SUPPLEMENTARY APPENDIX 5: Evidence Report

2022 American College of Rheumatology/American Association of Hip and Knee Surgeons Guideline for the Perioperative Management of Antirheumatic Medication in Patients with Rheumatic Diseases Undergoing Elective Total Hip or Total Knee Arthroplasty

Perioperative Guideline Update Evidence Tables (Glossary page 20)

PICO 1 (relates to more detailed, "voting PICOs" 1-3, 5-10)

In patients with RA, AS, PsA, JIA, severe or not severe SLE undergoing THA or TKA and who are receiving one or more of the candidate drugs, what is the effect of stopping the drug prior to surgery versus continuing?

Summary: There are 4 observational studies that provided indirect evidence to this PICO question, mostly with RA patients, three with primary THA/TKA (1-3) and one with TKA revision (4). In one study (1) the surgical site infections were not associated with continuing medication with DMARDs, but due to the low event rate this should be interpreted with caution. The rates of PJI (1.3%) and reoperation (1%) were low but no comparison was made with medications stopped. In a study (2) comparing groups with or without combination of DMARD's with GC, where DMARDs were stopped four weeks before operation, no significant differences were noted. In other study (3) discontinuation of a biologic > 2 dose intervals prior to surgery did not increase the risk of flares, but the use of MTX at the time of surgery did not independently protect against the risk of flares. Another study (4) compared to OA patients, RA patients treated with csDMARDs, TNFi and GC's with all medications stopped 14 days before revision TKA had similar post-operative results for the knee, despite the initial local joint status and general health status were worse in RA than in OA patients. However, postoperative complications were more frequent with RA.

Quality of evidence across all critical outcomes: Very low

Ref ID, Author, year	Study type	Duration	Population Description	Treatment given to relevant population	Results
14 Borgas, 2020 (1)	Case-series study	Follow-up 1 year	395 patients with RD, undergoing 494 THA/TKA operations	78% used Hydroxychloroquine, Methotrexate, or Sulfasalazine, 32% used TNFi perioperatively and continued treatment.	Surgical site infection rate was 3.8% (n = 19), 12 (2.4%) were superficial; periprosthetic joint infection rate was 1.4% (n = 7) after TKA. No correlation could be found between the total number of SSI and treatment with prednisolone, methotrexate, TNF-alpha inhibitors or a combination of these treatments.

					Periprosthetic joint infection occurred in only 1 patient medicating perioperatively with a TNF-alpha inhibitor and in 4 treated with MTX. Six deaths occurred within 1 year of surgery, none was linked directly to PJI or surgery. Four patients underwent reoperation within 1 year of surgery.
24 Ren, 2021 (2)	Case-control study	Average follow-up 11.4 years	56 RA patients undergoing 91 TKAs	A. Control group (20 patients, no anti-rheumatic drugs used); B. DMARD group (15 patients, conventional or biologic DMARD use with no GC) C. Co-therapy group (21 patients, DMARD and GC use). All bDMARDs were stopped 4 weeks before surgery and restarted at least 1 week postoperatively depending on medication, wound healing, and disease status.	GC with DMARDs (group C) achieved larger/increased range of motion (ROM) (C:122.17 vs A:108.31 vs B:108.07, p =0.001, partial eta squared (η2 p) = 0.18) at 1 year, better HSS score (C, 83.01 vs A, 79.23 vs B, 77.35, p = 0.049, η2 p =0.067), pain relief (C, 1.09 vs A, 1.17 vs B, 1.75, p = 0.02, η2 p = 0.094), and ROM (C, 130.81 vs A, 112.82 vs B, 113.58, p= 0.001, η2 p = 0.142).
84 Goodman, 2018 (3)	Case-series	6 weeks after surgery	120 RA patients undergoing THA/TKA	GC and MTX continued, a biologic discontinued > 2 dose intervals prior to surgery	Neither disease duration nor medication use, including biologics, increased the risk of flares; discontinuation of a biologic > 2 dose intervals prior to surgery did not increase the risk of flares. Use of MTX at the time of

					surgery did not independently protect against the risk of flares.
132 Hernigou, 2017 (4)	Case-series	10 years	45 RA patients who had undergone revision TKA	csDMARDs, TNFi and GC's stopped 14 days before TKA	5 and 10-year mortality rates, from 1998 to 2010, for RA patients were 11 % (5/45) and 20 % (9/45). The mean length of hospitalization for RA patients was 9.5 days. The rate of adverse events RA 38% (17/45). Wound healing at an average 23 days (range, 18–30) in RA knee. The mean overall changes in knee scores for the RA revision group 86 points ± 12; higher functional scores 11% (5/45); no improvement 4% (2/45). Revision among RA patients 9% (4/45).

