Factors Associated With Increasing Length of Stay for Rheumatoid Arthritis Patients Undergoing Total Hip Arthroplasty and Total Knee Arthroplasty

Kyle W. Morse, MD¹, Nicole K. Heinz, PA-C¹, Jeremy M. Abolade, BS¹, Joshua Wright-Chisem, MD¹, Linda Alice Russell, MD¹,², Meng Zhang, PhD³, Serene Mirza, BS¹, Diyu Pearce-Fisher, BS¹, Dana E. Orange, MD, MS¹,⁴, Mark P. Figgie, MD¹,², Peter K. Sculco, MD¹,², and Susan M. Goodman, MD¹,²

Abstract
Background: Total hip arthroplasty (THA) and total knee arthroplasty (TKA) are cost-effective procedures that decrease pain and improve health-related quality of life for patients with advanced symptomatic arthritis, including rheumatoid arthritis (RA). Patients with RA have a longer length of stay (LOS) after THA or TKA than patients with osteoarthritis, yet the factors contributing to LOS have not been investigated. Purpose: We sought to identify the factors contributing to LOS for patients with RA undergoing THA and TKA at a single tertiary care orthopedic specialty hospital. Methods: We retrospectively reviewed data from a prospectively collected cohort of 252 RA patients undergoing either THA or TKA. Demographics, RA characteristics, medications, serologies, and disease activity were collected preoperatively. Linear regression was performed to explore the relationship between LOS (log-transformed) and possible predictors. A multivariate model was constructed through backward selection using significant predictors from a univariate analysis. Results: Of the 252 patients with RA, 83% were women; they had a median disease duration of 14 years and moderate disease activity at the time of arthroplasty. We had LOS data on 240 (95%) of the cases. The mean LOS was 3.4 ± 1.5 days. The multivariate analysis revealed a longer LOS for RA patients who underwent TKA versus THA, were women versus men, required a blood transfusion, and took preoperative opioids. Conclusion: Our retrospective study found that increased postoperative LOS in RA patients undergoing THA or TKA was associated with factors both non-modifiable (type of surgery, sex) and modifiable (postoperative blood transfusion, preoperative opioid use). These findings suggest that preoperative optimization of the patient with RA might focus on improving anemia and reducing opioid use in efforts to shorten LOS. More rigorous study is warranted.

Keywords
rheumatoid arthritis, total knee arthroplasty, total hip arthroplasty, opioid usage, length of stay, inflammatory arthritis

Received September 1, 2021. Accepted November 5, 2021.

Introduction
Total hip arthroplasty (THA) and total knee arthroplasty (TKA) are cost-effective procedures that improve the health-related quality of life for patients with advanced symptomatic joint damage, including those with rheumatoid arthritis (RA) [11,17,31]. Patients with RA comprise just 0.5% to 1% of the general population but nearly 2% to 4% of those undergoing THA or TKA [10,12,23,36]. While the current rates of arthroplasty utilization among RA patients remain...
stable, these patients experience significant improvements following total joint arthroplasty (TJA) [8,22]. However, the use of TJA has led to a marked increase in overall cost, specifically postoperative inpatient costs, which is the largest expenditure for this procedure. As inpatient costs make up the largest proportion of expenditures for TKA, cost containment efforts need to address length of stay (LOS) [18,28]. Patients with RA have a longer LOS after THA or TKA, yet the factors contributing to LOS in patients with RA have not been identified [4].

Patient-related factors such as age and co-morbidities and hospital or surgeon-related factors may contribute to extended LOS [24]. Whether there are unique factors that contribute to LOS for RA patients undergoing TJA is unknown [6]. The purpose of this study was to identify the factors contributing to LOS for patients with RA undergoing THA or TKA at a single tertiary care orthopedic specialty hospital.

Methods

A retrospective review was performed from a prospectively collected observational cohort of 252 patients with RA undergoing either THA or TKA between October 2013 and November 2018 at a tertiary care center specializing in musculoskeletal health. Patients were identified and screened as part of the Perioperative Flare in Rheumatoid Arthritis study as detailed by Goodman et al [9] and Morse et al [20].

In brief, demographics, RA characteristics, medications, and disease activity were systematically collected. Demographics included age, gender, relevant past medical history, body mass index (BMI), RA duration, surgical type (THA or TKA), race, ethnicity, and employment status. The 2010 or 1987 American College of Rheumatology/European League Against Rheumatism criteria was used to classify RA. Additionally, a physical examination by one of the authors or another hospital rheumatologist confirmed the diagnosis. Medications recorded included the use of nonsteroidal anti-inflammatory drugs (NSAIDs), steroids, methotrexate or other conventional disease modifying anti-rheumatic drugs (DMARDs), opioids, and biologics. Recent opioid use was recorded as well as the opioid prescribed, but duration of opioid use and daily dose were not recorded. Perioperative management of the patient with RA included cessation of biologic DMARDs for 1 dose interval prior to surgery and continuation of methotrexate (MTX), other synthetic DMARDs, and glucocorticoids per institutional guidelines. Operative details were recorded from the 36 surgeons contributing patients; these included estimated blood loss (EBL, mL) and surgical duration (min). The posterolateral approach was used for all THAs and a midline incision with medial parapatellar approach was used for all TKAs. The use of drains varied with surgeon preference and was not recorded. Length of stay (hours) was recorded. All transfusions were recorded as well as the indication; institutional guidelines use an absolute transfusion trigger of 7 mg/dL. Transfusions were also given at the discretion of the surgeon or for patients who developed symptoms attributed to anemia during the postoperative period. Patients who had cleared physical therapy and were medically stable were deemed ready for discharge.

