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Current Perspectives on Arthroplasty in Systemic Lupus Erythematosus: Rates, Outcomes, and Adverse Events

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Abstract Systemic lupus erythematosus (SLE) is a chronic debilitating condition with significant impact on the musculoskeletal system. Arthroplasty may be indicated for damage related to active lupus or its treatment. As therapies for SLE have advanced, morbidity and mortality have declined, while the rate of joint replacement has increased. The age of SLE patients undergoing arthroplasty is increasing, and the indication for surgery is evolving—while avascular necrosis was previously the predominant indication for arthroplasty, osteoarthritis now accounts for a larger proportion of surgeries. Pain and functional outcomes of arthroplasty in SLE patients are comparable to those of the general population with osteoarthritis, but lupus remains an independent risk factor for post-hip arthroplasty complications and mortality. Further research is needed to characterize the impact of lupus disease activity and severity on arthroplasty outcomes.

Keywords Systemic lupus erythematosus · Arthroplasty · Joint replacement · Outcomes · Epidemiology

Introduction

Systemic lupus erythematosus (SLE) is an inflammatory autoimmune disorder that affects multiple organ systems but most commonly involves the musculoskeletal system. Arthroplasty is often a therapeutic consideration in SLE for joint damage related to active disease and its treatment. The rates, outcomes, and adverse events associated with arthroplasty in SLE will be discussed in this article.

Musculoskeletal Manifestations of SLE

Arthritis and arthralgias are the most frequent initial manifestations of SLE and occur in more than 90 % of patients over the course of their illness [1, 2]. Unlike rheumatoid arthritis, joint involvement in active SLE is typically non-erosive and non-destructive, although erosions can be identified on MRI that are not seen on plain radiographs [3]. Jaccoud's arthropathy, a reducible periarthritis characterized by ligamentous laxity and tenosynovitis, is a classic feature [4]. While the inflammatory arthritis associated with lupus is typically less destructive than the arthritis seen in rheumatoid arthritis, lupus patients may suffer from significant musculoskeletal damage, including osteoarthritis, avascular necrosis (AVN), osteoporosis, and vertebral fractures, which are debilitating complications of ongoing disease activity and treatment with glucocorticoids. Musculoskeletal damage is the most frequent long-term complication of SLE, with longitudinal cohorts reporting an incidence of 24 to 55 % over 10 to 15 years [2, 5]; the prevalence of AVN in SLE patients ranges from 4 to 30 % [6], and their risk of fracture is five times that of the general population [7]. Risk factors for fracture in patients with SLE include post-menopausal status, glucocorticoid use, duration of disease, and chronic anticoagulant and antiepileptic use [8]. Glucocorticoid therapy is the most significant risk factor for AVN, and is associated with disease activity and severity [9, 10]. Arthroplasty is the definitive treatment for AVN of the

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hip, knee, or shoulder [11] and is also frequently indicated for the management of fractures, which often involve the hip.

Rates of Arthroplasty in SLE

Given the high burden of AVN and fractures and improved mortality for patients with SLE, arthroplasty in this population is not unusual, although few studies have characterized the causes and frequency of arthroplasty in SLE (Table 1). Mourao et al. studied 500 SLE patients, in which 94 % suffered from arthritis, and found that 19 (3.8 %) underwent at least one total joint replacement over the 30 years in which data was collected [12]. In these 19 SLE patients, 46 joints were replaced, with hip (43.5 %) and knee (32.6 %) replacements most common. Several patients had elbows and shoulders replaced. Notably, AVN and rheumatoid arthritis overlap syndrome were the conditions most commonly associated with joint replacement, with 10 patients suffering from AVN and 11 with SLE/rheumatoid arthritis overlap syndrome and its characteristic erosive arthritis. Given the small number of cases in the case series, statistical significance for these associations was not achieved.

Two subsequent larger studies examined the rates and indications for arthroplasty in SLE. Mukherjee et al. conducted a case-control study utilizing the UK General Practice Research Database to examine the odds of having a hip or knee arthroplasty in patients with SLE versus those without [13•]. After excluding all patients with inflammatory arthritis and connective tissue diseases other than SLE, cases of total hip arthroplasty (THA) and total knee arthroplasty (TKA) were matched for age, gender, and location. The study found that SLE patients were younger at the time of joint replacement than patients with non-inflammatory arthritis (65.7 vs. 69.5 years for hips and 66.3 vs. 70.4 years for knees) and that the odds of having a THA or TKA are greater in SLE than in non-inflammatory conditions (odds ratio (OR) 1.43, 95 % confidence interval (CI) 1.13–1.81 for THA and OR 2.54, 95 % CI 1.94–3.33 for TKA). Odds ratios were recalculated after adjusting for risk factors for AVN (prior diagnosis of antiphospholipid syndrome, alcohol consumption, and previous use of steroids, but not disease activity) and the increased odds of THA disappeared, while the odds of TKA remained significantly higher (OR 1.91, 95 % CI 1.41–2.58). From this, the authors speculated that AVN may more frequently be an indication for THA, but not for TKA, findings that are confirmed by Mertelsmann-Voss et al. [14••].

