

Peri-arthroscopic Management of Immunosuppressive Medications in Patients With Rheumatic Disease: A Survey of Practice Trends Among Rheumatologists and Sports Medicine Orthopedic Surgeons

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Abstract

Background/purpose: Rheumatologists and orthopedic surgeons frequently collaborate on difficult decisions regarding perioperative management of immunosuppression in rheumatic disease patients, balancing risk of postoperative infection with risk of disease flares. Current evidence-based guidelines pertain specifically to arthroplasty, thus we sought to understand the trends and common practices regarding peri-arthroscopic use of immunosuppression.

Methods: Rheumatologists and sports medicine surgeons, from a variety of New York hospitals and serving a broad range of demographics, were surveyed on immunosuppressive medication management in rheumatic disease patients undergoing arthroscopic surgeries. Physicians preferences were elicited regarding the use of common anti-rheumatic medications with the lower risk meniscectomies and the higher risk anterior cruciate ligament (ACL) reconstructions and allografts. Physicians were asked specifically about peri-arthroscopic use of conventional synthetic disease-modifying drugs (csDMARDs), biologics, and janus kinase (JAK) inhibitors.

Results: During the survey period, 25 rheumatologists and 19 sports medicine fellowship-trained orthopedic surgeons completed their respective questionnaires. For lower-risk arthroscopies, rheumatologists favor continuing various csDMARDs (72-100%), biologics (50-64%) and JAK inhibitors (57%), while a majority of surgeons concurred for all 3 drug classes (csDMARDs 63%; biologics 53%; and JAK inhibitors 58%). For higher-risk arthroscopies, most rheumatologists prefer that patients continue csDMARDs (63-100%) but fewer support the use of biologics (28-39%) or JAK inhibitors (22%). Surgeons were more hesitant to endorse any class of immunosuppressive antirheumatic medications (22-27%) around these higher risk surgeries. The rheumatologists were most concerned about surgeries taking place too soon after the last dose of rituximab, recommending these higher risk surgeries not take place for 7.7 ± 8.8 weeks following the last infusion .

Conclusion: For lower-risk arthroscopies, most rheumatologists but only about half of orthopedic surgeons prefer patients continuing csDMARDs. Approximately half of both groups prefer patients hold biologics and JAK inhibitors. In more involved arthroscopies, most rheumatologists but few orthopedists support the continued use of csDMARDs, with consensus to hold all other immunosuppression when possible. While the duration medications were held perioperatively were somewhat reflective of the current guidelines for arthroplasty, there is a need for evidence-based guidelines specifically regarding peri-arthroscopy immunosuppression in rheumatic disease patients.

1.0 Introduction

Arthroscopy remains one of the most widely performed outpatient orthopedic procedures in the United States.(1–4) In patients with rheumatic disease, growing utilization of arthroscopic surgery is predicted as immunosuppressive treatment options enable these patients to lead longer and more functional lives, and as a result, sustain more activity-related injuries.

Physicians who manage patients' immunosuppressive anti-rheumatic medications – csDMARDs, biologics, JAK inhibitors, and glucocorticoids – will increasingly face difficult decisions surrounding perioperative management of immunosuppressive medications, as they aim to both maintain optimal disease control and minimize postoperative infection risk. Rheumatologists and orthopedic surgeons often collaborate on these management decisions, as evidenced by the American College of Rheumatology and American Association of Hip and Knee Surgeons (ACR/AAHKS) joint guidelines for perioperative management in total hip and knee arthroplasty. (5, 6) However, multiple studies have suggested that the ACR/AAHKS arthroplasty guidelines for immunosuppression management may not be applicable to arthroscopic procedures. The risk of perioperative infections varies given the range of arthroscopy patient risk profiles, variability in baseline rheumatic disease control, and the complexity of arthroscopic procedures (though all less invasive with lower risk than arthroplasty). (6, 7) In the absence of established, evidence-based guidelines for arthroscopy, it is important to understand current trends and common practices in perioperative immunosuppression management among multidisciplinary physician and surgeon teams managing rheumatic disease patients. (7) We aim to illustrate not only the complexity of arthroscopic surgery and associated risks but also the medication-specific considerations for these decisions with the goal of fostering productive dialogue among team-members to ensure most optimal outcomes for patients.

