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Reply

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To the Editor:

We are grateful to Dr. Jain and colleagues for their interest in our article. Jain et al raise an important point: not all joints in a patient with RA are affected equally at any given time, making it challenging to associate synovial findings from only 1 joint with assessments of

global patient symptoms. We had discovered that morning stiffness duration was associated with the presence of fibrin and neutrophils in synovium; however, neither of the questions used in this analysis focused on any particular joint, and it is likely that joints other than the replaced joint influenced patient responses.

We did also collect Hip disability and Osteoarthritis Outcome Scores (HOOS) (1) and Knee injury and Osteoarthritis Outcome Scores (KOOS) (2) questionnaires in our cohort, which queried patients specifically about hips or knees, the joints for which arthroplasty was performed in our study, and included questions regarding stiffness severity. Just as a large percentage (43%) of patients with <1 hour of morning stiffness reported relatively high general stiffness severity, 58% of patients who reported <1 hour of morning stiffness rated their HOOS/KOOS morning stiffness severity as either severe or extreme, supporting our conclusion that stiffness severity and duration represent different constructs. In an attempt to address the question raised by Jain et al, we evaluated responses to these 2 joint-specific questions in relation to synovial histologic features but did not find any significant associations between any of the synovial histologic features and stiffness severity in the morning or later in the day. This is consistent with our original finding that synovial fibrin and neutrophils were associated with prolonged duration of morning stiffness but not stiffness severity. We look forward to future studies comparing synovial histologic features to morning stiffness duration and physical examination findings from a specific joint.

Jain et al also note that it would be interesting to explore the role of NETosis in the interaction of neutrophils with fibrin in the putative pathogenesis of morning stiffness. Given that neutrophil-derived DNA impedes fibrinolysis and RA synovium contains NETs, we agree that NETs may contribute to prolonged morning stiffness, and this warrants further study.

Finally, there is a question regarding the number of patients in each of the 3 DAS28 categories. Thirty-six percent, 47%, and 15% of patients had DAS28 scores of low, moderate, or high, respectively. Since assessments of synovial neutrophils and fibrin can easily be performed in any clinical research setting, we are eager to learn whether their association with morning stiffness duration is reproducible by independent laboratories and look forward to future investigations to clarify the pathogenesis of this vexing symptom.

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