International Orthopaedics (2018) 42:1485–1490
https://doi.org/10.1007/s00264-018-3871-5

ORIGINAL PAPER

Is osteonecrosis due to systemic lupus erythematosus associated with increased risk of complications following total hip arthroplasty?

Dennis Q. Chen[1] · Jourdan M. Cancienne[1] · Brian C. Werner[1] · Quanjun Cui[1]

Received: 22 January 2018 / Accepted: 27 February 2018 / Published online: 17 March 2018

Abstract

Purpose As the medical treatment of systemic lupus erythematosus (SLE) has evolved, the rate of total hip arthroplasty (THA) in SLE patients has increased, with osteonecrosis (ON) being the primary indication for arthroplasty in a quarter of cases. Comparative literature evaluating outcomes following THA for patients with SLE and ON versus patients with non-SLE-related ON or patients with osteoarthritis (OA) is limited. The goal of the present study was to investigate the current trend in SLE patients undergoing THA and compare complications following THA for ON with SLE, ON without SLE, and OA.

Methods The PearlDiver patient records database (www.pearldiverinc.com, Colorado Springs, CO), a for-fee insurance-based patient records database, was utilized for this study. Two hundred forty-four patients who underwent THA for ON associated with SLE were identified and compared to control cohorts of 7836 patients with ON without SLE and 64,235 patients with OA using a multivariate analysis.

Results We found patients with SLE undergoing THA for ON experienced lower rates of infection and revision but a higher rate of medical complications compared to patients undergoing THA for non-SLE ON diagnoses. Patients with SLE undergoing THA for ON experienced decreased rates of infection but increased rates of transfusion and medical complications compared to patients undergoing THA for OA.

Conclusions Our data demonstrate that THA can be safely performed on SLE patients with ON without significantly increased morbidity compared to that in patients with non-SLE-associated ON or patients with OA.

Keywords Osteonecrosis · Systemic lupus erythematosus · Total hip arthroplasty

Introduction

Systemic lupus erythematosus (SLE) is an autoimmune systemic disease with a prevalence of 52.2–74.4 per 100,000 in the US population [1–3]. While the clinical manifestations of SLE are broad and multi-systemic, the most common orthopedic manifestations are arthritis and arthralgias, and affect up to 95% of patients with SLE [4, 5]. Osteonecrosis (ON) of the femoral head is a devastating complication that affects 4–30% of patients with SLE [4]. The pathophysiology behind SLE-associated ON remains unclear but is likely related to chronic steroid use and vasculitis [4, 6, 7]. Non-arthroplasty treatment options for the management of ON have produced variable results and include core decompression, fibular strut graft, and femoral osteotomy. Total hip arthroplasty remains the most reliable and effective definitive treatment for ON [7]. A recent study by Figgie et al. reviewed administrative hospital discharge databases from ten American states and found that 24% of THAs performed on SLE patients were for ON in 2005 [5]. In addition, modern medical advances in the treatment of SLE have indirectly led to increasing rates of THA among SLE patients by prolonging their life expectancy.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00264-018-3871-5) contains supplementary material, which is available to authorized users.

✉ Quanjun Cui
qc4q@hscmail.mcc.virginia.edu

Dennis Q. Chen
DC5AJ@hscmail.mcc.virginia.edu

Jourdan M. Cancienne
jc2yt@hscmail.mcc.virginia.edu

Brian C. Werner
BCW4X@hscmail.mcc.virginia.edu

[1] Department of Orthopaedic Surgery, University of Virginia Health System, 400 Ray C. Hunt Drive, Suite 330, Charlottesville, VA 22903, USA

Despite the expanding population of SLE patients with ON requiring THA, current evidence examining outcomes following THA for ON in SLE patients have been retrospective institutional observation studies limited by small sample sizes [8–14]. The goal of the present study was to use a national, administrative database to investigate the current trend in SLE patients undergoing THA and compare complications following THA for ON with SLE, ON without SLE, and osteoarthritis (OA).

