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Editorial

Preventing Cardiovascular Events in Patients With Inflammatory Arthritis: Are We Missing the Mark?

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See article by Kuriya et al., pages 1244–1252 of this issue.

Inflammation promotes atherogenesis at several points in the evolution of the disease process.[1] Consequently, individuals with chronic inflammation, such as those living with inflammatory arthritis—including rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis—have an increased lifetime risk of developing atherosclerotic cardiovascular disease (ASCVD).[1,2] This susceptibility is independent of traditional modifiable risk factors[1,2] including atherogenic lipoproteins, whose levels are variable in inflammatory arthritis patients and are influenced by anti-inflammatory therapies.[3] The 2021 Canadian Cardiovascular Society (CCS) Guidelines for management of dyslipidemia have recognized that patients with inflammatory arthritis are at increased risk of ASCVD[4] and recommend routine lipid screening for these people.[4] Additional markers of ASCVD risk, such as high-sensitivity C-reactive protein and coronary artery calcium score, can also be evaluated.[4] A discussion on prevention of ASCVD is appropriate with such patients, including possible statin use. Evidence from other jurisdictions suggests that risk of ASCVD in patients with inflammatory arthritis is frequently underestimated and suboptimally managed.[2]

To address this knowledge gap, in this issue of *Canadian Journal of Cardiology*, Kuriya et al. report a cross-sectional study of 302 patients (mean age 58 years, 71% female) with inflammatory arthritis; 59%, 32%, and 8% had rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis, respectively.[5] Patients were followed in a multidisciplinary cardio-rheumatology clinic in Toronto. In this primary prevention sample, no patient at entry had known ASCVD and none was taking statins. After stratifying patient risk using the Framingham risk score, one-half of the cohort was considered to be eligible for statin therapy; two-thirds of these were at low-risk but still qualified for statins because of excessive low-density lipoprotein cholesterol or apolipoprotein B levels. Among patients with intermediate risk, 91% met criteria for statin therapy based on a coronary artery calcium score > 0 or an elevated level of C-reactive protein. Other factors that raised the likelihood for recommendation of statin therapy included male sex and presence of hypertension. The authors observed that statin therapy was suboptimal among patients with inflammatory arthritis who met the criteria specified by the CCS dyslipidemia guidelines and concluded that more work was required to understand the barriers and challenges to implementation in these patients.

Increased ASCVD risk has long been recognized among patients with rheumatic diseases but acting to reduce risk has been hard to achieve. The study by Kuriya et al. arrives at an opportune moment, following upon the recent publication of the long-awaited **O**ral **R**heumatoid **A**rthritis Tria**l** (ORAL) Surveillance study.[6] ORAL Surveillance was a 4-year randomized, open-label, noninferiority, postauthorization, safety endpoint trial, which demonstrated that the risk of major adverse cardiovascular events (MACE) in patients with rheumatoid arthritis who were $\geq$ 50 years of age and had at least 1 additional ASCVD risk factor was higher (not noninferior) when taking Janus kinase inhibitors (tofacitinib) compared with tumour necrosis factor inhibitors.[6] A risk-factor dose-response was demonstrated in key secondary analyses, which showed that patients at the highest risk—that is, age > 65 years or ever smokers—had the greatest discrepancy in incidence rates of MACE between treatment arms.

The ORAL Surveillance study highlights the importance of assessing ASCVD risks in patients with rheumatoid arthritis and other inflammatory diseases, regardless of the treatment strategy.[6] The results of the study by Kuriya et al. uncover a substantial unmet need and opportunity to intervene for patients with inflammatory arthritis at increased risk of ASCVD with guideline-recommended therapies.[5] Furthermore, primary treatment of rheumatoid arthritis itself to lower disease activity or—ideally—remission concurrently lowers risk of

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ASCVD driven by systemic inflammation,[7] especially with tumour necrosis factor inhibitors.[8] Nevertheless, the persistent risk of MACE in patients with well-controlled rheumatoid arthritis must simultaneously be addressed by treating conventional ASCVD risk factors. Patients with inflammatory arthritis deserve every opportunity to achieve the best outcomes, although implementing risk-reduction strategies remains a challenge throughout the world.

Recognizing this challenge raises 2 key questions: Who is responsible for assessing ASCVD risk in patients with inflammatory rheumatic disease and who is responsible for treatment and monitoring ASCVD target achievement in patients at risk? Patients with well-controlled inflammatory arthritis in the Toronto study were followed in a multidisciplinary cardiology-rheumatology program within a tertiary care centre, providing them with exceptional access to experts in management of ASCVD risk. Despite this resource-rich setting, ASCVD risk remained undertreated. Notwithstanding the potential for improved access, the number and geographic distribution of patients with inflammatory arthritis (let alone other inflammatory diseases) in the general population makes it impractical for all high-risk patients to be managed in multidisciplinary tertiary care settings. Should individual rheumatologists be assessing ASCVD risk in all patients with inflammatory arthritis instead? If so, which tools are the most appropriate?

The European Alliance of Associations for Rheumatology (EULAR) 2017 recommended that ASCVD risk be assessed in all patients with inflammatory joint diseases at least once every 5 years[9] but leaves assignment of the responsibility to be defined locally according to different health care system and economic priorities. What is clear is that the international community recommends that the rheumatologist should at least ensure that ASCVD risk assessment is performed regularly, with documentation of who is performing it.

Fortunately, guidance from Canada provides a helpful example. In 2015, a set of 11 quality indicators for assessing and managing risk of ASCVD in patients with rheumatoid arthritis was reviewed by a task force of rheumatologists and cardiologists and found to be relevant, valid, and feasible.[10] Among the indicators, rheumatologists are recommended to assess risk of ASCVD within the first 2 years of diagnosis of arthritis, treat intermediate- to high-risk patients according to national ASCVD guidelines, and communicate to the primary care physician that patients with rheumatoid arthritis have an increased risk of ASCVD.[10] Additional indicators address contextual factors and how to address specific risks including lipids, smoking, and diabetes. Together, the quality indicators framework provides an important asset to the rheumatology field that should be acted upon urgently.

As highlighted by Kuriya et al., important gaps remain in identifying and preventing adverse ASCVD outcomes in patients with rheumatic diseases. The available set of quality indicators for ASCVD risk management in rheumatoid arthritis provides the tools needed to assess our current standards of practice, implement quality improvement initiatives in our clinics and models of care, and then periodically re-evaluate the impact of these initiatives to know if implementation has been effective or requires further adjustment. We also suggest that measuring outcomes including MACE should be included when evaluating the real-world effectiveness of practice changes to address risk of ASCVD.

It has been debated whether the primary care physician or the rheumatologist should be the quarterback providing ongoing treatment and monitoring of ASCVD risk factors.[11] In Canada and elsewhere, current shortages in the rheumatology workforce are expected to worsen over the coming decade because of the anticipated rate of retirements compared with training.[10] This real-world limitation threatens feasibility of management of ASCVD risk factors by rheumatologists alone. We thus emphasize that rheumatologists play a critical role in identifying patients who are at elevated risk of ASCVD. Furthermore, engagement of providers with expertise in ASCVD risk management including primary care providers, internists, cardiologists, endocrinologists, and others is needed to ensure adequate treatment and monitoring of risks of ASCVD for patients with inflammatory arthritis. Our collective commitment to provide collaborative high-quality care for patients with inflammatory arthritis will help to fill the critical unmet need spotlighted by Kuriya and colleagues.

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