2.0 Methods

We solicited participation from 50 rheumatologists and 28 sports medicine surgeons who specialize in knee arthroscopy across a wide array of hospitals and outpatient settings, including public county hospitals in cosmopolitan and suburban settings, a government veterans administration hospital, three university hospitals, and several affiliate outpatient offices. These centers encompass the diverse spectrum of demographics, care delivery settings, and insurance coverage, yet the survey distribution was limited to one medical center network to increase internal validity.

Both rheumatologists and orthopedic surgeons were surveyed regarding their peri-arthroscopic preferences about continuing versus holding the major groups of anti-rheumatic medications: (1) the conventional synthetic disease-modifying drugs (csDMARDs), (2) biologics, (3) janus kinase (JAK) inhibitors. Glucocorticoids were not addressed in this survey due to significant complexity and management considerations pertaining to the adrenal axis. Medication use in lower-risk arthroscopies (i.e. meniscectomies) was addressed separately from higher-risk surgeries (anterior cruciate ligament (ACL) reconstructions and allografts with meniscal transplants). While rheumatologists were surveyed regarding their preferences on continuing versus holding each of the commonly used medications within these groups of medications, orthopedists were surveyed regarding the use of the general groups of antirheumatic medications rather than individual drugs since they don't prescribe them. Orthopedists were asked granular questions regarding lower to higher-risk arthroscopies. Questions about individual rheumatological diseases were not asked in this survey as medications (and their continuation or interruption) are independent predictors of postoperative infection and flare. (4, 8) Surveys were intentionally designed to be of lower and higher specificity levels with regards to antirheumatic

medications to remain within the scope of practice of rheumatologists and orthopedic surgeons, respectively, since only the rheumatologists routinely manage these medications. In addition, through the synthesis of survey results, we sought to provide both groups necessary context regarding medical and surgical considerations to foster productive discussion on perioperative management of immunosuppression. Specific questions asked to rheumatologists and orthopedic surgeons can be found in Appendix Tables A and B.

Preference frequencies were calculated for each medication group and specific medication by provider type. Rheumatologists were asked to specify how many weeks before surgery they hold each specific medication and how many weeks after surgery they wait to restart each medication. These data for each medication were further grouped by the lower-risk versus higher-risk procedure categories and compared using the Student's t-test. R Version 4.1.0 was used for all statistical analyses.

This study was exempt from Institutional Review Board full review as it was a survey of physician practice patterns without involvement of any patient records. Surveys were designed, tested, and disseminated via institutional e-mail using the internet-based Qualtrics survey platform during the survey period of 8/2021–9/2021. Participants were informed regarding the survey period, investigators, storage and usage of data collected, and purpose of the study. They were made aware that submission of the survey indicated consent, that no identifying data would be collected, and no compensation would be provided for their voluntary participation. Completion of all survey questions was required for survey submission.

3.0 Results

3.1 Survey Respondents

During the survey period, 25 rheumatologists (50% completion rate) and 19 sports medicine surgeons with experience in arthroscopy (68% completion rate) fully completed their respective survey questionnaires.

3.2 Low-risk arthroscopies

For lower-risk arthroscopies, 72–100% of rheumatologists prefer to continue the various csDMARDs perioperatively. More than half prefer to continue biologics (50–64%) and JAK inhibitors (57%) (Table 1). Similarly, more than half of surveyed surgeons prefer continuing csDMARDs (63%), biologics (53%), and JAK inhibitors (58%) (Appendices C and D).