Materials and methods

Database

The PearlDiver patient records database (www.pearldiverinc.com, Colorado Springs, CO), a for-fee insurance-based patient records database, was utilized for this study. The database contains procedural volumes, patient demographics, and average charge information for patients with International Classification of Diseases, 9th Revision (ICD-9) diagnoses and procedures or Current Procedural Terminology (CPT) codes from several different insurers, including both Medicare and Humana (private insurer). The data for this study were derived from the Humana database in PearlDiver, which contained approximately 20 million individual patient records from 2007 to 2015 at the time of analysis. Access to the database was granted by PearlDiver Technologies for the purpose of academic research. The database was stored on a password-protected server maintained by PearlDiver. All data are de-identified and anonymous, and were thus exempt from institutional review board approval.

Study groups

The database was queried for all patients who underwent THA from 2007 to 2015 by using CPT code 27130 (arthroplasty, acetabular, and proximal femoral prosthetic replacement [total hip arthroplasty], with or without autograft or allograft). Patients with ON and SLE were then identified using ICD-9-CM diagnostic codes 733.42 (aseptic necrosis of the head and neck of femur) and 710.0 (systemic lupus erythematosus) to create our study cohort. A control cohort of patients undergoing THA for ON due to non-SLE diagnoses was created using ICD-9-CM diagnostic code 733.42 (aseptic necrosis of the head and neck of femur) and excluding 710.0 (systemic lupus erythematosus). A second control cohort was created with the remaining patients who underwent THA for non-ON diagnoses, of which the predominant diagnosis was OA. Three mutually exclusive patient cohorts were created in total (Fig. 1).

Patients in each cohort were queried for basic demographics including sex, age (< 65, 65–80, > 80 years), and smoking status. Comorbidities for each cohort were assessed, including obesity, morbid obesity, tobacco use, alcohol use, inflammatory arthritis, depression, hypercoagulable disorders, diabetes mellitus (DM), hyperlipidemia (HLD), hypertension (HTN), peripheral vascular disease (PVD), congestive heart failure (CHF), coronary artery disease (CAD), chronic kidney disease (CKD), chronic lung disease, and chronic liver disease (CLD), haemodialysis (HD), and hypothyroidism using ICD-9 codes for each disease.

Post-operative complications

Patients in each cohort were then queried for post-operative complications utilizing ICD-9 and CPT codes. Complications assessed within 90 days post-operatively were venous thromboembolism (VTE, including pulmonary embolism and deep vein thrombosis), infection (including diagnosis and/or operative procedure), blood transfusion, and other medical complications (including myocardial infarction, respiratory failure, cerebrovascular accident, urinary tract infection, pneumonia, acute renal failure, and cholecystitis). Hospital readmission for any reason (medical or surgical) was queried within 90 days post-operatively for all cohorts. Periprosthetic dislocation was assessed using both ICD-9 codes and CPT codes for a reduction procedure within six months post-operatively. Revision THA was assessed within the confines of the database (up to 8 years post-operatively). The CPT and ICD-9 codes used to identify all post-operative complications are listed in the Appendix.

Statistical analysis

A multivariate analysis controlling for age, gender, obesity, morbid obesity, tobacco use, alcohol abuse, inflammatory arthritis, depression, hypercoagulable state, DM, HLD, HTN, PVD, CHF, CAD, CKD, use of haemodialysis, chronic lung disease, CLD, and hypothyroidism was performed to compare complication rates. Adjusted odds ratios and 95% confidence intervals were calculated for each comparison. $P < 0.05$ was considered significant. An integrated statistical program based on open source R software within the PearlDiver database was used for all statistical calculations.

Results

Seventy-two thousand three hundred fifteen unique patients were identified who met the inclusion/exclusion criteria, of which 244 were patients with ON due to SLE, 7836 were patients with ON due to non-SLE diagnoses, and 64,235 were patients with non-ON diagnoses, of which the predominant diagnosis was OA. The number of THA performed in patients with SLE increased 190% over the time period studied