Bibliography:

1. Borgas Y, Gülfe A, Kindt M, Stefánsdóttir A**.** Anti-rheumatic treatment and prosthetic joint infection: an observational study in 494 elective hip and knee arthroplasties. BMC Musculoskeletal Disorders. 2020;21(1):410.
2. Ren Y, Yang Q, Luo T, Lin J, Jin J, Qian W, et al. Better clinical outcome of total knee arthroplasty for rheumatoid arthritis with perioperative glucocorticoids and disease-modifying anti-rheumatic drugs after an average of 11.4-year follow-up. Journal of Orthopaedic Surgery and Research. 2021;16(1):84.
3. Goodman SM, Bykerk VP, DiCarlo E, Cummings RW, Donlin LT, Orange DE, et al. Flares in Patients with Rheumatoid Arthritis after Total Hip and Total Knee Arthroplasty: Rates, Characteristics, and Risk Factors. The Journal of Rheumatology. 2018;45(5):604.
4. Hernigou P, Dubory A, Potage D, Roubineau F, Flouzat-Lachaniette CH**.** Outcome of knee revisions for osteoarthritis and inflammatory arthritis with postero-stabilized arthroplasties: a mean ten-year follow-up with 90 knee revisions. Int Orthop. 2017;41(4):757-63.

PICO 2 (relates to more detailed, "voting PICOs"4,11)

In patients with RA, AS, PsA, JIA, severe or not severe SLE undergoing THA or TKA who are receiving one or more of the candidate drugs in whom one has decided to stop the drug, what is the effect of stopping the drug early prior to surgery versus stopping late?

There are three studies that provided evidence to this PICO question. For people with hip fracture and other surgeries, there was no significant difference in the risk of mortality or readmission in patients who received their last infusion of intravenous abatacept <4 weeks before surgery compared with those who received the last infusion 4 to <8 weeks or ≥8 weeks before surgery (1), with 30-day readmission reference timing < 4 weeks vs. 4–8 weeks OR 1.00 (0.65–1.54), and < 4 weeks vs. ≥ 8 weeks 0.82 (0.46–1.47) (2). There were no significant differences in outcomes with ABA stop timing < 4 weeks vs. 4–8 weeks in hospitalized infections: <4 weeks: 67/732 (9.1%), 4-8 weeks: 67/862 (7.8%), non-urinary hospitalized infections <4weeks: 45/732 (6.2%), 4-8 weeks: 45/862 (5.2%), and PJI: 4 weeks: 13 (2.1 incidence per 100 person-years), 4-8 weeks 18 (2.5 incidence per 100 person-years). However, risk of prolonged length of stay was significantly greater in patients with ABA stop timing of 4–8 weeks, and patients with ABA stop timing < 2 weeks had greater risk of hospitalized infection [OR 1.63 (0.91–2.91)], PJI [HR 1.48 (0.45–4.93)], non-urinary hospitalized infection [OR 1.45 (0.70–2.99)] (2). One study of infliximab stop timing <4 weeks versus 8–12 weeks was not associated with an increase in infection within 30 days [OR 0.90, 95% CI 0.60–1.34)], the rate of PJI was 2.9 per 100 person-years and was not increased in patients with stop timing <4 weeks versus 8–12 weeks [HR 0.98, 95% CI 0.52–1.87)], and for hospitalized surgical-site infection within 90 days after surgery - infliximab stop timing <4 weeks was not associated with increased risk (OR 0.87 [95% CI 0.41–1.90]). (3). For prolonged length of stay > 5 days, infliximab stop timing <4 weeks versus 8–12 weeks was associated with lower risk of prolonged length of stay (OR 0.61 [95% CI 0.37–0.99]) (3).

Quality of evidence across all critical outcomes: Very low

Ref ID, Author, year	Study type	Duration	Population Description	Treatment given to relevant population	Results
94 George, 2020 (1)	Retrospective cohort study	Follow-up 2 years	2208 RA patients undergoing 3585 hip fracture repair (33%), 5025 abdominopelvic and 2167 cardiac surgeries	Intravenous abatacept or infliximab within 6 months of surgery	Among 2208 patients who received infliximab and 827 who received intravenous abatacept within 6 months of surgery, there was no significant difference in the risk of mortality or readmission in patients who received their last infusion <4 weeks before surgery compared with those who received the last infusion 4 to <8 weeks or ≥8 weeks before surgery after adjusting for potential confounders