Table 1
Rheumatologist Preferences for Perioperative Immunosuppression Management in Arthroscopy

Low-Risk Arthroscopy	Continued Medications	Weeks Held Before Surgery*	Weeks After Surgery Until Restarted*
Methotrexate	72% (n = 18)	1.2 ± 0.4	1.2 ± 0.4
Sulfasalazine	100% (n = 25)	NA	NA
Hydroxychloroquine	100% (n = 25)	NA	NA
Leflunomide	84% (n = 21)	1 ± 0	1 ± 0
Azathioprine	72% (n = 18)	1.2 ± 0.4	1 ± 0
Mycophenolate	72% (n = 18)	1.3 ± 0.8	1.2 ± 0.4
Adalimumab	50% (n = 11)	1.6 ± 0.7	1.5 ± 0.7
Etanercept	50% (n = 11)	1.2 ± 0.4	1.4 ± 0.7
Golimumab	50% (n = 11)	2.1 ± 1.3	1.8 ± 1
Certolizumab	50% (n = 11)	2.1 ± 1.2	1.6 ± 0.7
Infliximab	55% (n = 12)	2.7 ± 2.4	1.7 ± 1
Abatacept	55% (n = 12)	1.7 ± 0.9	1.5 ± 0.7
Tocilizumab	55% (n = 12)	1.8 ± 1	1.5 ± 0.7
Anakinra	55% (n = 12)	1.1 ± 0.3	1.2 ± 0.4
Secukinumab	55% (n = 12)	2.1 ± 1.3	1.6 ± 0.7
Ixekizumab	55% (n = 12)	2.1 ± 1.3	1.6 ± 0.7
Ustekinumab	59% (n = 13)	2.6 ± 2.3	1.6 ± 0.7
Rituximab	50% (n = 11)	4.8 ± 5.4	3 ± 4.6
Belimumab	64% (n = 14)	1.8 ± 1.1	1.4 ± 0.7
Tofacitinib	57% (n = 12)	1.1 ± 0.3	1.2 ± 0.4
Upadacitinib	57% (n = 12)	1.1 ± 0.3	1.2 ± 0.4
High-Risk Arthroscopy	Continued Medications	Weeks Held Before Surgery*	Weeks After Surgery Until Restarted*
Methotrexate	63% (n = 12)	1.3 ± 0.5	1.3 ± 0.5
Sulfasalazine	95% (n = 18)	1 ± 0	1 ± 0

* Average number of weeks, including only those providers who did not continue medications perioperatively

Low-Risk Arthroscopy	Continued Medications	Weeks Held Before Surgery*	Weeks After Surgery Until Restarted*
Hydroxychloroquine	100% (n = 19)	NA	NA
Leflunomide	63% (n = 12)	1.3 ± 0.5	1.3 ± 0.5
Azathioprine	68% (n = 13)	1.2 ± 0.4	1.1 ± 0.4
Mycophenolate	63% (n = 12)	1.2 ± 0.4	1.1 ± 0.4
Adalimumab	28% (n = 5)	1.7 ± 0.5	1.5 ± 0.5
Etanercept	28% (n = 5)	1.3 ± 0.5	1.2 ± 0.4
Golimumab	33% (n = 6)	2.4 ± 1.4	1.4 ± 0.5
Certolizumab	33% (n = 6)	2.2 ± 1.1	1.5 ± 0.5
Infliximab	33% (n = 6)	3 ± 2.3	1.8 ± 1.5
Abatacept	39% (n = 7)	2.1 ± 1.3	1.4 ± 0.5
Tocilizumab	33% (n = 6)	1.9 ± 1.1	1.4 ± 0.5
Anakinra	28% (n = 5)	1.2 ± 0.6	1.3 ± 0.5
Secukinumab	33% (n = 6)	2.5 ± 1.4	1.7 ± 0.9
Ixekizumab	28% (n = 5)	2.3 ± 1.2	1.7 ± 0.9
Ustekinumab	33% (n = 6)	4.3 ± 4.3	2.5 ± 3.2
Rituximab	39% (n = 7)	7.7 ± 8.8	3.4 ± 5.1
Belimumab	39% (n = 7)	2.7 ± 2	2 ± 1.8
Tofacitinib	22% (n = 4)	1 ± 0.4	1.1 ± 0.5
Upadacitinib	22% (n = 4)	1 ± 0.4	1.1 ± 0.5