Disease activity was measured using the Disease Activity Score (DAS28-ESR; score > 4.1 signifies high disease activity) and Clinical Disease Activity Index (CDAI; score > 22 signifies high disease activity). Patient-reported outcome measures (PROMs) included the Hip Disability and Osteoarthritis Outcomes Score (HOOS), Knee Injury and Osteoarthritis Outcomes Score (KOOS) and the Multi-dimensional Health Assessment Questionnaire (MDHAQ). The erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor (RF), and anti-citrullinated protein/peptide antibody (ACPA) levels were taken preoperatively and all PROMs were collected either on the day of surgery or at the time of preadmission testing within 2 weeks of surgery.

This study was approved by the Hospital for Special Surgery Institutional Review Board and all patients included signed informed consent. The study is reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist for cohort studies [34]. It was supported by the Clinical Translational Science Center (UL1-TR002384), Clinical Translational Science Award (# UL1TR001866), and the Accelerated Medicines Partnership (UH2- AR067691).

Statistical Analysis

Baseline characteristics were summarized using descriptive statistics and compared using $\chi^2$, Fisher’s exact test, 2-sample $t$-test, or Wilcoxon rank-sum test as appropriate. Significant variables ($P < .05$) associated with increased LOS in the univariate analysis were included in the multivariate analysis. The multivariate logistic regression analysis was then performed to explore the relationship between LOS and the predictors that were significant in the univariate model. The LOS outcome variable was log transformed and interpreted as the percentage change in the original scale of LOS with 1 unit increase of a continuous predictor, or a comparison of 1 category to the reference category for a categorical predictor.

Results

Patients with RA were predominantly women (83%), with prolonged disease duration (14.1 $\pm$12 years), and active disease (mean DAS28 = 3.7 $\pm$1.3, CDAI = 18.4 $\pm$ 10.9) (Table 1). For RA management, 53% were taking biologic...
Table 1. Baseline characteristics.

| Characteristic                  | RA patients (N = 252) |
|---------------------------------|-----------------------|
| Age, years (mean ± SD)          | 62.7 ± 11.0           |
| Female, n (%)                   | 209 (83.3)            |
| BMI (mean ± SD)                 | 29.3 ± 6.8            |
| Diagnosis Duration, years (mean ± SD) | 14.1 ± 12.0        |
| Type of surgery, n (%)          |                       |
| TKA                             | 146 (57.9)            |
| THA                             | 106 (42.1)            |
| Race, n (%)                     |                       |
| White                           | 186 (73.8)            |
| Black                           | 27 (10.7)             |
| Asian                           | 6 (2.4)               |
| Other                           | 33 (2.4)              |
| Smoking, n (%)                  | 115 (51.6)            |
| Education, n (%)                |                       |
| Less than College               | 31 (14.0)             |
| College or above                | 190 (86.0)            |
| Employment, n (%)               |                       |
| Employed                        | 84 (38.2)             |
| Unemployed, Disabled or Retired | 125 (56.8)            |
| Other                           | 11 (5.0)              |
| Ethnicity, n (%)                |                       |
| Hispanic or Latino              | 18 (7.7)              |
| Not Hispanic or Latino          | 211 (90.6)            |
| Do not wish to answer           | 4 (1.7)               |
| Criteria, n (%)                 |                       |
| Meet both criteria              | 101 (43.9)            |
| 1987                            | 32 (13.9)             |
| 2010                            | 54 (23.5)             |
| Does not meet criteria(diagnosis per PI) | 43 (18.7)        |
| Preoperative medications, n(%)  |                       |
| NSAIDS                          | 135 (57.2)            |
| Steroids                        | 87 (36.1)             |
| Methotrexate                    | 117 (48.8)            |
| DMARD                           | 70 (29.3)             |
| Opioids                         | 88 (37.0)             |
| Biologic                        | 128 (53.6)            |
| Preop hemoglobin, g/dl (mean ± SD) | 12.8 ± 1.5           |
|                                 | 268.0 ± 77.1          |
| Hx of previous transfusion, n (%) | 9 (3.9)              |
| Hx of DVT, n (%)                | 11 (4.7)              |
| Hx of PE, n (%)                 | 4 (1.7)               |
| Hx of CVA, n (%)                | 10 (4.3)              |
| Hx of Stroke, n (%)             | 7 (3.0)               |
| Hx of Malignancy, n (%)         | 21 (9.0)              |
| Hx of Hormone Therapy, n (%)    | 20 (8.6)              |
| History of Myocardial Infarction, n (%) | 2 (0.9)          |
| Estimated blood loss, mL (mean ± SD) | 188.8 ± 65.3       |
|                                 | 986.8 ± 74.1          |
|                                 | 2928.6 ± 323.3        |
| Surgery Duration, minutes (mean ± SD) | 92.4 ± 32.8       |