Table 1 Leading causes of arthroplasty in SLE patients

Cause of arthroplasty	Reference
Osteoarthritis	[14]
Avascular necrosis	[12, 14]
Fracture	[14]
Erosive arthritis/rheumatoid arthritis overlap	[12]

Mertelsmann-Voss et al. used data from administrative discharge databases from 10 states in the USA to examine population-based SLE arthroplasty rates as compared to non-inflammatory condition rates from 1991 to 2005 [14••]. The study found that rates of arthroplasty nearly doubled in both SLE (0.17 per 100,000 general population to 0.38 per 100,000) and non-inflammatory disease (124.5 per 100,000 to 247.5 per 100,000) over that time period. While age at the time of arthroplasty for patients with SLE was less than in non-inflammatory conditions (54.0 vs. 70.5 years), from 1991 to 2005 the mean age at arthroplasty increased in SLE while decreasing in non-inflammatory conditions. The proportion of SLE TKAs increased from 16 % in 1991 to 48 % in 2005, while the proportion of SLE THAs decreased from 66 to 40 %. A similar but less dramatic trend was seen in non-inflammatory arthroplasties with TKAs increasing from 39 to 54 % and THAs decreasing from 34 to 30 % over the same time frame. The indication for arthroplasty also shifted significantly in the SLE cases: in 1991, AVN accounted for 53 % of cases while osteoarthritis was the reason for 23 % of cases; by 2005, the relationship had reversed with AVN accounting for 24 % of cases and osteoarthritis explaining 61 % of cases. Fracture did not significantly change as an indication for arthroplasty over the years of the study. Of note, unlike Mourao et al., this study excluded arthroplasty cases that listed SLE and rheumatoid and juvenile idiopathic arthritis as comorbid conditions. As a result, erosive or inflammatory arthritis was not an indication for arthroplasty.

The authors hypothesized that advances in the treatment of SLE might explain the relative increase in osteoarthritis and decline of AVN as indications for arthroplasty, as well as the older age of SLE patients at arthroplasty. This hypothesis is supported by an increase in 5-year survival in SLE from 50 % in the 1950s to 95 % in 2000 [15]. Further, studies have shown that the risk of death from active lupus has decreased, while the risk of death from cardiovascular complications (a long-term sequela of lupus) has increased [16]. A longer lifespan in SLE may mean that patients are more likely to develop osteoarthritis requiring arthroplasty similar to their non-inflammatory counterparts.

In summary, SLE patients have greater odds of undergoing hip or knee replacement than patients with non-inflammatory conditions, and the rate of arthroplasty has doubled for both SLE patients and those with non-inflammatory arthritis. SLE patients are less likely to undergo surgery for AVN and more likely to undergo TKA for osteoarthritis than in 1991. Importantly, while SLE patients are still younger than those

undergoing arthroplasty for non-inflammatory conditions, the age is increasing for SLE patients and decreasing for those with non-inflammatory conditions.

Outcomes of Arthroplasty in SLE

SLE is a chronic systemic illness associated with poor health outcomes and health-related quality of life. Lupus patients have more medical comorbidities, including a significantly higher risk for cardiovascular disease and venous thromboembolism, and as a group have the sixth highest rate of all-cause hospital readmissions [17–19]. Adverse surgical outcomes are more common in lupus patients overall, with higher odds of 30-day post-operative acute renal failure, pneumonia, pulmonary embolism, stroke, infection, and mortality than in those without lupus [20••]. Few studies have systematically examined outcomes of arthroplasty in SLE. Given higher rates of medical comorbidities as well as worse baseline health-related quality of life and disability in SLE than in the general population, including those with other chronic conditions [21••, 22–24], it could be inferred that arthroplasty outcomes may be inferior, but existing data does not support this.

Surgeon- and Patient-Reported Outcomes

Most initial data on outcomes in SLE arthroplasty are derived from several case reports and case series of hip arthroplasties that lack standardized outcome measures, definitions of complications and adverse events, and comparator groups. Case series describe as few as 6 to as many as 33 THAs, often indicated for AVN of the hip, and document low complication and revision rates and good functional outcomes using surgeon-generated measures such as the Harris hip score or Mayo Clinic hip score [25–34]. A few of these studies examined patient-reported outcomes using the WOMAC and the SF-36, reporting improved post-surgical outcomes in these health-related quality of life measures, though not always to the level of the general population [33–36].