* Average number of weeks, including only those providers who did not continue medications perioperatively

3.3 Higher-risk arthroscopies

In higher risk arthroscopies, 63–100% of rheumatologists prefer that these patients continue the various csDMARDs, though they were otherwise consistent with the surgeons in that only a minority prefer the continued use of biologics (28–39%) and JAK inhibitors (22%). (Table 1). Conversely, relatively few surgeons supported continuation any antirheumatic immunosuppression, ranging from 22%-27% for the 3 medication categories.

3.4 Rheumatologists' timelines for perioperative holding and restarting medications

The rheumatologists all concurred that hydroxychloroquine and sulfasalazine should be continued before and after both lower and higher risk arthroscopies, and their recommended number of weeks to hold the other csDMARDs medications to prevent infection varied little within the group (Table 1, Fig. 1). For lower risk procedures, the rheumatologists who advocated holding the csDMARDs would do so for only 0.78 weeks ± 0.61 (range 0 to 1.3 weeks), and for the higher risk surgeries an average of 1.0 weeks ± 0.50 (range 0 to 1.3) before surgery. Following the lower risk surgeries, the rheumatologists who hold csDMARDs restart them after an average of 0.73 weeks ± 0.58 (range 0 to 1.2), and after lower-risk surgeries they ask patients to wait 0.97 weeks ± 0.49 (0 to 1.3).

Regarding the biologics, the rheumatologists who hold medication prefer to do so for much longer before arthroscopy. These hold times for lower-risk surgeries ranged from 1.1 ± 0.3 weeks (anakinra) to 4.8 ± 5.4 weeks (rituximab), and the wait before higher risk arthroscopies ranged from 1.2 ± 0.6 weeks (anakinra) to 7.7 ± 8.8 weeks (rituximab). For postoperative restarting of biologics with lower risk surgeries, rheumatologists prefer to restart medications after an average of 1.2 ± 0.4 weeks (anakinra) to 3.0 ± 4.6 (rituximab), and after higher risk surgeries the wait ranges from 1.2 ± 0.4 weeks (etanercept) to 3.4 ± 5.1 weeks (rituximab).

Rheumatologists who hold JAK inhibitors (tofacitinib and upadacitinib) prefer to do so for an average of 1.1 ± 0.3 weeks before lower-risk surgeries, and 1.0 ± 0.4 weeks before the higher risk surgeries. After arthroscopy, they wait an average of 1.2 ± 0.4 weeks for low risk surgeries and 1.1 ± 0.5 weeks for the higher risk surgeries.

For each of the medications, when preferred preoperative holding time and postoperative restart time were compared in low versus higher-risk surgeries, there were no statistically significant differences in times.

4.0 Discussion

The present study is the first to survey rheumatologists and orthopedic surgeons about peri-arthroscopic management of immunosuppressive medications in patients with rheumatic disease. Our overall findings demonstrate general agreement between the two groups of physicians in peri-arthroscopic immunosuppression management, for both lower-risk and higher-risk arthroscopies. While the management paradigm to date has focused on balancing the risk of infection with the risk of disease flares, our findings suggest that procedural complexity and associated infection risks are key management considerations for the physicians.

