

Outcomes in rheumatoid arthritis patients undergoing total joint arthroplasty

Rheumatoid arthritis (RA) is a systemic inflammatory disease that targets synovial joints and can lead to joint destruction. While most total knee and total hip arthroplasty procedures are performed in patients with osteoarthritis (OA), they are also effective in treating advanced joint destruction of the knee and hip in patients with RA, although differences have been reported between these groups. Patterns of use, complications and outcomes may differ for patients with RA compared with patients with OA. This review will address the change in utilization of arthroplasty in RA, differences in comorbidities and adverse events in patients with RA compared with OA, and the similarities and differences in pain and function outcomes after total knee arthroplasty and total hip arthroplasty.

Epidemiology: incidence of arthroplasty

The course of the rheumatoid arthritis (RA) has changed since the introduction and increasing use of potent disease-modifying antirheumatic drugs (DMARDs). The widespread use of DMARDs, which have the potential to arrest synovitis, have led to improvements in the overall status of patients with RA. Comparing patients in a 1985 cohort to RA patients 15 years later, Pincus and colleagues described significantly fewer swollen and tender joints, better function as measured by Health Assessment Questionnaires scores, and decreased erosions on radiographs for the later patients, findings associated with significantly higher utilization of DMARDs, particularly methotrexate [1,2]. The addition of biologic DMARDs such as the TNF- α inhibitors (TNFi) led to further improvements in the status of RA patients, with greater gains in function and health-related quality of life, and decreases in radiographic evidence of joint damage [3–6]. Others, however, have noted that contemporary patients at the time of presentation between 1995 and 2000 had lower disease activity scores and milder RA than patients presenting in 1985–1990. This observation

was made prior to the initiation of therapy, suggesting a change in the natural course of the disease [7], with evolution into a milder disease overall [8]. Whether attributable to milder disease or the widespread use of potent medications, a change in the utilization of total knee arthroplasty (TKA) and total hip arthroplasty (THA) surgery for RA patients has been described in association with the change in the course of RA.

Utilization of orthopedic surgery has historically been high for RA patients, with 30–50% of patients followed longitudinally undergoing orthopedic procedures, 24% of which were large joint arthroplasty [9,10]. Recent reports utilizing the Swedish National Inpatient Registry describe a significant 24% decrease in all RA-related hospital admissions for lower extremity surgery between 1987 and 1996, and 8% from 1997 to 2001 [11]. Similar declines in hip and knee arthroplasty rates were also reported using Finnish, as well as Swedish registry data [12,13]. Similar decreases in rates of joint surgery were reported for RA patients in Minnesota, where 27.3% of patients diagnosed with RA from 1980 to 1994 had joint surgery within 10 years of diagnosis, compared with 19.5% in a later cohort diagnosed between 1995 and

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2007 [14]. A study analyzing data from three different sources for ten states covering the years 1991–2005 noted minimal change in the rate of arthroplasty for RA, while over the same time period the rate of arthroplasty for osteoarthritis (OA) almost doubled from 124.5 per 100,000 up to 247.5 per 100,000 [15,16]. It appears that the change in utilization of TKA and THA for RA patients is leveling off [17]. In addition, the proportion of TKA performed for RA was 21% when assessed in 1991 [18] and is now 2.41–3.4% [15,16,19–21]. Although up to 13% of arthroplasty recipients were diagnosed with RA in a recent Canadian arthroplasty report – this report utilized data recorded by surgeons at the time of surgery, when the gross pathology of RA and OA may be similar (in some cases) [22]. Interestingly, the age at which RA patients undergo arthroplasty has increased significantly from 63.4 to 64.5, and the increase in age for juvenile inflammatory arthritis was even greater, increasing from 30.9 to 36.7 years of age, while the age of arthroplasty for those with non-inflammatory arthritis decreased from 71.5 to 69.0 [15,16]. Among patients with OA, the greatest increase in arthroplasty rates has been seen in individuals under 60 years of age [23]. Moreover, aging baby boomers expect to continue to participate in sports past the age of 80, and RA patients may have the same expectations. Sports injuries may contribute to the utilization of arthroplasty [24–26].

To summarize, the rates for TKA and THA have decreased for patients with RA, co-incident with a marked increase in the rates of TKA and THA for osteoarthritis. Importantly, the age at which RA patients undergo arthroplasty is increasing, while the opposite is true for patients with OA [23].

