SUPPLEMENTARY APPENDIX 1: Methods

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

Methodology Overview

This guideline was developed following the American College of Rheumatology (ACR) guideline development process (www.rheumatology.org/Portals/0/Files/ACR%20Guideline%20Manual_Appendices_updated%202015.pdf). This process includes the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology (www.gradeworkinggroup.org) (1-4).

Teams Involved

This project was a collaboration between the American College of Rheumatology (ACR) and the American Association of Hip and Knee Surgeons (AAHKS); all participating teams included representation from both organizations. A Core Leadership Team (four members) met weekly to supervise the project and was responsible for confirming the scope and clinical (Patient/Intervention/Comparator/Outcomes – PICO) questions, coordinating with the Literature Review Team, overseeing the voting process, and drafting the manuscript. The Core Team, together with the Literature Review Team, was comprised of individuals with content and methodological expertise.

The Literature Review Team (5 members) conducted a systematic search, screened papers for relevance, assessed study quality, extracted data, computed pooled estimates of outcomes, graded the quality of evidence, generated an evidence summary for each PICO, and compiled an evidence report (provided in Supplementary Appendix 3).

The Voting Panel consisted of 16 people, including rheumatologists, orthopedic surgeons, an SLE expert, an infectious disease expert, and two patient representatives. The

role of the Voting Panel was to vote on the drafted recommendation statements derived from the PICO questions, keeping the evidence report, their expertise and experience, and patient values and preferences in mind.

Patient Panel input from the 2017 guideline was used for this guideline update rather than forming a new panel, because the ACR and AAHKS believed patient values and preferences would not have changed in recent years. Two patients who were involved in the 2017 project were members of the Voting Panel for the update.

The ACR provided training for everyone involved in the development of this guideline, which included explanations of the ACR guideline process and GRADE methodology. See Supplementary Appendix 4 for team/panel rosters.

Disclosures and Management of Conflicts of Interest

Per ACR policy, everyone who was intellectually involved in the project (i.e., considered for guideline authorship) was required to disclose all relationships (https://www.rheumatology.org/Practice-Quality/Clinical-Support/Clinical-Practice-Guidelines/Perioperative-Management). Disclosures were evaluated to determine if any relationships were considered potential conflicts of interest for purposes of this project. Individuals whose primary employment (> 51% of work time/effort) was with a company that manufactured or sold therapeutics or diagnostics were not eligible to participate.

The project's principal investigators (PIs) and the literature review leaders had no relevant conflicts of interest for the full 12 months before this project began, and no guideline development team members had any relevant conflicts of interest for the duration of the project. Intellectual conflicts, such as a prior publication or scientific presentation on perioperative management, were recognized as important and were required to be disclosed, but because they were ubiquitous, intellectual conflicts were not counted as conflicted toward the allowed threshold.

Participant disclosures were shared with each project participant via email prior to the Voting Panel meeting. Updated participant disclosures are included online with this manuscript. Finally, author disclosures are also included in this paper.

Scope and Target Audience

The scope of this project included the perioperative use of disease modifying antirheumatic therapy, including traditional disease modifying antirheumatic drugs, biologic agents, targeted synthetic small molecule drugs, and glucocorticoids used for adults with rheumatoid arthritis (RA), spondyloarthritis (SpA), juvenile idiopathic arthritis (JIA), or systemic lupus erythematosus (SLE) who are undergoing elective total hip (THA) or total knee arthroplasty (TJA). It updates recommendations regarding when to continue, when to withhold, and when to restart these medications, and the optimal perioperative dosing of glucocorticoids.

The target audience is clinicians, including orthopedic surgeons, rheumatologists, and other providers, and patients undergoing THA or TKA. Derivative products may be developed in the future to facilitate implementation of this guideline to these audiences.

PICO Development

The Core Leadership Team confirmed that the set of PICO-formatted clinical questions for the guideline, including pre-specified outcomes for each PICO question, would be the same as for the 2017 guideline (see Supplementary Appendix 2).

Systematic Synthesis of the Literature

Literature Searches

To identify recently published evidence for the PICO questions since the 2017 guideline searches were done, a medical librarian, in collaboration with the Literature Review Team, performed systematic searches of the published English language literature. OVID Embase, PubMed, and Cochrane Library searches were updated for this guideline through August 26, 2021, capturing references since March 16, 2016 (See Supplementary Appendix 5).

Study Selection

The updated literature searches identified 249 references across all PICO questions, after duplicates and non-English publications were removed. After excluding 192 references through title and abstract screening (because they did not match study designs of interest, did not examine populations or interventions of interest, or did not report outcomes of interest), 57 full-text articles were screened. Of these, 29 were excluded (for same reasons as above), leaving 28 articles to be considered for the evidence report. In the end, 24 papers were matched to PICO questions and included in the final evidence report.