In lower-risk arthroscopies, rheumatologists are more in favor than orthopedists of continuing the various csDMARDs perioperatively. That said, rheumatologists were more closely aligned with orthopedists

regarding the continued use of biologics and JAK inhibitors in lower-risk arthroscopy. These preferences mirror recent ACR/AAHKS recommendations (for total joint arthroplasty) and suggest providers are more likely to follow these guidelines in lower-risk arthroscopic procedures (like meniscectomies) with a lower overall postoperative complication rate from all etiologies (2.8%), including not only infections but also surgical, anesthetic, and medical complications, and pulmonary emboli.(9) Additionally, where the risk of infection is low, physicians must consider the risk of *inducing* flares of autoimmune disease – and post-operative complications – from holding immunosuppression combined with the stress of surgery, especially in patients with higher baseline disease levels.(4, 10) This is a balancing act that more likely errs on the side of more immunosuppression to prevent flares in these arthroscopies.

In higher-risk arthroscopies like ACL reconstructions with higher overall complication rates (9.0%)(9), orthopedic surgeons prefer risk-reduction and holding of all medications but rheumatologists favor continuing csDMARDs and holding the other categories of immunosuppressive medication. While orthopedic surgeon preferences for arthroscopy are at odds with ACR/AAHKS arthroplasty guidelines which recommend continuation of csDMARDs and holding of other classes of immunosuppressive medications, they align with studies in the orthopedic literature that highlight significant variation in the incidence of infection and overall complications after arthroscopy. Furthermore, this variation may be attributable to procedural complexity and technique.(6, 9, 11, 12) Results of a study analyzing complication rates after orthopedic surgeries reported in the American Board of Orthopedic Surgery Database showed an increase in complication rates with rising procedural complexity from meniscectomy (2.8%) to ACL reconstruction (9.0%). In a retrospective review of a large insurance database, Yeranorian et al reported a higher rate of infections after procedures like rotator cuff repairs, possibly because they require implant placement in the subacromial space which has direct communication with the skin.(12) Given larger risks for infection inherent to procedure type with these more invasive and complicated arthroscopies, cessation of immunosuppressive medications perioperatively may be favored to mitigate risk if the risk of a resulting disease flare is low enough. However, with regards to the timing of holding and restarting medications perioperatively, our results show no significant differences when comparing higher-risk to lower-risk arthroscopic procedures.

Glucocorticoid management was not included in the current study due significant controversy in management. Historically, management of glucocorticoids was driven by the stress dose paradigm, adopted in reaction to adrenal insufficiency related deaths in patients whose long term glucocorticoids were discontinued preoperatively.(13) However, recent debate in the literature suggests that continuing patients' baseline daily doses may be enough to prevent adrenal insufficiency.(14–16) In addition, guidelines recommend the opposite of supraphysiologic doses – tapering of steroids to < 20 mg/day if possible due to infection risk.(5) Investigators have also suggested that recency of exposure may play an equally important role as the dose, including Baker et al who showed a dose-dependent risk of postoperative infection starts even lower doses of glucocorticoids (5–10 mg).(8) While the study averaged doses over 90 days and was thus limited in knowledge of whether patients received chronic low dose glucocorticoids or acute preop or postop high dose glucocorticoids, authors suggest that recent glucocorticoid exposure likely has a larger effect on postoperative complications than cumulative

exposure. Further investigation is needed to determine whether the current timing of perioperative holding and restarting of glucocorticoids is optimal and to what extent procedural complexity should impact perioperative medication timing.