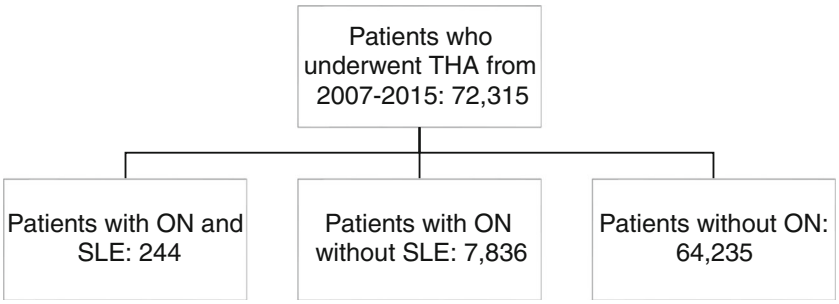

Fig. 1 Study cohorts

(Fig. 2). Patients with SLE undergoing THA for ON experienced lower rates of infection (OR 0.3; 95% CI 0.2–0.5) and revision (OR 0.71; 95% CI 0.6–0.9) but a higher rate of medical complications (OR 1.22; 95% CI 1.0–1.5) within 90 days compared to patients undergoing THA for non-SLE-related ON diagnoses (Table 1). Compared to patients undergoing THA for OA, SLE patients undergoing THA for ON experienced significantly higher rates of blood transfusion (OR 1.52; 95% CI 1.1–2.0) and medical complications (OR 1.59; 95% CI 1.2–2.2), but significantly lower rates of infection within 90 days (OR 0.32; 95% CI 0.1–0.7) (Table 2). There were no other significant differences in complications noted between these two cohorts.

Discussion

SLE patients with ON represent a unique subset of patients with distinct pathophysiology and medical comorbidities. The development of ON in SLE patients is likely due to a combination of chronic steroid use and vasculitis [4, 6, 7]. Following improvements in the medical treatment of SLE, the life span of SLE patients has dramatically improved from a 50% five year survival in 1950–1975 to a 78% 20-year survival in 1990–2004 [15]. As life expectancy increased, so has the demand for arthroplasty among SLE patients, doubling from 0.17/100,000 in 1991 to 0.38/100,000 in 2005. Furthermore, the primary indication in this series was ON in nearly a quarter of cases [5]. In our present study, we report a 190% increase in THA for ON in patients with SLE from 2007 to 2015.

Prior studies investigating the patients with ON due to SLE have been small observational studies and with conflicting results. A study by Hanssen reported a 15% incidence of delayed wound healing and 10% superficial wound infection following 29 THAs and 14 bipolar hemiarthroplasties in a cohort of 31 SLE patients, 27 of which had ON. More recently, Kang et al. have reported an infection rate of 11.1% following 28 arthroplasties performed on SLE patients with ON. However, other studies have found more favorable results. Shigemura et al. reported no superficial or deep infection and two dislocations in a group of 14 THA performed on SLE patients with ON [14]. Similarly, Prupas et al. reported on six patients with SLE ON treated with THA who experienced no serious complications at follow-up ranging from 23 to 76 months [8]. Woo et al. reported on 19 arthroplasties on SLE patients with ON who experienced no post-operative complications except for one revision for osteolysis at nine year follow-up [9].

The present study examined 244 patients with ON due to SLE and 7836 patients with ON due to non-SLE diagnoses and reports a lower incidence of infection and revision following THA for ON in SLE patients versus ON in non-SLE patients. This is consistent with a systematic review by Johannson which found a 4% revision rate in patients with ON secondary to SLE compared to 13% in the overall ON group [16]. We believe this result is largely reflective of the effect of multiple other risk factors associated with ON, rather than SLE having a protective effect. ON is associated with younger patient age, corticosteroid use, excessive alcohol consumption, smoking, HIV, sickle cell, and organ transplant [16]. The cumulative effect of these risk factors may be more influential in increasing the revision rate in patients with ON. For instance, Johannson found that the subset of patients with organ transplant and ON had a 33% revision rate. Patients with ON secondary to SLE likely have a lower infection and revision rate due to the lack of other risk factors associated with ON.

Interestingly, our study also demonstrated a decreased rate of infection in the ON SLE group when compared to that in the OA group. This is consistent with a systematic review by Kennedy et al. which also found a lower infection rate following THA in SLE patients compared to the general population [7]. Again, we do not believe this finding is reflective of a protective effect from SLE, but rather due to increased vigilance when treating this subgroup of patients. For example, Kang described employing a more aggressive prophylactic antibiotic regimen for THA in SLE patients [17]. Further, prior studies investigating THA in SLE patients have limited surgery to those patients with inactive or minimally active disease [17, 18]. Therefore, we believe the lower infection rate in SLE patients is due to a combination of careful patient selection and increased provider precautions rather than an intrinsic protective effect from the disease process.