Table 1. (continued)

| Characteristic                  | RA patients (N = 252) |
|---------------------------------|-----------------------|
| Post op transfusion needed?, Yes n (%) | 26 (11.2)            |
| BIHAHAQ, (mean ± SD)            | 3.8 ± 1.7             |
| DAS28—ESR, (mean ± SD)          | 3.7 ± 1.3             |
| CDAL (mean ± SD)                | 18.4 ± 10.9           |
| ESR result (mean ± SD)          | 20.4 ± 19.7           |
| CRP result (mean ± SD)          | 1.7 ± 2.5             |
| HOOS/KOOS Pain (mean ± SD)      | 40.3 ± 20.1           |
| HOOS/KOOS Function (mean ± SD)  | 46.2 ± 21.1           |
| Length of stay, hours (mean ± SD) | 81.8 ± 36.7           |

RA rheumatoid arthritis, BMI body mass index, TKA total knee arthroplasty, THA total hip arthroplasty, PI principal investigator NSAIDS nonsteroidal anti-inflammatory drugs, DMARD disease modifying anti-rheumatic drugs, DVT deep vein thrombosis, PE pulmonary embolus, CVA cerebrovascular accident, MDHAQ Multi-dimensional Health Assessment Questionnaire, DAS Disease Activity Score, ESR erythrocyte sedimentation rate, CDAI Clinical Disease Activity Index, CRP C-reactive protein, HOOS Hip Disability and Osteoarthritis Outcomes Score, KOOS Knee Injury and Osteoarthritis Outcomes Score.

therapies, 49% were taking MTX, and 36% were taking glucocorticoids. Eighty-eight (37%) patients reported taking opioids preoperatively, with 87 using short-acting opioids and 1 taking methadone. Overall LOS data were available for 240/252 (95%) with a mean LOS of 3.4 ± 1.5 days.

In the univariate analysis, postoperative blood transfusion (P = .01), baseline DAS 28 (P = .02), sex (P = .001), BMI (P = .03), employment status (P = .04), type of surgery (P < .001), opioid usage (P = .001), duration of surgery (P = .01), HOOS/KOOS baseline pain score (P = .02), HOOS/KOOS baseline function score (P = .003), duration of disease (0.03), baseline MD-HAQ (P = .01), and baseline ESR (P = .03) were significantly associated with length of stay (Table 2).

The multivariate analysis revealed that after controlling for the other risk factors, the major predictors of LOS were type of surgery (TKA vs THA), female sex, preoperative opioid use, and requirement for postoperative blood transfusion. Overall, LOS decreased by 19.75% (range 9.73%, 28.65%, P = .0002) for patients who underwent THA compared to TKA; increased by 19.72% (range 2.35%, 40.05%, P = .04) when comparing female to male; decreased by 18.13% (range 7.91%, 27.21%, P = .0007) for patients who did not take opioids; and decreased by 22% (range
Table 2. Univariate Analysis for predictors of length of stay following total hip and total knee arthroplasty in patients with rheumatoid arthritis.