196 George, 2019 (2)	Retrospective cohort study	Mean follow-up time of 2.5 years	1780 RA patients who underwent elective primary or revision THA or TKA	ABA reference stop timing < 4 weeks vs. 4–8 weeks or vs. > 8 weeks or vs. < 2 weeks	There were no significant differences in outcomes with ABA stop timing < 4 weeks vs. 4–8 weeks hospitalized infection OR 0.93 (0.65–1.34); < 4 weeks vs. ≥ 8 weeks OR 1.13 (0.73–1.77) Non-urinary hospitalized infection: reference timing < 4 weeks vs. 4–8 weeks OR 0.93 (0.60–1.44); < 4 weeks vs. ≥ 8 weeks OR 0.97 (0.57–1.66). PJI: < 4 weeks vs. 4–8 weeks: HR 1.29 (0.62–2.69), < 4 weeks vs. ≥ 8 weeks HR 1.20 (0.48–3.05) 30-day readmission reference timing < 4 weeks vs. 4–8 weeks OR 1.00 (0.65–1.54); < 4 weeks vs. ≥ 8 weeks 0.82 (0.46–1.47). Risk of prolonged length of stay was significantly greater in patients with ABA stop timing of 4–8 weeks [OR 1.74 (1.17–2.58)] or ≥8 weeks [OR 2.26 (1.41–3.62)] vs. < 4 weeks. Patients with ABA stop timing < 2 weeks had greater risk of hospitalized infection [OR 1.63 (0.91–2.91)], PJI [HR 1.48 (0.45–4.93)], non-urinary hospitalized infection [OR 1.45 (0.70–2.99)], and 30-day readmission [1.23 (0.60–2.51)] vs. stop timing 2–4 weeks.
143 George, 2017 (3)	Retrospective cohort study	90 days	Patients with RA, IBD, psoriasis, PsA, or AS who undergone THA or TKA	infliximab within 6 months of THA or TKA Infliximab stop timing <4 weeks versus 8–12 weeks	Infliximab stop timing <4 weeks versus 8–12 weeks was not associated with an increase in infection within 30 days (OR 0.90, 95% CI 0.60–1.34). The rate of PJI was 2.9 per 100 person-years and was not increased in patients with stop timing <4 weeks versus 8–12 weeks (HR 0.98, 95% CI 0.52–1.87). Prolonged length of stay >5 days in 197 surgeries (4.7%); infliximab stop timing <4 weeks versus 8–12 weeks was associated with lower risk of prolonged length of stay (OR 0.61 [95% CI 0.37–0.99]). Hospitalized surgical-site infection within 90 days after surgery - infliximab stop timing <4 weeks was not associated with increased risk (OR 0.87 [95% CI

0.41–1.90]). Mortality in 4 patients (0.1%) within 30 days, 14 (0.3%) within 90 days, and 55 (1.3%) within 1 year.

Bibliography:

1. George MD, Baker JF, Winthrop KL, Goldstein SD, Alemao E, Chen L, et al. Immunosuppression and the risk of readmission and mortality in patients with rheumatoid arthritis undergoing hip fracture, abdominopelvic and cardiac surgery. Ann Rheum Dis. 2020;79(5):573-80.
2. George MD, Baker JF, Winthrop K, Alemao E, Chen L, Connolly S, et al. Timing of Abatacept Before Elective Arthroplasty and Risk of Postoperative Outcomes. Arthritis Care Res (Hoboken). 2019;71(9):1224-33.
3. George MD, Baker JF, Hsu JY, Wu Q, Xie F, Chen L, et al. Perioperative Timing of Infliximab and the Risk of Serious Infection After Elective Hip and Knee Arthroplasty. Arthritis Care Res (Hoboken). 2017;69(12):1845-54.

PICO 3 (relates to more detailed, "voting PICOs" 12)

In patients with RA, AS, PsA, JIA, severe or not severe SLE undergoing THA or TKA who are receiving one or more of the candidate drugs in whom one has decided to stop the drug, what is the effect of restarting the drug early after surgery versus restarting late?

There are two observational case-control studies that provided indirect and direct evidence to this PICO question. In one study (1) the time of restart csDMARDs, TNFi and GC's was 14 days without comparator group, thus, making it unclear if the results could have been otherwise different. Another study (2) had infliximab restarted within 4 weeks, 4–8 weeks, 8–12 weeks, 12–16 weeks, and ≥16 weeks or never restarted in different patients, and it showed that patients who had restarted infliximab at any given time had lower rates of PJI than those who had not yet restarted (adjusted HR 0.50 [95% CI 0.28–0.89]).

Quality of evidence across all critical outcomes: Very low

Ref ID, Author, year	Study type	Duration	Population Description	Treatment given to relevant population	Results
132 Hernigou, 2017 (1)	Case-series	10 years	45 RA patients who had undergone revision TKA	csDMARDs, TNFi and GC's restarted 14 days after TKA	5 and 10-year mortality rates for RA patients were 11 % (5/45) and 20 % (9/45). The mean length of hospitalization for RA patients was 9.5 days. The rate of adverse events RA 38% (17/45). Wound healing at an average 23 days (range, 18–30) in RA knee. The mean overall changes in knee scores for the RA revision group 86 points ± 12; higher functional scores 11% (5/45); no improvement 4% (2/45). Revision among RA patients 9% (4/45).
143 George, 2017 (2)	Retrospective cohort study	90 days	4288 patients with RA, IBD, psoriasis, PsA, or AS who	Infliximab was restarted within 4 weeks, 4–8 weeks, 8–12 weeks, 12–16 weeks, and ≥16 weeks or never restarted.	Patients who had restarted infliximab at any given time had lower rates of PJI than those who had not yet restarted (adjusted HR 0.50 [95% CI 0.28–0.89]). Adding infliximab restart timing as a time-varying covariate to multivariable models did not change stoptiming associations.