The 2017 ACR/AAHKS guidelines for arthroplasties recommend that 1) csDMARDs (hydroxychloroquine, sulfasalazine, methotrexate, leflunomide) should be continued perioperatively, 2) biologics and targeted therapies should be stopped one dosing interval before surgery, 3) JAK inhibitors like tofacitinib should be stopped for seven days before surgery, 4) glucocorticoids should be tapered to < 20 mg/day, 5) medications should not be restarted until at least 14 days after surgery in order to ensure proper wound healing and avoid infection. Recent studies in the orthopedic literature, however, have challenged this status quo. Ibrahim et al's 2019 meta-analysis found significantly increased risk of infection in rheumatoid arthritis (RA) patients who continued methotrexate therapy at the time of total joint arthroplasty, in contrast to several previous studies suggesting a lower frequency of infections. It remains unknown whether these risks remain in higher-risk surgeries including total joint arthroplasties and more involved arthroscopic procedures like ACL reconstructions compared to lower-risk arthroscopies. In a cohort study of Medicare and MarketScan data investigating postoperative complications in RA patients exposed to biologics and glucocorticoids before total joint arthroplasty, Baker et al showed that various biologic medications all have similar infection risks, in contrast to previous reports in the literature. As most patients included in the study were chronically on biologic therapy and likely had well-controlled RA, the authors suggest that the differences between various biologics may not be present among patients on chronic therapy due to well-controlled disease. Given that disease control may impact postoperative complication risk and that infection risk with biologics is greatest in the months after initiation, the extent to which poorly controlled disease drives risk compared to chronic biologic therapy exposure itself remains to be investigated.

There were some limitations of the current study. While this was a diverse multicenter study within one network, which increases internal validity of the findings, it limits the generalizability of the findings since physicians in other networks may adjust their patients' immunosuppression differently around the time of arthroscopy. In addition, we used two separate surveys to target questions to rheumatologists and orthopedists, ultimately preventing statistical analyses beyond descriptive statistics to compare the two groups. However, this allowed for appropriate illustration of the groups' differences in perspective given their respective emphasis on medical and surgical considerations. Finally, the survey focused on patients with disease controlled on baseline immunosuppression at the time of surgery, and rarer cases of disease flaring at baseline near the time of surgery were not addressed by this survey as they would require more case specific discussions.

5.0 Conclusion

For lower-risk arthroscopies, rheumatologists are more likely than orthopedists to recommend patients continue csDMARDs, while both groups of physicians show similar concern about the use of biologics and JAK inhibitors. In more involved arthroscopies with higher-risk, most rheumatologists but few

orthopedists support the continued use of csDMARDs, with consensus to hold biologics and JAK inhibitors and to minimize steroid doses when possible. However, given that procedural complexity and associated risk is likely a driver of infection risk, further investigation of infectious complications by procedure risk is required. Before such data are available, we have summarized our current recommendations (Table 2). Overall, these findings underscore the need for evidence-based guidelines regarding peri-arthroscopy management of immunosuppression in rheumatic disease patients.

Table 2: Recommendations for peri-arthroscopy management of immunosuppressive medications in rheumatic disease patients

- In all arthroscopies, continue conventional synthetic disease modifying antirheumatic drugs.
- For lower-risk arthroscopies, continue biologics and JAK inhibitors.
- For higher-risk arthroscopies, hold biologics and JAK inhibitors.

Declarations

Ethics approval and consent to participate: This study was exempt from NYU Langone Health Institutional Review Board full review as it was a survey of physician practice patterns without involvement of any patient records. All methods were carried out in accordance to institutional guidelines. Informed consent was obtained from all participants.

Consent for publication: Informed consent for publication of deidentified data was obtained from all participants.

Availability of data and materials: The datasets generated and/or analyzed during the current study are not publicly available due to institutional preferences but are available from the corresponding author on reasonable request.

Competing interests: LMJ receives fellowship support from Arthrex, Smith & Nephew, and AANA. JS and KV have no conflicts of interest to report.