| Univariate variable       | Level                                      | Estimated model coefficient (standard error) | Percentage change in the original scale of length of stay with 1 unit increase of a continuous predictor, or a comparison of one category to the reference category for a categorical predictor* (95% CI) | P value |
|---------------------------|--------------------------------------------|---------------------------------------------|--------------------------------------------------------------------------------------------------|---------|
| Age                       |                                            | 0.002 (0.002)                                | 0.2% (~0.19%, 0.59%)                                                                            | .47     |
| Sex                       | Female vs. Male                            | 0.22 (0.07)                                  | 24.61% (~8.63%, 42.93%)                                                                         | .001    |
| Race                      | Asian vs White                             | −0.10 (0.17)                                 | −9.51% (~35.16%, 26.26%)                                                                        | .56     |
|                           | Black vs. White                            | 0.11 (0.09)                                  | 11.63% (~6.42%, 33.16%)                                                                         | .19     |
|                           | Other vs. White                            | −0.03 (0.08)                                 | −2.96% (~17.03%, 13.52%)                                                                        | .75     |
| Ethnicity                 | Hispanic or Latino vs Not Hispanic nor Latino | 0.06 (0.10)                                | 6.18% (~12.72%, 29.18%)                                                                         | .55     |
| BMI                       | No vs. Yes                                 | 0.008 (0.004)                                | 0.8% (~0.02%, 1.60%)                                                                            | .03     |
| Have you ever smoked      | College or above vs. Less than college      | −0.02 (0.08)                                 | −1.98% (~16.21%, 14.66%)                                                                        | .74     |
| cigarettes                | Employed vs. Unemployed or Disabled or Retired | −0.11 (0.05)                                | −10.42% (~18.77%, −1.19%)                                                                       | .04     |
|                           | Other vs. Unemployed or Disabled or Retired | 0.08 (0.13)                                 | 8.33% (~16.04%, 39.77%)                                                                         | .53     |
| RA Criteria               | criteria 1987 vs Meets BOTH criteria       | −0.02 (0.09)                                 | −1.98% (~17.83%, 16.93%)                                                                        | .83     |
|                           | criteria 2010 vs Meets BOTH criteria       | −0.02 (0.07)                                 | −1.98% (~14.55%, 12.43%)                                                                        | .79     |
| TXA                       | No vs. Yes                                 | −0.014 (0.06)                                | −1.39% (~12.33%, 10.92%)                                                                        | .81     |
| Type of Surgery           | Hip vs. Knee                               | −0.22 (0.05)                                 | −19.75% (~27.24%, −11.49%)                                                                      | .0001   |
| NSAIDs                    | No vs. Yes                                 | 0.09 (0.05)                                  | 9.42% (~0.79%, 20.68%)                                                                          | .10     |
| Opioid                    | No vs. Yes                                 | −0.19 (0.05)                                 | −17.3% (~25.02%, −8.79%)                                                                        | .001    |
| Methotrexate              | No vs. Yes                                 | 0.09 (0.05)                                  | 9.42% (~0.80%, 20.68%)                                                                          | .10     |
| Steroids                  | No vs. Yes                                 | −0.09 (0.06)                                 | −8.60% (~18.74%, 2.80%)                                                                         | .09     |
| Biologic                  | No vs. Yes                                 | −0.002 (0.05)                                | −0.20% (~9.52%, 10.08%)                                                                         | .96     |
| Other DMARD               | No vs. Yes                                 | 0.01 (0.06)                                  | 1.01% (~10.20%, 13.61%)                                                                         | .85     |
| Prior Transfusion         | No vs. Yes                                 | 0.004 (0.14)                                 | 0.40% (~23.69%, 32.10%)                                                                         | .98     |
| Postoperative Transfusion | No vs. Yes                                 | −0.24 (0.08)                                 | −21.34% (~32.75%, −7.98%)                                                                       | .01     |
| Prior DVT                 | No vs. Yes                                 | −0.23 (0.13)                                 | −20.54% (~38.42%, 2.31%)                                                                        | .06     |
| History of PE             | No vs. Yes                                 | −0.24 (0.21)                                 | −21.33% (~47.88%, 18.72%)                                                                       | .25     |
| History of CVA            | No vs. Yes                                 | 0.10 (0.13)                                  | 10.52% (~14.34%, 42.59%)                                                                        | .46     |
| History of Stroke         | No vs. Yes                                 | 0.14 (0.16)                                  | 15.03% (~15.94%, 57.40%)                                                                        | .37     |
| History of Malignancy     | No vs. Yes                                 | −0.05 (0.09)                                 | −4.88% (~20.26%, 13.47%)                                                                        | .59     |
| History of Hormone        | No vs. Yes                                 | −0.07 (0.10)                                 | −6.76% (~23.36%, 13.43%)                                                                        | .49     |
| Therapy                   |                                            |                                             |                                                                                                |         |
| History of Myocardial     |                                            |                                             |                                                                                                |         |
| Infarction                |                                            |                                             |                                                                                                |         |
| Hemoglobin at baseline    |                                            |                                             |                                                                                                |         |
| Platelet count            |                                            |                                             |                                                                                                |         |
| Estimated blood loss      |                                            |                                             |                                                                                                |         |
| Duration of Surgery       |                                            |                                             |                                                                                                |         |

(continued)
Table 2. (continued)

| Univariate variable                  | Level                      | Estimated model coefficient (standard error) | Percentage change in the original scale of length of stay with 1 unit increase of a continuous predictor, or a comparison of one category to the reference category for a categorical predictor* (95% CI) | P value |
|-------------------------------------|----------------------------|---------------------------------------------|-------------------------------------------------------------------------------------------------|---------|
| HOOs/KOOS pain at baseline          | −0.003 (0.001)             | −0.30% (−0.49%, −0.10%)                      | .02                                                                                             |         |
| HOOs/KOOS function at baseline      | −0.004 (0.001)             | −0.40% (−0.59%, −0.20%)                      | .003                                                                            |         |
| Duration of disease                 | 0.005 (0.002)              | 0.5% (0.11%, 0.90%)                          | .03                                                                                             |         |
| MD−Haq at baseline                  | 0.04 (0.02)                | 4.08% (0.08%, 8.24%)                         | .01                                                                                             |         |
| DAS28_esr at baseline               | 0.05 (0.02)                | 5.13% (1.09%, 9.33%)                         | .02                                                                                             |         |
| CDAI at baseline                    | 0.004 (0.003)              | 0.4% (−0.19%, 0.99%)                         | .11                                                                                             |         |
| CRP result at baseline              | −0.007 (0.01)              | −0.70% (−2.62%, 1.27%)                       | .58                                                                                             |         |
| ESR result at baseline              | 0.003 (0.001)              | 0.3% (0.1%, 0.50%)                          | .03                                                                                             |         |
|                                    | 0.0001 (0.0001)            | 0.01% (−0.01%, 0.03%)                       | .34                                                                                             |         |
|                                    | 0.0001 (0.0001)            | 0.01% (−0.01%, 0.03%)                       | .20                                                                                             |         |

Table 3. Multivariate analysis for predictors of length of stay following total hip and total knee arthroplasty in patients with rheumatoid arthritis.