undergon
e THA or
TKA

Bibliography:

1. Hernigou P, Dubory A, Potage D, Roubineau F, Flouzat-Lachaniette CH**.** Outcome of knee revisions for osteoarthritis and inflammatory arthritis with postero-stabilized arthroplasties: a mean ten-year follow-up with 90 knee revisions. Int Orthop. 2017;41(4):757-63.
2. George MD, Baker JF, Hsu JY, Wu Q, Xie F, Chen L, et al. Perioperative Timing of Infliximab and the Risk of Serious Infection After Elective Hip and Knee Arthroplasty. Arthritis Care Res (Hoboken). 2017;69(12):1845-54.

PICO 4 (relates to more detailed, "voting PICOs" 13)

In patients with RA, AS, PsA, JIA, severe or not severe SLE undergoing THA or TKA who are receiving chronic glucocorticoids, what is the effect of administering supra-physiologic doses of glucocorticoids perioperatively (stress-dose corticosteroids) vs. continuing the usual glucocorticoid dose?

One study (1) found for this PICO, where pre-operative use of stress-steroid dose was not significantly associated with an increase in adverse events in SLE patients undergoing, but the sizes of the patient groups were small. Another study (2) concluded that patients with higher GC exposure were more likely to have hyperglycemia and other complications and that the risk of short-term complications is increased by 8.4% for every 10-mg increase in GC dose.

Quality of evidence across all critical outcomes: Very low

Ref ID, Author, year	Study type	Duration	Population Description	Treatment given to relevant population	Results
191 Fein, 2016 (1)	Case-control study	26 weeks follow-up	52 SLE patients with TKA	16 patients on stress-dose GCs, and 36 no GC	AEs were not increased among patients on stress-dose steroids: 37.5% of SLE patients on stress-dose steroids had any AE vs. 38.9% of SLE patients not on stress-dose steroids.
Chukir, 2021 (2)	Retrospective case-control	Short postoperative	432 RA patients who underwent THA and TKA	387 on stress-dose GC, 45 non-GC	Hypotension: GC 55 (14%), non-GC 5 (11%) 0.57 Vasopressor use: GC 40 (10%), non-GC 3 (7%) 0.44 LOS, midnights [IQR]: GC 3.0 [2.0-4.0], non-GC 3.0 [2.0-4.0] Complications: GC 63 (16%), non-GC 8 (2%) Hyperglycemia: GC 49 (78%), non-GC 7 (88%) CAUTI: GC 6 (10%), non-GC 0 Sepsis: GC 3 (5%), non-GC 0 PJI: GC 2 (3%), non-GC 0 SSI: GC 2 (3%), non-GC 1 (12%) DVT: GC 1 (2%), non-GC 0

Bibliography:

1. Fein AW, Figgie CA, Dodds TR, Wright-Chisem J, Parks ML, Mandl LA, et al. Systemic Lupus Erythematosus Does Not Increase Risk of Adverse Events in the First 6 Months After Total Knee Arthroplasty. J Clin Rheumatol. 2016;22(7):355-9.
2. Chukir T, Goodman SM, Tornberg H, Do H, Thomas C, Sigmund A, et al. Perioperative Glucocorticoids in Patients With Rheumatoid Arthritis Having Total Joint Replacements: Help or Harm? ACR Open Rheumatol. 2021.

PICO 5 (this PICO is really background data and not a true PICO, it was background on risk of DMARDs overall- NOT surgically associated risk)

No new evidence available

PICO 6 (this PICO is background data and not a true PICO, and is risks of surgery for rheumatic disease patients without analysis of medication risks)

What is the background risk for adverse events associated with THA or TKA in patients with RA, SpA, JIA, or SLE independent of the use of anti-rheumatic medications of interest?