Several case-control studies have provided more information about hip and knee arthroplasty outcomes in SLE with overall favorable results (Tables 2 and 3). Zangger et al. examined the 2-year outcomes of 26 THAs in 19 patients with SLE and AVN compared to those of 29 THAs in 19 control patients, the majority with inflammatory arthritis, osteoarthritis, or developmental dysplasia of the hip [37]. They found no significant difference in surgeon-derived (average Harris hip score 86.7 in SLE vs. 81.9 in controls, scored 1–100, higher is better) or patient-reported outcome measures (average visual analogue scale score 2.00 in SLE vs. 1.97 in controls (maximum 10), average SF-36 sub-scale score of 63.4 in SLE vs. 60.5 in controls (maximum 100)).

A larger study conducted by Shah et al. included 54 SLE THAs and 45 SLE TKAs matched to osteoarthritis controls by age, gender, and presence of AVN [21]. Though baseline WOMAC pain and function scores were worse in SLE THAs than controls, scores 2 years post-operatively were no different. Notably, SF-36 physical component scores (PCS) were significantly lower in SLE patients than controls both pre- and post-operatively, perhaps reflecting general lupus disease burden. The authors found similar baseline and post-operative WOMAC scores in SLE patients and controls undergoing TKAs, but the SF-36 PCS was again significantly lower in SLE than controls. Multivariable regression showed that SLE was not an independent risk factor for poor pain or function following THA or TKA.

Issa et al. compared the outcomes of 34 TKAs in lupus patients with non-lupus patients matched 1:3 by age, gender, body mass index, surgical indication, and follow-up time [38•]. After an average of 6 years of follow-up, there was no difference in the post-operative surgeon-derived Knee Society Score or the SF-36 PCS or mental component score (MCS) between lupus patients and controls. Though the numbers in these studies are relatively small, they suggest there is no significant difference in pain or functional outcomes of arthroplasty between SLE patients and those with inflammatory or osteoarthritis.

Complications and Adverse Events

Multiple studies have looked at the rates of complications and adverse events in SLE arthroplasty, finding notable differences between THAs and TKAs. Domsic et al. evaluated inpatient mortality associated with arthroplasty in SLE using the Nationwide Inpatient Sample from 1993 to 2006 [22]. Lupus patients undergoing TKA or THA were compared to rheumatoid arthritis and general population patients, and the odds of inpatient mortality were determined after controlling for confounders (age, gender, comorbidities, surgical indication, and location of surgery). Compared to controls, SLE patients had a significantly higher risk of post-operative mortality with hip replacements (OR 4.0, 95 % CI 1.9–8.0), with the highest risk in non-elective hip surgery (OR 4.9, 95 % CI 2.2–10.9), but this was a non-significant trend following knee replacements (OR 1.2, 95 % CI 0.2–7.5). Notably, there was no increased mortality associated with rheumatoid arthritis compared to controls.

While case series have reported varied rates of complications and revisions [27, 30, 31, 39], the few case-control studies examining this question have generally found higher arthroplasty complication rates in patients with SLE undergoing hip, but not knee, replacements. Roberts et al. evaluated 6-month complication rates in 58 SLE THA cases matched 2:1 to osteoarthritis controls by age, gender, and year of surgery [40•]. After adjusting for comorbidities, lupus patients had