| Multivariate variable               | Level                      | Estimated model coefficient (standard error) | Percentage change in the original scale of length of stay with 1 unit increase of a continuous predictor, or a comparison of one category to the reference category for a categorical predictor* (95% CI) | P value |
|-------------------------------------|----------------------------|---------------------------------------------|-------------------------------------------------------------------------------------------------|---------|
| Sex                                 | Female vs. Male            | 0.18 (0.08)                                 | 19.72% (2.35%, 40.05%)                                                                       | .04     |
| TXA                                 | No vs. Yes                 | 0.04 (0.07)                                 | 4.08% (−9.26%, 19.38%)                                                                       | .61     |
| Type of Surgery                     | Hip vs. Knee               | −0.22 (0.06)                                | −19.75% (−28.65%, −9.73%)                                                                   | .0002   |
| Opioid                              | No vs. Yes                 | −0.20 (0.06)                                | −18.13% (−27.21%, −7.91%)                                                                   | .0007   |
| Postoperative Transfusion           | No vs. Yes                 | −0.25 (0.09)                                | −22.11% (−34.71%, −7.10%)                                                                   | .006    |
| Hemoglobin at baseline              | 0.03 (0.02)                | −2.96% (−6.69%, 0.92%)                       | .18                                                                                             |         |
| DAS28_esr at baseline               | 0.07 (0.04)                | 7.25% (−0.84%, 16.00%)                      | .053                                                                                        |         |
| CDAI at baseline                    | −0.003 (0.004)             | −0.30% (−1.08%, 0.49%)                      | .51                                                                                             |         |

TXA tranexamic acid, CI confidence interval, CDAI Clinical Disease Activity Index.

*Percentage change in the original scale of length of stay with 1 unit increase of a continuous predictor, or a comparison of one category to the reference category for a categorical predictor: (exponential [estimated model coefficient]-1)*100. Multivariate analysis included all characteristics found significant in the univariate analysis.

7%, 34.71%, P = .006) when patients did not have a post-operative transfusion (Table 3). Neither disease activity nor baseline pain and function were significant predictors of LOS in the multivariate adjusted model.

Discussion
Patients with RA undergoing TJA require greater health care resources than patients with OA [16,19]. The largest portion of health care expenditures occurs during the inpatient stay.
For this reason, we sought to identify risk factors for increased LOS in RA patients undergoing THA or TKA at a single institution. The results of this study demonstrated that independent predictors for increased LOS in patients with RA were undergoing TKA, being female, using opioids preoperatively, and requiring postoperative blood transfusions.

This study has several limitations. First, we did not collect data on opioid dosage or length of use and therefore could not stratify our data by this important variable. Second, we did not collect data on hospital readmission, emergency department visits, or discharge destination (inpatient rehabilitation vs home). Third, we did not report on added cost for increased LOS. Fourth, we did not collect data on the method of anesthesia, although it is our institution’s protocol that most patients undergo surgery using neuraxial anesthesia with pain managed postoperatively by the acute pain service. Finally, as with any observational study, there may be other unmeasured confounding variables that affected our primary outcome (overall LOS). Despite these limitations, we believe that this large cohort of patients with RA undergoing THA and TKA at a single institution highlights important associations between certain modifiable and non-modifiable factors and the risk for prolonged LOS.

Prior reports have identified risk factors for increased LOS after THA or TKA; however, few studies have specifically evaluated RA patients undergoing TJA. In a meta-analysis evaluating LOS in patients undergoing TKA, Shah et al [26] reported that age > 70, female gender, BMI > 30, non-white race, an American Society of Anesthesiologist score of 3 to 4, Charlson Comorbidity Index (CCI) score > 0, and preoperative hemoglobin < 13.0 g/L as risk factors for increased LOS. Similarly, Styron et al [29] reported female gender and higher CCI as risk factors for longer LOS in patients undergoing THA or TKA. Farley et al [7] reported that postoperative anemia was the greatest risk factor for > 3 days of LOS with a OR of 3.27. Similar to these studies, we found in our RA TJA cohort that female sex and postoperative blood transfusion led to increased LOS. Surprisingly, although we have previously shown that disease activity is a risk factor for transfusion [20], higher disease activity was not an independent predictor of LOS. Also unexpected was our finding that worse baseline pain or function scores did not independently increase the risk of prolonged LOS, although both were significant in the univariate analysis.

Requiring a transfusion is a potentially modifiable risk factor for prolonged LOS. Anemia is the most frequent extra-articular manifestation of RA and is present in two-thirds of patients [35]. While anemia of chronic diseases (ACD) is most common, anemia is multifactorial in patients with RA; iron deficiency may also play a role and can be difficult to confirm in the presence of ACD [13]. There is frequently overlap in simple red blood cell indices such as mean corpuscular hemoglobin between the ACD and iron deficiency [27]. While a low ferritin level is the hallmark of iron deficiency, inflammation influences the level of ferritin, and so more complex measures such as the calculated ratio of the soluble transferrin receptor/log ferritin index can predict a response to iron therapy in patients with RA [30,35]. Replacing iron, either orally or intravenously, may be needed prior to surgery [5]. However, the use of erythropoiesis stimulating agents is more controversial due to the risk of venous thromboembolism [25].