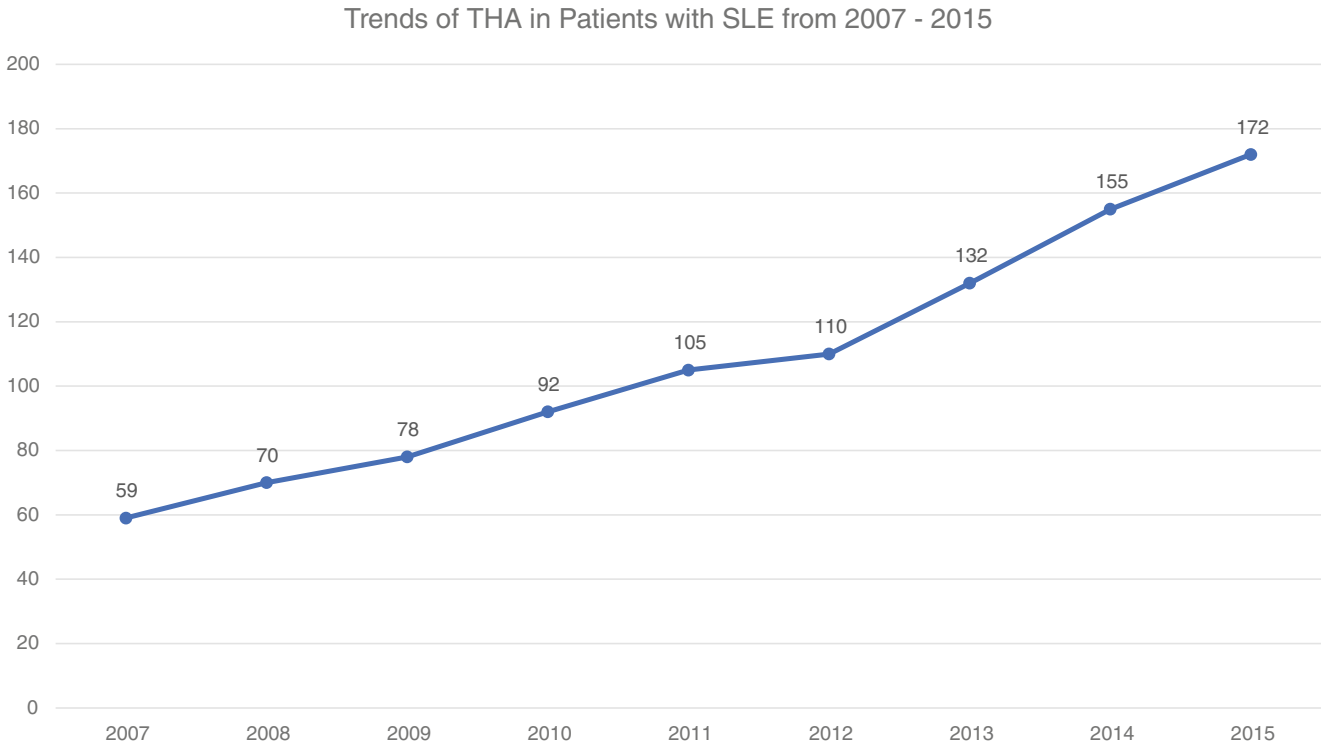

Fig. 2 Trend of THA in patients with SLE from 2007 to 2015

Although SLE is the sixth most common condition resulting in 30-day all-cause readmissions in the USA, our study did not find a high incidence of readmission among the SLE cohort [19]. However, our study did find that patients with ON and SLE have a higher incidence of medical complications within 90 days when compared to the overall group of patients with ON or when compared to patients with OA and this is likely reflective of the medical complexity of patients with SLE.

We found patients with SLE and ON to have a higher incidence of blood transfusion following THA compared to the OA population. This may be due to a lower starting pre-operative haemoglobin in SLE patients compared to that in the OA population as reported by Merayo-Chalico [18]. In addition, SLE is known to be associated with abnormal platelet aggregation and antibodies against coagulation factors, thus increasing the risk of peri-operative bleeding [20].

