(31)	4.22(85)	
Corticosteroid, %(N)	0.73(50)	12.00(274)	<0.0001
Osteonecrosis of the hip, %(N)	2.61(179)	15.81(361)	<0.0001
Spasm of muscle, %(N)	0.20(14)	0.44(10)	0.059
Gait abnormality, %(N)	0.35(24)	0.66(15)	0.0517
Contracture of joint, pelvic region and thigh, %(N)	0.15(10)	0.09(2)	0.7417
Hospital region, %(N)			<0.0001
South	20.94(1435)	44.22(1,010)	
Northeast	3.58(245)	15.89(363)	
Midwest	62.27(4267)	22.42(512)	
West	13.21(905)	17.47(399)	
Vitamin D deficiency, %(N)	1.50(103)	1.66(38)	0.5899
Surgery Type, %(N)			<0.0001
THA	30.75(2107)	36.56(835)	
TKA	69.25(4745)	63.44(1,449)	
Charlson comorbidity index, mean(sd)	0.62(0.95)	1.61(0.91)	<0.0001

proportion of patients undergoing total hip arthroplasty (THA) as compared to non-SLE patients (36.6% vs 31.7%, p<0.0001). Prior to matching, SLE patients were 1.5 times more likely to have any complication (OR 1.5, p<0001), 1.7 times more likely to have a medical complication (OR 1.7, p<0.001) and 1.3 times more likely to have a surgical complication (OR 1.3, p<0.0001). Specifically, SLE was associated with a nearly three-fold increase in sepsis (CI 1.214-7.103, p<0.017), and significant increased odds of thrombocytopenia, transfusion, genitourinary complications, fever and pulmonary insufficiency (Table II). SLE patients also had a 0.3 day increased length of stay as well as increased rate of discharge to a care facility with an OR of 1.2 (Table III).

After 3:1 matching of Non-SLE to SLE patients, demographic data including age, gender, and race distributions remained relatively the same when comparing to un-matched data (Table IV). Corticosteroid use and osteonecrosis was similarly unchanged (Table IV). In the matched cohort, SLE patients were 1.5 time more likely to have any complication (OR 1.5, p<0.0001), 1.3 times more likely to have a surgical complication, (OR 1.3, p<0.0001) and 1.9 times more likely to have a medical complication (OR 1.9, p<0.0001). When looking at specific complications, SLE patients were 1.3 times more likely to have acute postoperative anemia (OR 1.3, p<0.0001), 1.6 times more likely to have fever (OR 1.6, p=0.0008), 3 times more likely to have altered mental status (OR 3.0, p=0.0196), 1.4 times more likely to have thrombocytopenia (OR 1.4, p=0.023), 1.7 times more likely to have genitourinary complications (OR 1.7, p<0.0001), 4 times more likely to have sepsis (OR 3.8, p=0.0487) and 2 times more likely to receive a transfusion (OR 2.1, p<0.0001) (Table V). Additionally, SLE patients were twice as likely to discharge to a facility than non-SLE patients (OR 2.1, p<0.0001) (Table VI).

TABLE V. Logistic regression analysis of SLE-related perioperative complications (Matched cohort)

	3:1 Matched Cohort	
Variables	**Odds ratio (95% Confidence interval)**	**P-value**
Any complication	1.476(1.340,1.627)	<0.0001
Surgical complications	1.273(1.146,1.414)	<0.0001
Medical complications	1.871(1.679,2.084)	<0.0001
Individual Complications		
Acute postoperative hemorrhagic anemia	1.249(1.123,1.390)	<0.0001
Hematoma/seroma	1.471(0.882,2.455)	0.1395
Wound infection	0.937(0.343,2.562)	0.8996
Mechanical complication of implant	1.634(0.933,2.862)	0.086
Periprosthetic infection	1.000(0.104,9.618)	1
Dislocation of prosthetic joint	3.002(0.423,21.322)	0.2718
Fever	1.600(1.215,2.106)	0.0008
Altered mental status	3.008(1.193,7.587)	0.0196
Thrombocytopenia	1.362(1.027,1.806)	0.032
Central nervous system	1.500(0.136,16.552)	0.7406
Cardiac	1.429(0.826,2.472)	0.2022
Peripheral vascular	0.333(0.042,2.630)	0.297
Gastrointestinal	0.309(0.094,1.017)	0.0533
Genitourinary	1.653(1.343,2.034)	<0.0001
Sepsis	3.756(1.008,13.999)	0.0487
Pulmonary embolism	0.651(0.247,1.715)	0.3856
Deep venous thrombosis	1.503(0.750,3.010)	0.2505
Transfusion	2.054(1.811,2.329)	<0.0001