Summary: There are 14 observational studies that provided indirect evidence to this PICO question, comparing inflammatory rheumatic diseases to osteoarthritis. One study (1) concluded that patients with AS are at increased risk for complications after THA. Another study (2) concluded that spondyloarthritis was associated with a higher risk of implant infection after TKA, but not THA, and was associated with lower in-hospital mortality rates after THA/TKA. The studies that compared RA with OA as a reference population concluded that during perioperative period patients with RA did not suffer increased odds of most in-hospital complications and in-hospital mortality for a revision TKA (3), but other studies concluded that RA was a risk factor for infection after THA/TKA (4), had an increased proportion of patients requiring blood transfusions, had a longer mean length of stay and the incidence of pneumonia and postoperative bleeding that required transfusion was higher in RA patients, and RA patients had higher rates of wound infections, pulmonary embolisms, and deep vein thrombosis, however, these findings were not significant (5). In other study (4) comparing RA patients with OA patients, RA patients had no increased risk of post-surgical myocardial infarction and stroke, and had a lower risk of VTE following THA/TKA with the latter possibly explained by increased prevalence of obesity and more frequent use of NSAIDs in the OA cohort. Patients with IA have significantly higher risk of transfusion, mechanical complications, infection, and readmission following THA (6). One study concluded that flares are frequent in patients with RA undergoing arthroplasty and that higher baseline disease activity significantly increases the risk of flares (7) and the risk for radiographic loosening after THA/TKA in patients with RA (8), and that RA patients were 47% more likely to develop a post-operative infection, compared to patients with OA (9). In the longer term, patients with RA undergoing primary TKR had excellent 2-year outcomes, comparable with OA, in spite of worse preoperative pain and function, and RA was not an independent risk factor for poor outcomes (10). Patients with RA had a decreased 10-year risk of revision while the risk of death and PJI was increased compared with patients with OA following THA/TKA (11). Studies on patients with SLE concluded that SLE is an independent risk factor for adverse postoperative outcomes, mainly immediate complications, but the long-term outcome is good enough to offer surgical treatment (12), but is not an independent risk factor for increased AEs at six months after TKA (13). Another study on risk factors concluded that SLE with other connective tissue disease, age > 45 years, high temperature, positive anti-dsDNA antibody and SLICC/ACR Damage Index > 3 were the risk factors of complications during hospitalization; and that bilateral THA, low hemoglobin and abnormal renal function were the risk factors of transfusion (14). One study attempting to evaluate the role of biologics in developing late postoperative infections concluded that biological drug therapy, especially TNFi, may be associated with an increased rate of late deep infections (15).

Quality of evidence across all critical outcomes: Very low

Ref ID, Author, year	Study type	Duration	Population Description	Treatment given to relevant population	Results
13 Blizzard, 2017 (1)	Case-control study	Follow-up 2 years	1002 patients with AS who subsequently underwent THA and 660240 controls (all patients undergoing primary THA without a diagnosis of AS and age- and gender matched control population)	THA	At 90 day in the AS group compared with the control cohort the rate of broken prosthetic joint (RR, 2.50), wound complications (RR, 2.21), cellulitis or seroma (RR, 1.90), remained a significant increase in the rate of broken prosthetic joint (RR, 2.54), wound complications (RR, 1.84), and cellulitis or seroma (RR, 1.67), elevated RR in the rate of prosthetic hip dislocation (RR, 1.44), periprosthetic infection (RR, 1.56), and THA revision (RR, 1.46). At 2 years, the rate of wound complications (RR, 2.44) followed by osteolysis or polyethylene wear (RR, 2.32), broken prosthetic joint (RR, 1.99), THA revision (RR, 1.69) and prosthetic hip dislocation (RR, 1.67). Relative to the matched control group, the greatest RR was seen in broken prosthetic joint (RR, 2.54), followed by osteolysis or polyethylene wear (RR, 2.14), wound complication (RR, 1.95), prosthetic hip dislocation (RR, 1.47), and THA revision (RR, 1.42).
187 Singh, 2020 (2)	Retrospective cohort study	N/A	70,708 SpA patients who had THA, 84,658 SpA patients who had TKA, 4,045,776 non-SpA patients who had THA, 8,042,624 non-SpA patients who had TKA	csDMARDs, bDMARDs, GC	Patients with SpA had higher odds ratio (OR (95% CI) of the following post-THA and post-TKA, respectively: (1) discharge to care facility, THA 1.16 (1.12, 1.21) and TKA 1.14 (1.11, 1.18); (2) hospital stay > 3 days, THA 1.15 (1.11, 1.20) and TKA 1.05 (1.01, 1.10); and (3) transfusion, THA 1.16 (1.12, 1.21) and TKA 1.10 (1.05, 1.14); but lower odds of (1) mortality, THA 0.78 (0.64, 0.96) and TKA 0.40 (0.19, 0.84); and (2) hospital charges above the median, THA 0.49 (0.46, 0.53) and TKA 0.48 (0.45, 0.51). SpA was associated with higher odds of implant infection, 3.02 (2.27, 4.03) post-TKA, not post-THA.