DistillerSR software (https://distillercer.com/products/distillers-systematic-review-software) was used to aid screening the literature search results. Teams of two independent reviewers performed duplicate screening of each title and abstract with articles identified as potentially eligible passing to review of full text. Eligible articles underwent full-text screening by two independent reviewers. Selected manuscripts were then matched to PICO questions. See Supplementary Appendix 6 for details related to the study selection process.

Data Extraction and Analysis

Data from RCTs for each PICO question was extracted into RevMan software (http://tech.cochrane.org/revman). Risk of bias of each primary study was assessed using the Cochrane risk of bias tool (http://handbook.cochrane.org/). The critical/important outcomes selected for this guideline were binary, and they were analyzed using the Mantel-Haenszel method in a random effects model and reported as relative risks with 95% confidence intervals.

In clinical scenarios not addressed by RCT data, data from observational cohort studies was used to estimate relative effects. In situations in which the intervention had not been tested in the specific situation in question but had been tested in a more general situation or population, the effect sizes from that study were applied, postulating that the effect could be generalizable but rating down the quality of evidence for indirectness.

Evidence Report Formulation

Extracted data was reviewed and level of evidence determined. The limited literature did not lend itself to formulate a GRADE Summary of Findings (SoF) table for each PICO question; in these cases, the evidence was summarized as clearly as possible. The quality of evidence for each outcome was evaluated using GRADE quality assessment criteria (1) with discordance resolved by discussion. The Core Leadership Team reviewed the evidence report (Supplementary Appendix 3) and addressed possible evidence gaps prior to presentation to the Voting Panel.

Moving from Evidence to Recommendations

GRADE methodology specifies that panels make recommendations based on a consideration of the balance of benefits and harms of the treatment options under consideration, the quality of the evidence (i.e., confidence in the effect estimates), and patients' values and preferences. Key to the recommendation is the trade-off between desirable and undesirable outcomes; recommendations require estimating the relative value patients place on the outcomes.

A recommendation could be either in favor of or against the proposed intervention and either strong or conditional. According to GRADE, a recommendation is categorized as strong if the panel is very confident that the benefits of an intervention clearly outweigh the harms (or vice versa); a conditional recommendation denotes uncertainty regarding the balance of benefits and harms, such as when the evidence quality is low or very low, or when the decision is sensitive to individual patient preferences, or when costs are expected to impact the decision. Thus, conditional recommendations refer to decisions in which incorporation of patient preferences is a particularly essential element of decision making.

Judgments are based on the experience of the clinician panel members in shared decision making with their patients, on the experience and perspectives of the 2017 guideline Patient Panel members and, to a considerable extent, on the results of discussion with the patient group.

Consensus Building

The Voting Panel received the evidence report for review before it met to discuss and decide on the final recommendations. Individual online voting took place first, to ascertain initial consensus, followed by a virtual webinar meeting of the Voting Panel, where they reviewed the evidence and provided votes on the direction and strength of each drafted recommendation. The webinar voting process was conducted using Poll Everywhere software (www.polleverywhere.com). A 70% consensus was used as the threshold for a recommendation; if 70% consensus was not achieved during an initial vote, the panel members held additional discussions before re-voting until at least 70% consensus was achieved.

Final Review and Approval of the Manuscript by the ACR

In addition to journal peer reviews, the manuscript was reviewed by the following committees and subcommittees of the ACR and AAHKS: ACR Guideline Subcommittee; ACR Quality of Care Committee; ACR Board of Directors; AAHKS Evidence Based Medicine Committee; and AAHKS Board of Directors. These ACR and AAHKS oversight groups did not make or mandate that specific recommendations be made within the guideline, but rather, served as peer reviewers.

Moving from Recommendations to Practice

These recommendations are designed to support health care providers who work with patients with rheumatic diseases undergoing THA/TKA. Health care providers and patients must take into consideration not only clinical phenotype and level of disease activity, but also comorbidities, response and tolerance of prior therapies, patient's values and preferences, and patient's functional status and functional goals in choosing the optimal therapy for an individual patient at the given point in treatment.

REFERENCES

1. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008;336(7650):924-6.
2. Andrews J, Guyatt G, Oxman AD, Alderson P, Dahm P, Falck-Ytter Y, et al. GRADE guidelines: 14. Going from evidence to recommendations: the significance and presentation of recommendations. J Clin Epidemiol. 2013;66(7):719-25.
3. Andrews JC, Schunemann HJ, Oxman AD, Pottie K, Meerpohl JJ, Coello PA, et al. GRADE guidelines: 15. Going from evidence to recommendation-determinants of a recommendation's direction and strength. J Clin Epidemiol. 2013;66(7):726-35.
4. Guyatt GH, Oxman AD, Kunz R, Atkins D, Brozek J, Vist G, et al. GRADE guidelines: 2. Framing the question and deciding on important outcomes. J Clin Epidemiol 2011;64:395-400.