Comorbidities & adverse events

THA and TKA are extremely successful operations, and rates for complications and adverse events are low. However, significant complications may occur, such as venous thromboembolism (VTE), infection, dislocation and death. While there are provider-related risk factors for increased adverse events such as hospital and surgeon volume [19,27,28], patient level factors also contribute to risk [29]. Certain comorbidities, which contribute to perioperative risk such as cardiovascular disease and VTE risk, are increased in patients with RA, yet the impact of this high risk status on complications of THA and TKA is not clear. While age, complicated diabetes mellitus and poor preoperative status determined by the American Society of Anesthesiologists score are recognized as risk factors for short-term complications after THA and TKA [28,30], the risk contributed by RA has not been as well defined. In fact, when the current literature was reviewed

systematically, patients with RA were at increased risk for infection after TKA, and dislocation after THA when compared with OA [29], but other complications such as VTE and cardiac events were not increased in RA. Importantly, 90-day mortality was not increased in RA patients after THA or TKA in comparison to OA patients [20,21,29].

RA increases the overall risk of VTE compared with non-RA, with an incidence rate of 6.1/1000 patient years, which was 2.4% higher than non-RA [31]. While the risk of VTE is increased in RA patients [32], the increase in VTE risk associated with hospitalization is no different for RA than for the general population [33]. Additional information regarding VTE risk pertaining to THA and TKA was gained when large administrative databases were queried to determine the rate of complications by comparing RA to OA. For RA patients undergoing TKA, there was no increase in VTE compared with OA patients after controlling for potential confounders, and cumulative aggregated adverse events (pulmonary embolism, deep venous thrombosis, cerebrovascular event, pulmonary compromise, sepsis, cardiac adverse events) were no greater for RA patients [20,21]. For RA patients undergoing THA, there was no difference in VTE risk for RA patients compared with OA, but cumulative aggregate adverse events were higher for RA patients [20]. Other studies have also failed to find an increase in rates of VTE in RA patients undergoing THA and TKA compared with OA patients [29]. One study found that THA recipients with RA were actually at decreased risk for VTE relative to those with OA [1]. This suggests that although patients with RA are at increased risk for VTE, perioperative management decisions may have mitigated the risk.

Cardiac events are a serious potential complication of TKA and THA. Arthroplasty is considered an intermediate risk procedure by the American College of Cardiology/American Heart Association, which indicates a 5% risk of cardiac events such as myocardial infarction [34]. A perioperative myocardial infarction rate of 0.6% was described in a study of approximately 8000 inpatient surgeries. This risk increased to 6.5% for patients with a prior history of cardiovascular disease [35] such as arrhythmia, coronary artery disease or valvular cardiac disease [36]. RA is a recognized independent risk factor for cardiovascular disease with a reported incidence rate of myocardial infarction of 3.97 [37–41]. In addition to traditional risk factors such as hypertension, hypercholesterolemia, diabetes mellitus and cigarette smoking, other factors which increase cardiac risk among patients with RA include poor functional status and disability, RA-related damage and RA disease activity [42,43]. In

fact, the risk of myocardial infarction in RA has been shown to be as high as the risk seen in diabetes mellitus [44]. However, when large administrative databases have been used to identify postoperative complications, no increase in cardiovascular events complicating TKA and THA has been observed for RA patients [20,21]. In fact, when RA patients were directly compared with patients with diabetes mellitus or patients with neither condition in regard to perioperative mortality and cardiac events, RA patients were significantly less likely than diabetes mellitus patients to have a postoperative cardiac event, and RA was not an independent risk factor for a cardiac event or perioperative mortality [45]. Traditional cardiac risk assessment tools are less useful for RA, as they depend on cholesterol levels, which are typically low in RA [46]. Patients prior to arthroplasty are rarely able to demonstrate adequate functional capacity (four metabolic equivalents) through exercise to gauge cardiac reserve [34], it nonetheless appears that current clinical practices for cardiovascular screening and therapy are sufficient to normalize the risk of perioperative cardiac complications for RA.

Prosthetic joint infection is a serious complication of arthroplasty. According to an analysis of the Nationwide Inpatient Sample data from 2001 to 2010, there is an overall 2.4% incidence of infection following TKA, and an incidence of 2.0% following THA [47]. RA patients are at nearly double the risk of hospitalization for infection compared with patients in the general population [48] and the specific risk of revision TKA for prosthetic joint infection is 1.6-times greater than OA [49,50]. An overall infection rate of 3.7% for RA after arthroplasty has been reported, which increased to 5.9% in revision arthroplasty cases. The most significant risk factor for infection was a prior prosthetic joint infection, with 30% of infections occurring in a joint which was previously infected [51]. Medications used for the therapy of RA have clear associations with increased infection risk [52,53]. However, while use of TNFi therapy has been associated with prosthetic joint infection in some studies, the effect has not been consistently described [54–57]. Given the standardized infection ratio for THA of 0.46 at a single high volume center, an estimated 55,890 cases would be needed to demonstrate a significant increase in infection risk between patients on versus not on TNFi therapy [58].