Table 2 Hip arthroplasty outcomes in systemic lupus erythematosus

Author and year	Study design	SLE arthroplasties (*n*)	Mean age (years)	Patient-reported outcomes	Complications (%, odds ratio (95 % CI))	Revision (%)	Mortality (odds ratio (95 % CI))	Conclusions
Shah et al. 2015 [21]	Case-control	54	54	WOMAC pain: pre- 42.5/post- 91.1 WOMAC function: pre- 38.8/ post- 86.4 SF-36 PCS: pre- 25.0/post- 40.5 SF-36 MCS: pre- 45.2/post- 51.4	NR	NR	NR	No difference in pain or functional outcomes compared to OA controls
Gonzalez-Contreras et al. 2015 [41]	Case-control	58	34	NR	36.2 %[b], 5.42 (2.39 to 12.30)	NR	NR	SLE independent risk factor for complications; higher immediate complications compared to RA and OA controls
Roberts et al. 2014 [40]	Case-control	58	52	NR	50 %[c], 3.77 (1.74 to 8.16)	5.2 %	NR	SLE independent risk factor for complications; higher 6-month complications compared to OA controls
Woo et al. 2014 [43]	Case-control	19	41	NR	0 %	0	NR	No difference in complications or revision rate over average 8-year follow-up compared to non-SLE avascular necrosis controls
Issa et al. 2013 [42]	Case-control	60	42	NR	1.7 %, 0.68 (0.06 to 7.65)	1.7 %	NR	No difference in complications or revision rate over 7-year follow-up compared to non-SLE avascular necrosis controls
Domsic et al. 2010 [22]	Case-control	3150	55[a]	NR	NR	NR	3.96 (1.95–8.04)	Higher mortality compared to non-SLE and RA controls
Zangger et al. 2000 [37]	Case-control	26	46	SF-36 PF post: 55.3 SF-36 MH post: 74.9	23.1 %, 8.4 (0.94 to 75.31)	3.8 %	NR	Trend towards higher complications over 4-year follow-up between SLE avascular necrosis THAs and controls[d]

WOMAC Western Ontario McMaster University Osteoarthritis Survey [35], *SF-36 PCS and MCS* Short Form-36 Physical Component Score and Mental Component Score [36], *SF-36 PF and MH* Short Form-36 Physical Function Score and Mental Health Score [36], *NR* not reported, *OA* osteoarthritis, *RA* rheumatoid arthritis

[a] Reflects mean age of combined hip and knee arthroplasty cohorts

[b] Complications = transfusion requirement, hematoma, thrombosis, infections, aseptic loosening, or prosthesis dislocation during initial hospitalization

[c] Complications = fall, acute renal disease, DVT, infection, or revision surgery within 6 months of surgery

[d] Controls = 18 inflammatory arthritis, 5 osteoarthritis, 4 developmental dysplasia of the hip, 1 avascular necrosis, and 1 post-traumatic arthritis

Table 3 Knee arthroplasty outcomes in systemic lupus erythematosus

Author and year	Study design	SLE arthroplasties (*n*)	Mean age (years)	Patient-reported outcomes	Complications (%, odds ratio (95 % CI))	Revision (%)	Mortality (odds ratio (95 % CI))	Conclusions
Shah et al. 2015 [21]	Case-control	45	62	WOMAC pain: pre- 42.6/post- 85.7 WOMAC function: pre- 42.1/post- 83.7 SF-36 PCS: pre- 27.3/post- 40.2 SF-36 MCS: pre- 48.1/post- 54.5	NR	NR	NR	No difference in pain or functional outcomes compared to OA controls
Issa et al. 2015 [38]	Case-control	34	53	SF-36 PCS: post- 47 SF-36 MCS: post- 51	8.8 % 1.90 (0.99–13)	8.8 %	NR	No difference in complications or patient-reported outcomes compared to non-SLE controls
Fein et al. 2015 [44]	Case-control	52	58	NR	37.7 %, 1.52 (0.70–3.76)	NR	NR	No difference in complications compared to OA controls
Domsic et al. 2010 [22]	Case-control	2435	55[a]	NR	NR	NR	1.21 (0.20–7.49)	No difference in mortality compared to non-SLE and RA controls
Mont et al. 1997 [39]	Case series	25	36[b]	NR	NR	56.0 %	NR	Lower rate of successful outcomes in SLE compared to non-SLE avascular necrosis cases

WOMAC Western Ontario McMaster University Osteoarthritis Survey [35], *SF-36 PCS and MCS* Short Form-36 Physical Component Score and Mental Component Score [36], *NR* not reported

[a] Reflects mean age of combined hip and knee arthroplasty cohorts

[b] Reflects mean age of cohort of 21 patients with steroid-associated avascular necrosis, 17 of whom had lupus

greater risk of adverse events (OR 3.77, 95 % CI 1.74–8.16) with 50 % suffering from falls, deep vein thrombosis, acute kidney injury, superficial wound infections, or revisions. González et al. conducted a similar case-control study matching 58 cases of SLE THA to controls with rheumatoid or osteoarthritis [41•]. They also found that lupus was an independent risk factor for immediate post-operative complications (hazard ratio 2.8, 95 % CI 1.2–6.8) with 36 % of SLE THA cases experiencing transfusion requirements, hematoma, thrombosis, infections, aseptic loosening, and prosthesis dislocation. Both studies found the SLE patients had a longer length of hospital stay. Zangger et al. also found a trend towards higher SLE complications over an average of 4 years of follow-up in their smaller case-control study of 26 SLE THAs for AVN compared to controls with mostly inflammatory and osteoarthritis (OR 8.40, 95 % CI 0.94–75.31) [37]. When compared to THAs performed for AVN of other etiologies, two case-control studies (with 60 and 19 SLE cases each) found no increase in complications in SLE THA cases [42, 43].