Much attention has been given to the use of opioids prior to orthopedic surgery and to their associated morbidity with chronic use. Over one-third of patients in our RA cohort reported using opioids preoperatively, and preoperative opioid use was associated with increased LOS following surgery. Similarly, Tan et al [33] reported that 34.9% of their patient cohort used opioids prior to THA. These patients were at a 4 times increased risk of filling a second prescription and 12 times increased risk for continued opioid use following surgery. Kim et al [14] reported that patients who used opioids preoperatively and underwent TKA had a higher comorbidity score (OR 1.5, 95% CI 1.20–1.65) and were at increased risk for prolonged postoperative opioid use for 1 year. They did not report specifically on RA patients. In addition, 72% of patients who used opioids preoperatively for at least 80% of a 4-month duration became persistent opioid users postoperatively. Bonner et al [3] compared patients undergoing THA who used opioids preoperatively and those who did not and found preoperative opioid users had an increased average LOS (2.38 days vs 1.99 days, respectively), reported lower outcome scores, and were more likely to be discharged to a rehabilitation facility.

Blevins Peratikos et al [2] reported that overall preoperative opioid users had increased LOS, were more likely not to be discharged home, and experienced higher postsurgical complications including surgical site infection, 30-day readmission, and revision. Additionally, in chronic opioid users the median in medical costs was $1,084 and patients had a 64% lower rate of opioid cessation. Bell et al [1] reported that preoperative opioid use was associated with increased total episode of care costs compared to non-users ($19,229 vs $17,552) with increased cost of care of $789.00 and postacute care costs were increased 70%. This has not previously been assessed in patients with RA. A limitation of this study is that we did not collect information on the duration or dose of opioid use preoperatively but rather only recent opioid use; our findings are consistent with usage rates found in these studies. Our results reinforce these findings that preoperative opioid use is associated with prolonged LOS, and preoperative opioid cessation/reduction efforts should be made.

Chronic opioid use among patients with RA is prevalent; we found a 37% rate of preoperative opioid use in our study. It is associated with high disease activity,
severe pain, anti-depressant usage, and high disability
[15]. Effective disease control is essential to control pain and reduce opioid use [21]. The mean disease activity scores in this cohort with long-standing disease revealed moderate disease activity, with a mean CDAI of 18 and a mean DAS-28 of 3.7. Multiple other strategies have been implemented to reduce preoperative opioid usage. Dlott et al [6] implemented a preoperative risk factor screening tool that included identification of patients’ daily opioid usage (among other risk factors) to optimize patients prior to THA or TKA. The authors report a decreased LOS of 1.81 days and no transfusions in a cohort of patients who went through the optimization process compared to a historical cohort with LOS of 2.55 [6]. Tamboli et al [32] reported that the initiation of a perioperative tapering protocol can decrease opioid use over 6 weeks. Postoperative counseling on opioid reduction remains as important as preoperative opioid cessation counseling/strategies, but this has not been shown in a RA cohort and patients with long standing polyarticular RA may receive opioids for multiple affected joints rather than the operative joint alone.

In conclusion, in this cohort of 252 patients with RA undergoing THA or TKA, we found that undergoing TKA, being female, using opioids preoperatively, and needing a postoperative blood transfusion were associated with increased LOS. While type of surgery (TKA) and female sex are non-modifiable risk factors, preoperative optimization focusing on preoperative anemia and blood transfusion triggers may reduce overall LOS. In addition, patients with a recent history of opioid use should undergo preoperative counseling in conjunction with multimodal perioperative pain management in order to reduce perioperative opioid use; this may prevent the increased LOS reported in our study.

CME Credit
Please go to HSS eAcademy at https://bit.ly/HSSJCME to find all journal-related CME, complete the online post-test, and claim CME credit.

Declaration of Conflicting Interests
The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Kyle W. Morse, MD, Nicole K. Heinz, PA-C, Jeremy M. Abolade, BS, Joshua Wright-Chisem, MD, Meng Zhang, PhD, Serena Mirza, BS, Linda Alice Russell, MD, and Diyu Pearce-Fisher, BS have declared no potential conflicts of interest. Dana E. Orange, MD, MS, reports relationships with Astra Zeneca MedImmune and Pfizer. Mark P. Figgie, MD, reports relationships with Wishbone, Lima, Insight Medical, HSZ, and Mekanika. Peter K. Sculco, MD, reports relationships with EOS Imaging, Intellijoint Surgical, DePuy Synthes, Lima Corporate, and Zimmer Biomet. Susan M. Goodman, MD, reports relationships with Novartis and Horizon Pharmaceuticals.

Funding
The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This study was supported by the Accelerated Medicines Partnership (AMP) (UH2-AR067691) and Clinical Translational Science Center (UL1-TR002384), Clinical Translational Science Award (# UL1TR001866).

Human/Animal Rights
All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2013.

Informed Consent
Informed consent was obtained from all patients included in this study.

Level of Evidence
Level IV, Prognostic Study

Required Author Forms
Disclosure forms provided by the authors are available with the online version of this article as supplemental material.