Surprisingly, given the complexity of the surgery for patients with RA undergoing THA and TKA, most surgeries are performed at nonteaching hospitals, in similar proportions to OA patients. 78% of RA and 79% of OA undergo TKA in nonteaching hospitals. For THA, 76% of RA and 75% of OA receive their surgery in nonteaching hospitals.

Additional RA-specific factors complicate this analysis. Corticosteroids, which are frequently used in RA, clearly increase overall infection risk. The effect on infection risk for corticosteroid is highest with current use, but cumulative and absolute dose also influence the risk [59,60]. When biologic DMARDs are discontinued, corticosteroids may be used to treat flares in disease activity, which may contribute to infection risk [48]. However, active RA is also a risk factor for infection and could further complicate analysis [61]. When current literature was systematically reviewed and the analysis was adjusted for potential confounders, the increase in infection risk for RA patients could only be demonstrated after TKA, not THA [29]. This was further demonstrated in a study utilizing large administrative databases, which found an increased risk for infection following TKA in persons with RA relative to those with OA (adjusted hazard ratio [HR]: 1.47; 95% CI: 1.05–2.05; $p = 0.03$) [62].

Additional factors may contribute to the risk of infection in RA. Anemia is common in RA [63], and RA patients are more likely to require transfusion with TKA and THA [20,21] than OA. Since allogeneic transfusion is a risk factor for prosthetic joint infection [64], preoperative evaluation and therapy of anemia prior to arthroplasty might improve outcomes for RA patients. RA is highly associated with smoking [65], and smoking is a known risk factor for surgical complications, including infection [66–68]. Smoking cessation can be recommended prior to arthroplasty. The prevalence of periodontal disease is increased in patients with RA, correlating with RA severity [69,70]. RA patients are more likely to have *Staphylococcus aureus* colonization of the oropharynx than healthy controls, 56 versus 24% [67,68]. While coagulase-negative staphylococcus is the most common causative organism overall in prosthetic joint infection, in RA, *S. aureus* is the more frequent pathogen [71]. Given the tremendous morbidity and expense of prosthetic joint infection, additional interventions are clearly still needed to decrease the risk of infection for RA, and attention to smoking cessation, oral hygiene and anemia might improve infection risk for RA.

Dislocation following THA was recently recognized as a risk in patients with RA after THA. A systematic review of complications after THA for RA versus OA patients, meta-analysis of unadjusted comparative data revealed an increased risk of dislocation for RA with an odds ratio of 2.74 (95% CI: 1.73–4.34). This finding persisted in four additional studies in which the data were adjusted for age, sex, surgical approach and surgical volume (odds ratio: 2.16; 95% CI: 1.52–3.07) [29]. This was further demonstrated in a study utilizing administrative databases, which found

an increased risk for dislocation following THA in persons with RA (adjusted HR: 1.91; 95% CI: 1.29–2.82; $p = 0.001$) [29].

Volume–outcome relationships for the occurrence of complications (e.g., mortality, deep vein thrombosis, early revision) following joint replacement have been demonstrated [22], with the risk for complications roughly inversely proportional to the volume of the operating surgeon [19,72–74]. A recent study that utilized administrative data demonstrated that increased surgeon experience in persons with RA (defined as the number of total joint arthroplasty (TJA) procedures in patients with RA performed by the surgeon annually) was associated with a reduced risk for complications following TJA in persons with RA (adjusted HR: 0.81 per 10 cases; 95% CI: 0.71–0.93; $p = 0.002$), even after controlling for surgeon volume overall (adjusted HR: 0.84 per additional 10 RA TJA cases; 95% CI: 0.69–0.95; $p = 0.009$). This indication-specific benefit of experience is consistent with the unique challenges posed by performance of TJA in persons with RA, including bone destruction and tendon rupture [75–92].

An additional concern for the surgeon operating on a patient with polyarticular disease is to consider the sequence of surgery when multiple joints have reached an end stage. Position and function of the limb to be addressed informs this decision. If the patient has a flexion contracture of the knee and an equinus deformity of the foot, the foot may be addressed first to produce a pain free and plantigrade foot, necessary to rehabilitate the replaced knee. Similarly, the hip should be replaced prior to knee replacement to facilitate rehabilitation. In general, the lower extremity should be addressed prior to the upper extremity so that the patient is free of assistive devices such as canes or walkers prior to upper extremity surgery [93].

Outcomes

While the majority of THA and TKA are performed for patients with OA, THA and TKA remain important therapeutic options for patients with RA who develop end-stage joints. Historically, patients with RA had significant relief of pain after THA and TKA, but less improvement in function and health-related quality of life [7–8,94–97]. Since RA has become a milder disease [7], related to therapy [2], as well as a possible change in the natural history of the disease [8], it is possible that the differences in THA and TKA for patients with RA might have changed as well. Examining a contemporary cohort of RA patients with a high utilization of DMARD use, pain and function outcomes after TKA were as good as outcomes for OA patients, and RA was not an independent risk factor for poor outcomes after adjusting for confounders such as age and gender [98].

