More May Not Be Better — But Is Less Enough?

Joint inflammation is the principal clinical feature of juvenile idiopathic (formerly rheumatoid) arthritis (JIA). The American College of Rheumatology (ACR) has defined an active joint as one that has swelling, or in the absence of swelling, that is painful and shows limitation in range of motion on physical examination. At present, for both clinical care and research, a total of 75 joints are assessed for determining the extent of JIA involvement. In the context of the formal joint count the tarsometatarsal joints and cervical, thoracic and lumbar spine are all considered single joints. Some of these 75 joints cannot be examined for presence of swelling, including the sacroiliac joints, joints of the spine and hips, and the subtalar joints. Similarly, limitation in range of motion of the sternoclavicular, acromioclavicular, and sacroiliac joints cannot be assessed. Thus, based on constrained assessment of swelling and limitation of motion on physical examination, the sacroiliac joints can never be “active” using the ACR criteria above, leaving a child with JIA with a maximum of 73 possible active joints when employing the traditional “full joint count” approach.

Although, theoretically, all joints can be involved with JIA, similarly to rheumatoid arthritis (RA), there are certain joints that are more commonly targeted by JIA than others. In this issue of The Journal the measurement properties of several alternative reduced joint counts for JIA are investigated by Bazso, et al. Their work is an important step in the desired direction of developing a valid reduced joint count, despite some limitations.

The authors’ stated purpose of these focused joint assessments is their use in research, rather than for daily practice, and in preparation of the development of a measure of absolute disease activity of JIA. These reduced joint counts were selected after discussions among experienced investigators from a single center and under consideration of the frequency of joint involvement in several large JIA cohorts, all collected by the investigators’ group in the past. For reasons not completely clear, Bazso, et al use a “semi full-joint count” as a reference measure or criterion standard for their validation analyses as they disregard thoracic and lumbar spine assessment, ending up with 71 possibly active joints in a child with JIA.

Limiting the scope of disease features when measuring absolute disease activity has precedence in other rheumatic diseases, even those not primarily affecting the joints; an example might be the Systemic Lupus Erythematosus Disease Activity Index, a measure of absolute disease activity whose 24 dichotomous items identify disease activity well in the majority of SLE phenotypes. Bazso’s work is reminiscent of the approach taken with the development of the Disease Activity Scale-28 for RA, where inflammatory changes of only 28 joints (shoulders, elbows, wrists, metacarpophalangeal joints, proximal interphalangeal joints, and knees) are considered in the calculation of the RA disease activity score.

Given the large differences among JIA phenotypes, however, an inherent risk of limiting joint counts when measuring JIA disease activity may be to unjustly classify those children who are “special,” i.e., those whose JIA is not playing by the rules and involves less commonly affected joints. Even if such “special” patients were few and far between, such cases need to be investigated to make us aware not only of advantages but also of potential pitfalls of focused joint counts.

Bazso, et al address the validity of reduced joint counts in 3 ways. First, the joints considered in the focused joint assessment were all taken from a pool of commonly affected joints as per several large JIA cohorts; joints included in the 45, 35 and 27, and 10 reduced joint counts were then selected from this pool after extensive discussions among this group of investigators. Given the approach taken, it is not astonishing, but is nonetheless comforting, to observe that correlation coefficients of the 71 semi full-joint count...
to other JIA outcomes are comparable to those of the focused joint counts. Second, the authors present the effects of considering reduced joint counts when assessing JIA response to medications using the ACR Pediatric Criteria for Improvement⁴. In the context of these criteria, reduced joint counts would have changed the interpretation of the disease course in no more than 4% of the overall group of patients included in these studies, thus not to an important degree. Third, Bazso, et al provide initial evidence of the validity of reduced joint counts in children with very low (10 or fewer) and with very high (28 or more) joint counts. Results support that for children with 10 or fewer active joints, limited joint counts perform as well as the 71 joint count. At least to some extent, this is expected, given the methodological approach taken when selecting candidate reduced joint counts.

Careful assessment of the performance of focused joint count in children with very high joint counts appears especially important, since those children in particular are often enrolled in clinical trials of biologic medications. Unfortunately, reduced joint counts produce less than pleasing results, in terms of correlation coefficients, when children with high joint counts are evaluated as compared to children with 10 or fewer active joints. Additionally, although the presentation of Spearman correlations is important, a more interesting analysis might have been to determine what proportion of children with at least 28 active joints would have been “reclassified,” in terms of their response to therapy (ACR Improvement Criteria), when using the focused as compared to the full joint count.

As suggested by the ACR Quality Measure Committee, any outcome measure for rheumatic diseases needs to be rigorously validated prior to use in clinical care or pivotal studies, with specific steps to be taken detailed in the publications of the Committee⁵,⁶. Similar to the development of other rheumatology disease measures, a single study cannot provide all validation steps necessary to support the use of a new measure in clinical trials. Additional investigations of the validity of reduced joint counts must be provided in future studies and will need to include assessing the performance of the reduced joint counts in other datasets and patient cohorts. Receiver-operating characteristic curve analysis should be entertained to more accurately assess agreement between joint assessment approaches and diagnostic accuracy throughout the range of active joints in the various JIA subtypes. Using other datasets, additional research is necessary to identify and validate the best combination, and the optimal number of joints to be considered in a reduced joint count. Such analyses may help to support the choice of the “right” reduced joint assessment for JIA, as the “one size fits all” approach may not be best under all circumstances.

It is conceivable that for different study questions or objectives, certain types of focused joint counts are more appropriate than the 27 limited joint count championed by the investigators. The ultimate goal of medical interventions is to control disease signs and symptoms in an effort to improve the child’s health-related quality of life. Thus, an alternative approach to candidate reduced joint counts for JIA might be one that preferentially considers joints whose involvement has the largest influence on patient health and/or physical functioning.

Nonetheless, the work of Bazso and colleagues is an important step in the direction of developing a valid reduced joint count. Despite some limitations, the work of Bazso, et al is an exciting initial step toward the development of reduced joint counts for JIA clinical trials. The study provides an excellent starting point for the validation of new, urgently needed JIA outcome measures that will hopefully help limit variations in joint assessment among investigators, and serve as the foundation of an elusive JIA disease activity measure.

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