References
1. Bell KL, Detweiler M, Yayac S, Chen AF. Preoperative opioid use increases the cost of care in total joint arthroplasty. J Am Acad Orthop Surg. 2021;29:310–316. https://doi.org/10.5435/JAAOS-D-20-00316.
2. Blevins Peratikos M, Weeks HL, Pisansky AJB, Yong RJ, Stringer EA. Effect of preoperative opioid use on adverse outcomes, medical spending, and persistent opioid use following elective total joint arthroplasty in the United States: a large retrospective cohort study of administrative claims data. Pain Med. 2020;21(3):521–531. https://doi.org/10.1093/pm/pnz083.
3. Bonner BE, Castillo TN, Fitz DW, Zhao JZ, Klemt C, Kwon YM. Preoperative opioid use negatively affects patient-reported outcomes after primary total hip arthroplasty. J Am Acad Orthop Surg. 2019;27(22):e1016–e1020. https://doi.org/10.5435/JAAOS-D-18-00658.
4. Burn E, Edwards CJ, Murray DW, et al. Trends and determinants of length of stay and hospital reimbursement following knee and hip replacement: evidence from linked primary care and NHS hospital records from 1997 to 2014. BMJ Open. 2018;8(1):e019146. https://doi.org/10.1136/bmjopen-2017-019146.
5. Chen WS, Liu CY, Lee HT, et al. Effects of intravenous iron saccharate on improving severe anaemia in rheumatoid arthritis patients. Clin Rheumatol. 2012;31(3):469–477. https://doi.org/10.1007/s10067-011-1885-0.
6. Dlott CC, Moore A, Nelson C, et al. Preoperative risk factor optimization lowers hospital length of stay and postoperative emergency department visits in primary total hip and knee arthroplasty patients. J Arthroplasty. 2020;35(6):1508–1515. e2. https://doi.org/10.1016/j.arth.2020.01.083.
7. Farley KK, Anastasio AT, Premkumar A, Boden SD, Gottschalk MB, Bradbury TL. The influence of modifiable, postoperative patient variables on the length of stay after total hip arthroplasty. *J Arthroplasty*. 2019;34(5):901–906. https://doi.org/10.1016/j.arth.2018.12.041.

8. Fujimura K, Haraguchi A, Sakurai R, et al. Have the radiographic characteristics of total knee arthroplasty recipients in rheumatoid arthritis changed after the induction of biologic disease modifying anti-rheumatic drugs? [published online ahead of November 29, 2021]. *Mod Rheumatol*. https://doi.org/10.1093/mr/roa114.

9. Goodman SM, Bykerk VP, DiCarlo E, et al. Flares in patients with rheumatoid arthritis after total hip and total knee arthroplasty: rates, characteristics, and risk factors. *J Rheumatol*. 2018;45(5):604–611. https://doi.org/10.3899/jrheum.170366.

10. Harb MA, Solow M, Newman JM, et al. Have the annual trends of total knee arthroplasty in rheumatoid arthritis patients changed? *J Knee Surg*. 2018;31(9):841–845. https://doi.org/10.1055/s-0037-1615822.

11. Hawker G, Wright J, Coyte P, et al. Health-related quality of life after knee replacement. *J Bone Joint Surg Am*. 1998;80(2):163–173. https://doi.org/10.2106/00004623-199802000-00003.

12. Helmick CG, Felson DT, Lawrence RC, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part I. *Arthritis Rheum*. 2008;58(1):15–25. https://doi.org/10.1002/art.23177.

13. Khalaf W, Al-Rubaie HA, Shihab S. Studying anemia of chronic disease and iron deficiency in patients with rheumatoid arthritis by iron status and circulating hepcidin. *Hematol Rep*. 2019;11(1):7708. https://doi.org/10.4081/hr.2019.7708.

14. Kim SC, Choudhry N, Franklin JM, et al. Patterns and predictors of persistent opioid use following hip or knee arthroplasty. *Osteoarthritis Cartilage*. 2017;25(9):1399–1406. https://doi.org/10.1016/j.joca.2017.04.002.

15. Lee YC, Kremer J, Guan H, Greenberg J, Solomon DH. Chronic opioid use in rheumatoid arthritis: prevalence and predictors. *Arthritis Rheumatol*. 2019;71(5):670–677. https://doi.org/10.1002/art.40789.

16. Liao CY, Chan HT, Chao E, Yang CM, Lu TC. Comparison of total hip and knee joint replacement in patients with rheumatoid arthritis and osteoarthritis: a nationwide, population-based study. *Singapore Med J*. 2015;56(1):58–64. https://doi.org/10.11622/smedj.20150111.

17. Losina E, Walensky RP, Kessler CL, et al. Cost-effectiveness of total knee arthroplasty in the United States: patient risk and hospital volume. *Arch Intern Med*. 2009;169(12):1113–1122. https://doi.org/10.1001/archinternmed.2009.136.

18. Maradit Kremers H, Visscher SL, Moriarty JP, et al. Determinants of direct medical costs in primary and revision total knee arthroplasty. *Clin Orthop*. 2013;471(1):206–214. https://doi.org/10.1007/s11999-012-2508-z.

19. March LM, Barcenilla AL, Cross MJ, Lapsley HM, Parker D, Brooks PM. Costs and outcomes of total hip and knee joint replacement for rheumatoid arthritis. *Clin Rheumatol*. 2008;27(10):1235–1242. https://doi.org/10.1007/s10067-008-0891-3.