Two case-control studies examining outcomes of TKAs in SLE found no increase in complications compared to osteoarthritis controls. Fein et al. matched 52 SLE TKAs 1:2 with osteoarthritis controls by age, gender, and year of the procedure [44•]. There was no significant increased risk of adverse events in SLE patients compared to controls (OR 1.52, 95 % CI 0.70–3.76) with 38 % of SLE subjects suffering any complication over 6 months of follow-up. Similarly, Issa et al. matched 34 SLE TKAs 1:3 with non-SLE TKAs by age, gender, body mass index, year, and indication for the procedure and found no statistically significant difference in complications (OR 1.90, 95 % CI 0.99–13.0) over 6 months of follow-up [38•].

The similar outcomes of SLE TKAs to those in the general population may reflect the distinct population of SLE patients who undergo knee rather than hip replacement—that is, patients who are older, likely with better disease control, and increasingly undergoing knee arthroplasty for osteoarthritis rather than active inflammatory disease or AVN. Though AVN is declining as an indication for arthroplasty, it still accounts for a large percentage of the THAs represented in these studies (32 to 68 %) [21••, 42]. Avascular necrosis may be a marker of more severe lupus, or higher lupus disease activity, which may contribute to the increased post-operative mortality and complications observed in THAs.

Though none of the arthroplasty studies directly evaluate the impact of lupus disease activity and severity on outcomes, a study utilizing the Taiwan National Health Insurance Research Database provided data on adverse outcomes after any major surgery including orthopedic procedures for 4321 patients with SLE, and used SLE-related hospitalizations and SLE-related glucocorticoid injections as surrogates for disease activity and severity. This study demonstrated a significant increase in adverse events including sepsis, pulmonary embolism, and acute renal failure associated with SLE hospitalizations or glucocorticoid use prior to surgery in a dose-dependent fashion. The OR of developing acute renal failure after major surgery was 1.54 (95 % CI 0.93–2.56) in those with SLE treated as an outpatient, increased to an OR of 5.87 (95 % CI 3.76–9.17) for those with a lupus-related hospitalization within 24 months, and increased further for those with a hospitalization for SLE within 6 months of major surgery to 7.23 (95 % CI 4.52–11.6), with similar dose-dependent increases seen in the risk of pulmonary embolus, stroke, and septicemia [20••].

In summary, SLE patients have excellent pain and functional outcomes, as measured by both surgeon-derived and patient-reported instruments, that do not differ significantly from those of the general population undergoing hip and knee replacements. Additionally, they do not face higher complication rates after knee replacements, perhaps reflecting more similar indications for surgery (namely osteoarthritis, rather than active inflammatory disease). However, SLE patients face higher rates of adverse events, including revisions and post-operative mortality, following hip arthroplasty than their inflammatory arthritis and osteoarthritis counterparts.

Table 4 Take-home points

- •Arthroplasty rates in SLE patients are increasing.
- •Osteoarthritis has replaced avascular necrosis as the most common indication for arthroplasty in SLE patients.
- •Pain and functional outcomes in SLE patients undergoing arthroplasty are comparable to those of the general population.
- •SLE is an independent risk factor for post-hip arthroplasty complications and mortality.
- •Further studies are needed to characterize the impact of SLE disease activity and severity on adverse events and to identify perioperative risk reduction strategies.

Conclusions

As treatment and outcomes for patients with SLE have advanced, the need for arthroplasty and the reported complications associated with arthroplasty have also changed over time (Table 4). Lupus patients are generally younger at the time of arthroplasty than those with primary inflammatory arthritis or osteoarthritis, but age is increasing. The proportion of arthroplasties performed for AVN is declining, while those for osteoarthritis is rising. Outcomes of arthroplasty in lupus are overall excellent, with pain and functional measures at 2 years equivalent to those in the general population. Knee replacements are well tolerated, with complication rates in lupus patients comparable to those with primary osteoarthritis. Still, SLE confers an increased risk of death and complications following hip replacement, perhaps reflective of the greater

disease severity of those who require this procedure. Although there are no studies addressing perioperative risk reduction strategies specifically for patients with SLE undergoing arthroplasty, increased awareness of their high-risk status in particular in regard to venous thromboembolism and cardiovascular risk, combined with increased perioperative vigilance, may help mitigate the risks. Further studies are needed to characterize the impact of disease activity and severity on outcomes, particularly as the need for arthroplasty in SLE continues to increase with improving life expectancy.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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