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Figures

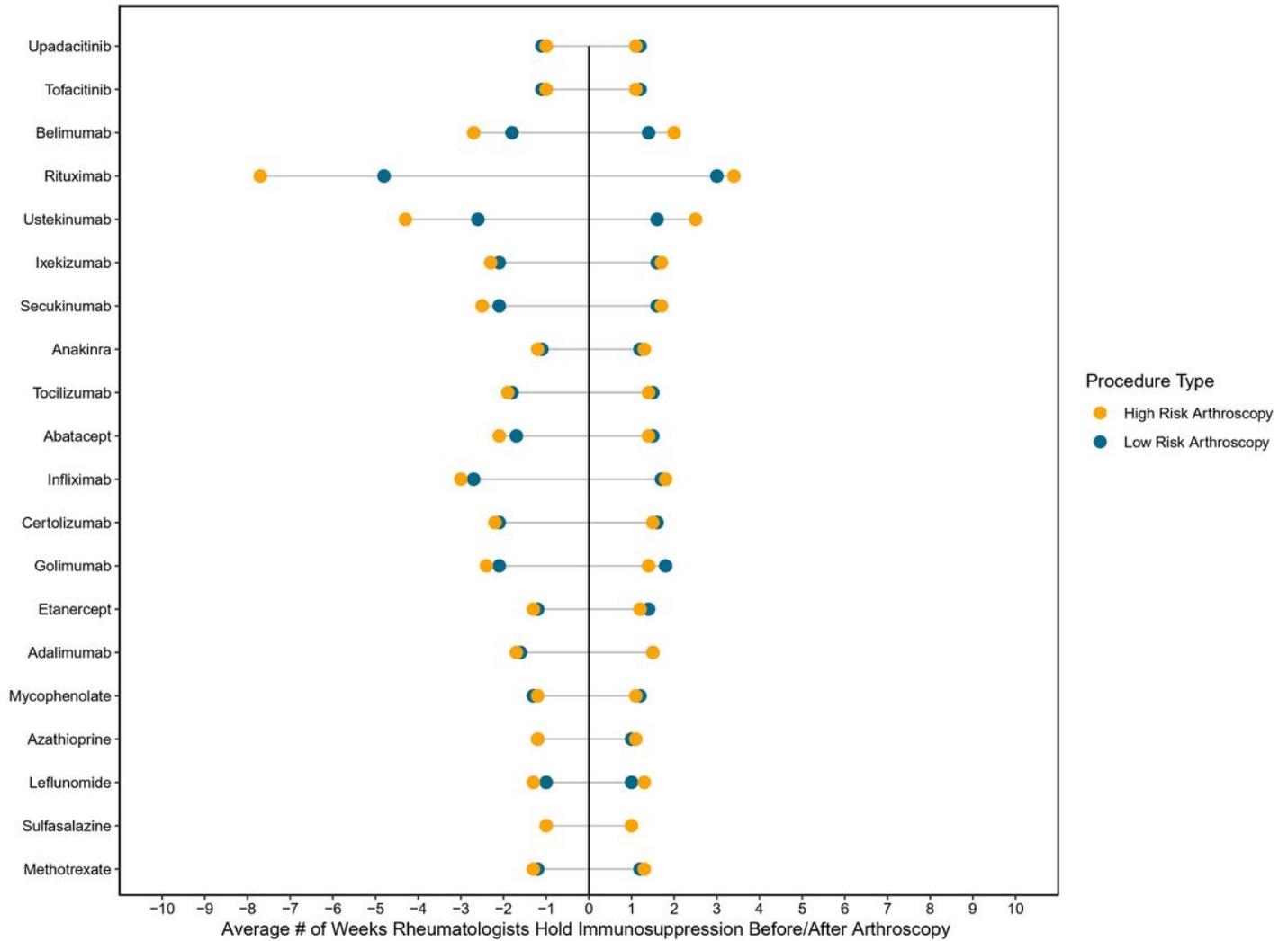


Figure 1

Rheumatologist Preferences for Holding and Restarting Immunosuppression during Arthroscopy

Illustration of surveyed rheumatologists' mean hold and restart times per immunosuppressive medication that belongs to one of the three classes – csDMARDs, biologics, and JAK inhibitors. Surgery date serves as the central reference point, and both lower and higher risk procedures categories are visualized.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Appendix.docx](#)