20. Morse KW, Heinz NK, Abolade JM, et al. Tranexamic acid does not reduce the risk of transfusion in rheumatoid arthritis patients undergoing total joint arthroplasty. *J Arthroplasty*. 2020;35(9):2367–2374. https://doi.org/10.1016/j.arth.2020.04.029.

21. Muilu P, Rantalaiho V, Kautiainen H, Virta LJ, Puolakka K. Opioid use among patients with early inflammatory arthritides compared to the general population. *J Rheumatol*. 2020;47(8):1285–1292. https://doi.org/10.3899/jrheum.190355.

22. Nettotruf JF, Bailey BS, Burch MB, et al. Arthroplasty rates not increasing in young patients with rheumatoid arthritis: a national database review, 2005 versus 2014. *Arthroplast Today*. 2021;8:118–123. https://doi.org/10.1016/j.artd.2021.02.002.

23. Onuoha KO, Solow M, Newman JM, et al. Have the annual trends of total hip arthroplasty in rheumatoid arthritis patients decreased? *Ann Transl Med*. 2017;5(suppl 3):S35. https://doi.org/10.21037/atm.2017.11.15.

24. Piuzzi NS, Smrdaj GJ, Sakr Esa WA, et al. The main predictors of length of stay after total knee arthroplasty: patient-related or procedure-related risk factors. *J Bone Joint Surg Am*. 2019;101(12):1093–1101. https://doi.org/10.2106/JBJS.18.00758.

25. Ruan RX, Bai CW, Zhang L, et al. Does subcutaneous administration of recombinant human erythropoietin increase thrombotic events in total hip arthroplasty? a prospective thrombelastography analysis. *J Orthop Surg Res*. 2020;15(1):546. https://doi.org/10.1186/s13018-020-02083-w.

26. Shah A, Memon M, Kay J, et al; for McMaster Arthroplasty Collective (MAC) Group. Preoperative patient factors affecting length of stay following total knee arthroplasty: a systematic review and meta-analysis. *J Arthroplasty*. 2019;34(9):2124–2165.e1. https://doi.org/10.1016/j.arth.2019.04.048.

27. Skikne BS, Punnonen K, Caldron PH, et al. Improved differential diagnosis of anemia of chronic disease and iron deficiency anemia: a prospective multicenter evaluation of soluble transferrin receptor and the sTfR/log ferritin index. *Am J Hematol*. 2011;86(11):923–927. https://doi.org/10.1002/ajh.22108.

28. Stranges E, Russo CA, Friedman B. Procedures with the most rapidly increasing hospital costs, 2004–2007: statistical brief #82. Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality; 2006. Available at: http://www.ncbi.nlm.nih.gov/books/NBK53597/. Accessed October 13, 2020.

29. Styrion JF, Koroukian SM, Klika AK, Barsoum WK. Patient vs provider characteristics impacting hospital lengths of stay after total knee or hip arthroplasty. *J Arthroplasty*. 2011;26(8):1418–1426.e1–e2. https://doi.org/10.1016/j.arth.2010.11.008.

30. Suominen P, Möttönen T, Rajamäki A, Irjala K. Single values of serum transferrin receptor and transferrin receptor ferritin index can be used to detect true and functional iron deficiency in rheumatoid arthritis patients with anemia. *Arthritis Rheum*. 2000;43(5):1016–1020. https://doi.org/10.1002/1529-0131(200005)43:5<1016::AID-ANR9>3.0.CO;2-3.

31. Suter LG, Paltiel AD, Rome BN, et al. Placing a price on medical device innovation: the example of total knee arthroplasty: rates, characteristics, and risk factors. *Clin Orthop Relat Res*. 2010;468(11):2355–2365. https://doi.org/10.1093/crj/roq106.

32. Tamboli M, Mariano ER, Gustafson KE, et al. A multidisciplinary patient-specific opioid prescribing and tapering
protocol is associated with a decrease in total opioid dose prescribed for six weeks after total hip arthroplasty. \textit{Pain Med}. \textcopyright 2020,21(7):1474–1481. https://doi.org/10.1093/pm/pnz260.

33. Tan TL, Rondon AJ, Wilt Z, et al. Understanding opioid use after total hip arthroplasty: a comprehensive analysis of a mandatory prescription drug monitoring program. \textit{J Am Acad Orthop Surg}. 2020;28(20):e917–e922. https://doi.org/10.5435/JAAOS-D-19-00676.

34. Vandenbroucke JP, von Elm E, Altman DG, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. \textit{Int J Surg}. 2014;12(12):1500–1524. https://doi.org/10.1016/j.ijjsu.2014.07.014.

35. Weiss G, Schett G. Anaemia in inflammatory rheumatic diseases. \textit{Nat Rev Rheumatol}. 2013;9:205–215. https://doi.org/10.1038/nrrheum.2012.183.

36. Young BL, Watson SL, Perez JL, McGwin G, Singh JA, Ponce BA. Trends in joint replacement surgery in patients with rheumatoid arthritis. \textit{J Rheumatol}. 2018;45(2):158–164. https://doi.org/10.3899/jrheum.170001.