Study finds opioids double risk of venous thromboembolism in rheumatoid arthritis patients
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New research presented this week at ACR Convergence 2022, the American College of Rheumatology's annual meeting, found that adult RA patients starting opioids had twice the risk of venous thromboembolism (VTE) compared to patients starting nonsteroidal anti-inflammatory drugs (NSAIDs). Venous thromboembolism is a serious, but preventable, condition that occurs when a blood clot forms in a vein.

Pain management is a priority for most patients with rheumatoid arthritis (RA). Even with well-controlled disease, around 60% of patients continue to experience pain, with few safe pharmacological strategies, including NSAIDs and opioids, to help manage it. One concern with NSAIDs is the increased risk of major cardiovascular events, which is already heightened in patients with RA.

And while many potential harms of opioids—addiction, overdose, and death—are well known, the risk of major adverse cardiovascular events is not as clear. This new-user active comparator cohort study aimed to assess the cardiovascular risk in RA patients taking opioids compared to NSAIDs.

"One of the arguments for choosing opioids over NSAIDs is less impact of opioids on cardiovascular disease. However, no data supports that opioids have a safer profile than NSAIDs in addition to their other risks," explains Gulsen Ozen, MD, a rheumatology fellow at University of Nebraska Medical Center and the study's lead author.

"Therefore, we wanted to investigate cardiovascular risks associated with opioids compared to NSAIDs to show if they are as safe as perceived."

The study cohort included adults with RA who participated in FORWARD, The National Databank for Rheumatic Diseases, for one year or more between 1998 and 2021. FORWARD collects patient-reported data on socioeconomics, disease activity, treatment outcomes, disability, hospitalizations and other key information about rheumatic conditions.

For the study, 4,778 opioid initiators were matched with 11,218 NSAID initiators by propensity scores, a statistical matching technique that attempts to estimate the effect of a treatment, policy, or other intervention by accounting for the covariates that predict receiving the treatment. Baseline characteristics in the matched cohort were
balanced except for CVD medications including aspirin, anti-hypertensives and statin cholesterol-lowering drugs.

Patients were followed for major adverse cardiovascular outcomes including myocardial infarction, stroke, heart failure, venous thromboembolism and death as well as all-cause mortality.

Although major cardiovascular incidents and all-cause mortality were lower among NSAID initiators compared to opioid initiators (392 and 228 vs. 133 and 95, respectively), the risk was similar in propensity score weighted models. The one exception was a two-fold increased risk of venous thromboembolism in the opioid group.

"We were anticipating a similar cardiovascular diseases risk and somewhat increased all-cause mortality risk with opioids compared to NSAIDs. However, we were not expecting increased venous thromboembolism risk," Dr. Ozen says. "Although our opioid and NSAID groups were well-balanced in recent hospitalizations, there may be differences in reasons for hospitalization requiring opioid versus NSAID initiation."

Dr. Ozen explains that while they didn't have data on why patients were hospitalized, data in the general public suggests that patients undergoing hip arthroplasty who are on long-term opioids have more venous thromboembolism events than non-users do.

Dr. Ozen notes that opioid prescribing in the rheumatology community decreased before the COVID-19 pandemic but has since ticked up and remains a problem for many patients with rheumatic diseases.

"Addressing pain in patients with rheumatoid arthritis is challenging as it is not always dependent on disease activity," Dr. Ozen says.

"Although we don't have direct evidence for patients with rheumatoid arthritis, we know from patients with osteoarthritis that chronic opioid use can intensify pain without improvement of function. Our study suggests that opioids can cause significant cardiovascular morbidity and even death in patients with [rheumatoid arthritis]."

"We hope our findings can decrease opioid prescriptions for pain in patients with inflammatory rheumatic diseases. We have to remember that pain in inflammatory rheumatic diseases is multifactorial, and we should utilize non-pharmacological methods more often in this patient population."

More information: Conference abstract: [acrabstracts.org/abstract/maj ... heumatoid-arthritis/](acrabstracts.org/abstract/majo ... heumatoid-arthritis/)

Conference: [www.rheumatology.org/Annual-Meeting](www.rheumatology.org/Annual-Meeting)

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