168 Pan, 2021 (3)	Case-control study	N/A	6363 RA patients and 132405 control patients with OA undergoing THA/TKA	RA therapy-related medications	Patients with RA had acute postoperative anemia (odds ratio [OR] = 1.196), blood transfusion (OR =1.179), prolonged hospitalization (OR = 1.049), and higher total cost (OR = 1.145), but had decreased odds of acute renal failure (OR = 0.804) and urinary complications (OR = 0.467)
176 Cordtz, 2020 (4)	Case-control study	90 days follow-up	2899 and 112,571 patients with RA and OA who had THA/TKA	csDMARDs, bDMARDs, GC	RA patients had higher HR of 1.29 (1.03 to 1.61) for infection following THA/TKA, but lower risk of deep vein thrombosis and pulmonary embolism and consequently VTE following TKA (HR of 0.60 (0.26 to 0.98)). Biologics treated RA patients had a HR of 1.35 (0.65 to 2.80) for infection and 4.82 (1.67 to 13.90) for VTE compared with non-biologics treated RA patients. RA patients had no increased risk of post-surgical myocardial infarction and stroke (HR 1.16, 0.76 to 1.78) compared with OA patients.
195 Jauregui, 2016 (5)	Retrospective case-control study	30 days follow-up	RA patients (n=141) and OA patients (n=7125) who had a primary TKA	RA medications	Superficial wound infection RA 1.4 %, OA 0.4% Deep incisional infection RA 0.7 %, OA 0.2% Pneumonia RA 2.1%, OA 0.003% Pulmonary Embolism RA 0.7%, OA 0.9% Bleeding requiring transfusions RA 14.2 %, OA 0.06% DVT RA 0.7%, OA 0.7%
106 Richardson, 2019 (6)	Case-control	Minimum of 90 days after THA.	1462 patients with inflammatory arthritis and 66,886 patients with OA undergoing THA. The IA cohort had	Patients with IA were treated with a DMARD, biologic, or SLE-specific medication within the year before THA.	Compared to OA, patients with IA had higher risk of transfusion (odds ratio [OR], 1.29; P < .01), mechanical complications (OR, 1.35), infection (OR, 1.96), and 90-day readmission (OR, 1.35). There were no differences in risk of venous thromboembolism or medical complications.

			more comorbidities.		
84 Goodman, 2018 (7)	Case-series	6 weeks after surgery	120 RA patients undergoing THA/TKA. Flarers vs non-flarers.	GC and MTX continued, a biologic discontinued > 2 dose intervals prior to surgery	By week 6: 75 (63%) of patients flared, but baseline disease activity (DAS28-CRP, Clinical Disease Activity Index (median 20.0 vs 15.0), and RAPID-3 (mean 17.0 vs 13.1)), inflammatory markers (CRP and ESR), as well the number of tender and swollen joints were higher in those who flared. The baseline DAS28 (OR 2.11) and log-transformed RADAI joint score (OR 2.97) were independent predictors of MD-validated patient report of flare. Increasing levels of CRP increased the risk of flares (OR 4.24). Neither disease duration nor medication use, including biologics, increased the risk of flares; discontinuation of a biologic > 2 dose intervals prior to surgery did not increase the risk of flares. Use of MTX at the time of surgery did not independently protect against the risk of flares. There was no significant difference in baseline HOOS activity scores (mean 37.3 vs 48.8), although baseline KOOS was lower (worse) (38.3 vs 51.5) in flarers. MD-HAQ function was worse (mean 4.1 vs 3.4) in flarers but the change from baseline to 6 weeks was similar between groups (mean –0.5 vs –0.5). High disease activity by DAS28-ESR (values > 5.1) were over 25-times more likely to report a flare over the subsequent 6 weeks compared to patients with low disease activity/remission (DAS28-ESR ≤ 2.6; OR 25.59). Elevated RAPID-3 was associated with an increased risk of flare (OR 1.18). A decreased risk of flare was seen with CRP ≤ 1.5 mg/dl and ≤ 2.0 mg/dl (OR 0.29, and OR = 0.17). Patients with normal ESR values also had a lower risk of flare (OR 0.30). Increased levels of CRP increased the risk of flares (OR 4.24).
167 Bohler, 2020 (8)	Case-control study	Mean follow-up 73 months	49 RA patients vs 88 OA	csDMARDs, bDMARDs, GC	SDAI over time was significantly higher in patients with RCL (median; 25th and 75th percentile: 10.8 months; 8.6 and 15.8; vs 7.0 months; 2.7 and 15.5; p = 0.043). In the