DISCUSSION

The current study shows SLE patients undergoing TJA are at markedly increased risk for medical complications and surgical complications post-operatively. Musculoskeletal manifestations of SLE include high rates of arthritis and osteonecrosis. Given the increase in arthroplasty in SLE patients in recent years and improved disease survival in this patient population, it is imperative to understand the perioperative outcomes and complications associated and inherent to SLE surgical candidates.

Our results show an increase in overall postoperative complications (OR 1.5, p<0.001) in SLE patients. This in in agreement with previous literature which also showed increased rates of complications in SLE patients.[14,20,24,25] Elevated hematologic complications in SLE included increased rates of acute postoperative hemorrhagic anemia (OR 1.35, p<0.0001), thrombocytopenia (OR 1.8, p<0.0001) and blood transfusion (OR 1.7, p<0.0001). Aggressive blood preservation programs should be employed in this population. Our results are further corroborated by literature suggesting SLE has been implicated in platelet dysfunction and antibodies to coagulation factors.[4,26–28] With SLE patients vulnerable to both the inherent bleeding from major joint and SLE induced platelet dysfunction including antibodies against coagulation factors—it is no wonder SLE patients show increased odds of perioperative anemia, thrombocytopenia and transfusion requirements in our study. Therefore, surgeons should take care to limit bleeding in SLE patients.

SLE patients had a 4 times higher rate of sepsis compared to patients without SLE. Previous rheumatology studies on SLE patients have found that infectious etiology accounts for 37% of hospitalizations and one-third of deaths in SLE patients.[29–34] The most common reasons for hospitalization being pneumonia, urinary tract infections, and skin infections—while bacteremia and sepsis complicated by organ failure are leading causes of mortality.[35–39] Tektonidou et al. reported the risk of hospitalization for serious infections in SLE patients were 12-24

times higher than in the general population.[29] These high rates of postoperative infections are in stark contrast to expected rates of postoperative infection in primary hip and knee arthroplasty of 0.5-3%[40–43] and <1%[44] respectively.

Corticosteroid use, however, continues to be a major confounder in the literature. Unfortunately, the risk of complications due to corticosteroids alone is nearly impossible to determine, and the question remains, "are complications secondary to steroids alone or to the underlying condition?" The literature is mixed regarding corticosteroid use in SLE patients and postoperative complications. Migliaresi et al, and Fein et al. concluded ON and adverse events were not related to steroid use.[21,45] Furthermore, Migliaresi et al. suggest complications are dose dependent and some doses may be protective.[45] On the contrary, multiple studies point to corticosteroid use as a major risk factor of ON and complications in SLE patients.[46–50] The current study showed the proportion of SLE patients on corticosteroids was significantly greater than non-SLE patients (12% vs 0.72%, $p<0.0001$).

There are several limitations of this study inherent to the retrospective study design and database utilization. There is significant heterogeneity of the hospitals and surgeon factors included in the NIS database. Furthermore, the NIS database only accounts for data collected from the surgical procedure date until discharge—thus relevant to the immediate and short-term postoperative periods only. Therefore, it is likely that the findings in this study underestimate the postoperative complications on a global level. Lastly, it is not feasible to control for all patient variables leaving the study vulnerable to confounding, however, the large sample size, patient matching, and multivariate analyses all contribute to a reduction in the confounding effects.

Overall, SLE patients undergoing TJA have increased rates of early postoperative surgical and medical complications. SLE patients are particularly vulnerable to postoperative anemia, thrombocytopenia, transfusion, genitourinary complications, and sepsis. SLE were also found to have longer lengths of stay and higher rates of discharge to a facility. As SLE patients continue to become a growing part of the total joint arthroplasty population, it is important to optimize medical and surgical risk factors in SLE patients to decrease the risk of complications in this susceptible patient population.

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