Including only patients with surgery performed after 2007 may explain the improved outcomes seen in this study, possibly due to improved surgical techniques and advances in implant design, as well as the improved status of contemporary RA patients. Similar improvements in function, as well as pain have been reported for RA patients undergoing lower extremity surgery, when cases operated on between 2007 and 2009 were studied [99], while recent studies utilizing cohorts dating to 1993 continue to report poorer function for RA patients undergoing TKA compared with OA patients [95]. However, surprisingly, for THA drawn from the same contemporary arthroplasty registry, RA remained a significant risk factor for poor function [100]. Defining poor function as a Western Ontario and McMaster University Osteoarthritis Index (WOMAC) score ≤ 60 , function after THA for RA patients operated on after 2007 was more likely to be poor. Other factors might contribute to the disparity in outcomes such as baseline function, or contralateral or ipsilateral joint involvement [101–103], but these factors should have been similar in patients drawn from the same cohort undergoing TKA. Age, BMI, baseline WOMAC function and use of DMARDs were similar between the RA patients undergoing THA compared with the RA patients undergoing TKA. Multiple factors associated with poorer outcomes for OA patients such as increased comorbidity, poor baseline function and female gender [101,104,105] were adjusted for in the analysis, and were not risk factors for RA patients, for either TKA or THA.

Other differences between OA and RA patients, which might influence arthroplasty outcomes, have emerged. Higher expectations of pain relief independently predict better outcomes for OA patients at 1 year [106] and most patients with OA expect significant improvements in pain and function from TKA [107]. However, expectations for improvement were lower for RA patients, despite matching for factors known to influence expectations such as age, gender, prior surgery and preoperative function [106,108,109]. Additional analysis revealed that the differences were driven by the RA patients not on biologic DMARDs. Patients on biologic DMARDs had expectations that were no different from the expectations of OA patients, while those on synthetic DMARDs or no therapy had significantly lower expectations [110].

The overall economic burden of RA is significantly greater than OA at the individual level [111,112], a finding also seen in relation to arthroplasty. Although THA and TKA are considered cost-effective procedures [113], cost was increased for RA undergoing THA and TKR compared with OA. Hospital charges (mean US\$) were higher for RA patients for THA, 49,821

versus 47,110 ($p = 0.001$). Hospital costs were also higher for TKA; RA patient's costs were US\$16,678 versus US\$16,188 ($p = 0.001$) for OA patients [20,21]. The cost differential was also seen in Australian RA patients, and while cost diaries revealed a significant decrease in out-of-pocket costs after surgery for RA and OA patients, RA patients' costs remained almost double the costs of OA patients [114]. Not surprisingly, the decrease in arthritis attributable healthcare costs seen after arthroplasty may not be seen in patients with a systemic polyarticular disease [115].

Conclusion & future perspective

In conclusion, THA and TKA are important options for appropriately selected patients with RA, who can expect significant improvement in pain and function. However, differences in adverse events, cost and outcomes persist when RA patients are compared with OA patients, and outcomes for RA patients undergoing

THA continue to be poorer than for OA patients. Improved outcomes for RA patients undergoing arthroplasty may be linked to improved disease management. One can speculate that increasingly effective therapy for RA may lead to fewer differences between RA and OA. Medication management in the perioperative period will likely remain a challenge, as the perioperative cost of increased infection risk will continue to be balanced against disease flare.

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Executive summary

Epidemiology

- Patients with rheumatoid arthritis (RA) have better overall function, associated with high utilization of disease-modifying therapy.
- RA patients continue to utilize arthroplasty at a high rate.
- The age of arthroplasty is increasing for RA, while the age of arthroplasty is decreasing for patients with osteoarthritis.

Comorbidities & adverse events

- RA patients have a higher prevalence of atherosclerotic cardiovascular disease, but do not have a higher incidence of cardiac events after arthroplasty.
- Prosthetic joint infection is increased in RA patients undergoing total knee replacement.
- Dislocation rates are increased in RA patients undergoing total hip replacement.
- Experience specifically with patients with RA, not just overall surgical experience is important in optimizing arthroplasty outcomes for patients with RA.
- Medications taken at the time of surgery may contribute to the risk of infection.

Outcomes

- RA patients undergoing total hip arthroplasty (THA) are more likely than osteoarthritis patients to have poor outcomes measuring pain and function 2 years after THA.
- RA is an independent predictor of poor function for THA.
- RA patients undergoing total knee arthroplasty have worse baseline pain and function, but have 2-year outcomes which are just as good as osteoarthritis patients.

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