			patients with a THA/TKA		regression model, each unit of mean SDAI over time significantly increased the risk of RCL (HR 1.125, 95% CI 1.021-1.241; p = 0.018). Patients treated with biological had a lower risk of RCL than those treated with traditional DMARDs (HR 0.192, 95% CI 0.042-0.891; p = 0.035). In the 88 matched OA patients, the RCL rate was significantly lower than in the RA group (13.6%; p = 0.002).
125 Salt, 2017 (9)	Retrospective case-control study	Median follow-up 555 days	170 RA patients and 1,814 OA patients	csDMARD's, TNFi's	RA patients were 47% more likely to develop a post-operative infection, compared to patients with OA (OR = 1.47). RA patients not taking immunosuppressive medications were 130% more likely to develop an infection compared with OA patients (OR = 2.30, 95% CI: 1.37 – 3.30).
136 Goodman, 2016 (10)	Case-control study	2 years follow-up	136 RA and 4320 OA patients who had TKA	csDMARD's, biologics	Despite having worse pre-operative WOMAC pain and function scores in RA patients, WOMAC scores at 2 years were equivalent, with excellent function scores (17.4 vs. 14.7) for both groups. There was no independent association of RA with 2-year pain (p-value=0.18) or function (p-value=0.71).
148 Cordtz, 2018 (11)	Case-control study	Mean follow-up 5.47 years	3913 patients with RA with THA/ TKA were compared with 120499 patients with OA.	bDMARD's, csDMARD's, GC's	Patients with RA had decreased risk of revision (SHR 0.71 (0.57–0.89)), but increased risk of PJI (SHR=1.46 (1.13–1.88)) and death (HR=1.25 (1.01–1.55)). Surgical revision for reasons other than PJI within 10 years of primary THA/TKA in 81/3913(crude ratio 0.82 (95% CI 0.66 to 1.03)) patients with RA. Prosthetic joint infection in 63/3913 RA patients with a final adjusted SHR of 1.46 (95% CI 1.13 to 1.88). Death in 2.2% (86/3013) RA patients and RA was associated with increased mortality risk (HR in final adjusted model 1.25; 95% CI 1.01 to 1.55).

199 Merayo-Chalico, 2017 (12)	Retrospective cohort study	Mean follow-up 8 years	58 SLE patients, 58 RA patients and 58 OA patients who had THA	Immunosuppressives, GC	Hospital stay SLE 11.3 ± 0.86, RA 8.4 ± 0.20, OA 7.9 ± 0.18, p = .001) Days until immediate complications: SLE 0.52 ± 0.16, RA 0.07 ± 0.06, OA 0 Blood transfusion, units: SLE 0.64 ± 0.15, RA 0.21 ± 0.08, OA 0.09 ± 0.06 (P = 0.004). Global complications SLE 36.2%, RA 15.5%, OA 5.1%. Risk factors for THA complications were: SLE (HR 2.8, 95% CI 1.2-6.8; p = 0.018) and low postoperative hemoglobin (HR 0.77, 95% CI 0.73-0.83; p < .0001). Long-term complications after THA were similar among groups.
191 Fein, 2016 (13)	Case-control study	26 weeks follow-up	52 SLE TKA and 104 OA TKA	Stress-dose GCs	Major AEs SLE 25.0% vs. OA 19.2%; P-value = 0.41, minor AEs 15.4% vs. 10.6%; P-value = 0.39, total Aes 38.5% vs. 27.9%; p-value = 0.18. AEs were not increased among patients on stress-dose steroids. In a multiple logistic regression analysis controlling for comorbidities and diagnosis, SLE was not an independent predictor of minor (OR 1.98, 95% CI 0.68–5.79), major (OR 1.14, 95% CI 0.47–2.75), or total AEs (OR 1.61, 95% CI 0.74–3.50), the number of Charlson-Deyo comorbidities was also not a predictor of minor, major, or total AEs.
173 Li, 2019 (14)	Retrospective case-series	N/A	100 SLE patients after THA	GCs, scDMARDs, bDMARDs, immunosuppressives	Risk factors for perioperative complications were: age > 45 years (OR = 18.1, 95% CI 3.29–99.63, p = 0.001), SLE with other connective tissue diseases (OR=9.3, 95% CI 1.26–68.52, p = 0.029), high temperature (OR = 9.73, 95% CI 1.25–75.96, p = 0.03), positive anti-dsDNA antibody (OR = 6.99, 95% CI 1.07–45.94, p = 0.043), SLICC/ACR Damage Index > 3 ((OR = 8.297, 95% CI 1.72–40.10, p = 0.008). Independent risk factors for perioperative transfusion were bilateral THA (OR = 2.94, 95% CI 1.12–7.76, p = 0.029),

					low hemoglobin (OR = 3.83, 95% CI 1.23-11.94, p = 0.021) and abnormal renal function (OR = 3.06, 95% CI 1.18–7.95,p = 0.021).
171 Hayashi, 2017 (15)	Retrospective cohort study	Minimum 2 years of follow-up	99 RA patients who undergone THA	Biologics (mostly TNFi), csDMARDs, GCs	Late deep infection after THA: biological drugs: OR: 9.5, 95% CI: 1.0–88.8; TNF inhibitor: OR: 11.7, 95% CI: 1.2–109.7

Bibliography:

1. Blizzard DJ, Penrose CT, Sheets CZ, Seyler TM, Bolognesi MP, Brown CR**.** Ankylosing Spondylitis Increases Perioperative and Postoperative Complications After Total Hip Arthroplasty. The Journal of Arthroplasty. 2017;32(8):2474-9.
2. Singh JA, Cleveland JD**.** Spondyloarthritis is associated with higher healthcare utilization and complication rates after primary total knee or total hip arthroplasty. Clinical Rheumatology. 2020;39(8):2345-53.
3. Pan X, Wang J, Shi Z, Cheng H, Lin Z, Wu X, et al. Rheumatoid Arthritis Versus Osteoarthritis in Patients Receiving Revision Total Knee Arthroplasty in the United States: Increased Perioperative Risks? A National Database-Based Propensity Score–Matching Study. JAAOS - Journal of the American Academy of Orthopaedic Surgeons. 2021.
4. Cordtz R, Odgaard A, Kristensen LE, Overgaard S, Dreyer L**.** Risk of medical complications following total hip or knee arthroplasty in patients with rheumatoid arthritis: A register-based cohort study from Denmark. Seminars in Arthritis and Rheumatism. 2020;50(1):30-5.
5. Jauregui JJ, Kapadia BH, Dixit A, Naziri Q, Hip-Flores DJ, Harwin SF, et al. Thirty-day complications in rheumatoid patients following total knee arthroplasty. Clin Rheumatol. 2016;35(3):595-600.
6. Richardson SS, Kahlenberg CA, Goodman SM, Russell LA, Sculco TP, Sculco PK, et al. Inflammatory Arthritis Is a Risk Factor for Multiple Complications After Total Hip Arthroplasty: A Population-Based Comparative Study of 68,348 Patients. The Journal of Arthroplasty. 2019;34(6):1150-4.e2.
7. Goodman SM, Bykerk VP, DiCarlo E, Cummings RW, Donlin LT, Orange DE, et al. Flares in Patients with Rheumatoid Arthritis after Total Hip and Total Knee Arthroplasty: Rates, Characteristics, and Risk Factors. The Journal of Rheumatology. 2018;45(5):604.
8. Böhler C, Weimann P, Alasti F, Smolen JS, Windhager R, Aletaha D**.** Rheumatoid arthritis disease activity and the risk of aseptic arthroplasty loosening. Seminars in Arthritis and Rheumatism. 2020;50(2):245-51.
9. Salt E, Wiggins AT, Rayens MK, Morris BJ, Mannino D, Hoellein A, et al. Moderating effects of immunosuppressive medications and risk factors for post-operative joint infection following total joint arthroplasty in patients with rheumatoid arthritis or osteoarthritis. Semin Arthritis Rheum. 2017;46(4):423-9.
10. Goodman SM, Johnson B, Zhang M, Huang WT, Zhu R, Figgie M, et al. Patients with Rheumatoid Arthritis have Similar Excellent Outcomes after Total Knee Replacement Compared with Patients with Osteoarthritis. J Rheumatol. 2016;43(1):46-53.

11. Cordtz RL, Zobbe K, Højgaard P, Kristensen LE, Overgaard S, Odgaard A, et al. Predictors of revision, prosthetic joint infection and mortality following total hip or total knee arthroplasty in patients with rheumatoid arthritis: a nationwide cohort study using Danish healthcare registers. Ann Rheum Dis. 2018;77(2):281-8.
12. Merayo-Chalico J, Gónzalez-Contreras M, Ortíz-Hernández R, Alcocer-Varela J, Marcial D, Gómez-Martín D**.** Total Hip Arthroplasty Outcomes: An 18-Year Experience in a Single Center: Is Systemic Lupus Erythematosus a Potential Risk Factor for Adverse Outcomes? The Journal of Arthroplasty. 2017;32(11):3462-7.
13. Fein AW, Figgie CA, Dodds TR, Wright-Chisem J, Parks ML, Mandl LA, et al. Systemic Lupus Erythematosus Does Not Increase Risk of Adverse Events in the First 6 Months After Total Knee Arthroplasty. J Clin Rheumatol. 2016;22(7):355-9.
14. Li Z, Du Y, Xiang S, Feng B, Bian Y, Qian W, et al. Risk factors of perioperative complications and transfusion following total hip arthroplasty in systemic lupus erythematosus patients. Lupus. 2019;28(9):1134-40.
15. Hayashi S, Hashimoto S, Takayama K, Matsumoto T, Takebe K, Terashima Y, et al. Risk factors for late deep infection after total hip arthroplasty in patients with rheumatoid arthritis. Acta Reumatol Port. 2017;42(2):150-4.

Glossary

AE: Adverse event

AS: Ankylosing Spondyloarthritis

BDMARDS: Biologic Disease modifying anti-rheumatic drugs

Charlson-Deyo comorbidities: an index used to predict survivorship

CsDMARDS: Conventional Synthetic Disease modifying anti-rheumatic drugs

DMARDS: Disease modifying anti-rheumatic drugs

IA: Inflammatory Arthritis

JIA: Juvenile Idiopathic Arthritis

PJI: Prosthetic Joint Infection

RA: Rheumatoid arthritis

RCL: radiographic signs of component loosening

SDAI: Simplified Disease Activity Index

SLE: Systemic Lupus Erythematosus

SLICC/ACR Damage Index: Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index (SDI)

SpA: Spondyloarthritis

THA: Total Hip Arthroplasty

TKA: Total Knee Arthroplasty

VTE: Venous Thromboembolism