Table 1 Post-operative complication rates following THA for AVN in patients with SLE vs. non-SLE AVN

Complication	Odds ratio	95% CI	*P*
DVT within 90 days	1.2	[0.8–1.8]	0.352
Infection within 90 days	0.3	[0.2–0.5]	*< 0.001*
Transfusion within 90 days	1.14	[0.9–1.4]	0.225
Medical complications within 90 days	1.22	[1.0–1.5]	*0.045*
Dislocation within 90 days	0.74	[0.4–1.3]	0.291
Overall dislocation	0.77	[0.5–1.2]	0.228
Overall revision THA	0.71	[0.6–0.9]	*0.027*
Readmission within 90 days	0.89	[0.7–1.1]	0.294

P values <0.05

The present study has several strengths. This is the largest study evaluating post-operative complications after THA in patients with ON and SLE. By utilizing an administrative national database to create our study cohort of 244 patients, we avoided the limitations of small sample size and the biases that may result from underpowered single-centre observational studies. Further, this study offers two comparison cohorts, which helps to further delineate complications inherently associated with performing THA in patients with ON and SLE. Another benefit of the PearlDiver database is that it allows tracking of 90-day post-operative complication rates after hospital discharge, compared to other databases such as the National Inpatient Sample, which only allows reporting of in-hospital complications.

Limitations of this study include those inherent to all retrospective database studies: the accuracy and strength of our conclusions are limited by the quality of coding data. Therefore, any miscoding or noncoding by physicians or billers is a potential source of error. Although there are no data reflecting the coding accuracy in the Humana dataset, a 2016 report by the Centers for Medicare and Medicaid Services showed an overall coding error rate of 1.1% [21]. Therefore, although this is a major potential limitation when using administrative databases such as PearlDiver, the overall coding error rate likely mirrors that in larger Medicare populations. In addition, although we attempted to capture a large representative sample of patients with ON and SLE, we cannot assure that our data represent a true cross section of the US

Table 2 Post-operative complication rates following THA for AVN in patients with SLE vs. OA

Complication	Odds ratio	95% CI	*P*
DVT within 90 days	1.12	[0.6–1.9]	0.689
Infection within 90 days	0.32	[0.1–0.7]	*0.007*
Transfusion within 90 days	1.52	[1.1–2.0]	*0.004*
Medical complications within 90 days	1.59	[1.2–2.2]	*0.003*
Dislocation within 90 days	1.39	[0.7–2.8]	0.352
Overall dislocation	1.12	[0.6–2.0]	0.715
Overall revision THA	0.89	[0.5–1.5]	0.65
Readmission within 90 days	1.27	[0.9–1.7]	0.13

P values <0.05

population as only one insurer's (Humana) data were included in the analysis. Further, due to the administrative nature of this study, the severity of a patient's SLE symptoms is not reflected in the ICD-9 codes, and therefore the effect of SLE disease severity on clinical outcomes could not be assessed. Also, while we tried to correct for confounding variables by multivariate analysis, there remain confounding variables (operative time, antibiotic cement use, hospital volume) not identifiable within the database that contribute to the outcomes studied. Finally, at the time of the study, the PearlDiver database indexed data from 2007 through 2015, and data for patients with end points outside this window would thus not be captured.

In this database study, patients with SLE undergoing THA for ON experienced lower rates of infection and revision but a higher rate of medical complications compared to patients undergoing THA for non-SLE ON diagnoses. Patients with SLE undergoing THA for ON experienced decreased rates of infection but increased rates of transfusion and medical complications compared to patients undergoing THA for OA. Overall, our study demonstrates that THA for ON in SLE patients is not associated with significantly increased rates of infection or revision but is associated with increased incidence of medical complications post-operatively. Historically, experience has been limited in this small subset of patients but our data is reassuring that THA can be safely performed on SLE patients with ON without significantly increased morbidity compared the standard population.

Compliance with ethical standards

Conflict of interest Dr. Cui or an immediate family member serves as a paid consultant to Exactech; has received research or institutional support from National Institute of Health, Department of Defense and Exactech; and serves as a board member, owner, officer, or committee member of the Virginia Orthopaedic Society, Journal of Arthroplasty; received royalties from Elsevier. None of the following authors or any immediate family member has received anything of value from or has stock or stock options held in a commercial company or institution related directly or indirectly to the subject of this article: Dr. Cancienne, Dr. Chen, and Dr. Werner.

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