Burying the White Blood Cell Count: Using the Neutrophil-to-Lymphocyte to Determine the Severity of Pediatric Musculoskeletal Infection

Brian Q. Hou[1], Anoop S. Chandrashekar[1], Naadir H. Jamal[1], Stephen W. Chenard[1], Stephanie N. Moore-Lotridge[2,6], Jonathan G. Schoenecker[2,3,4,5,6]
[1]Vanderbilt university School of Medicine, Nashville, TN [2]Department of Orthopedics, Vanderbilt University Medical Center, Nashville, TN, [3]Department of Pharmacology, [4]Department of Pathology, Microbiology, and Immunology, [5]Department of Pediatrics, [6]Center of Bone Biology, Vanderbilt University Medical Center, Nashville, TN
Brian.hou@vanderbilt.edu

Disclosures: Funding for this work was supported by the Caitlin Lovejoy Fund, the Vanderbilt University Medical Center Department of Orthopaedics, the Vanderbilt School of Medicine Research Immersion Program, and the Burroughs Wellcome Fund Physician-Scientist Institutional Award to Vanderbilt University (ID: 1018894). The Schoenecker laboratory is likewise supported by the NIH (5R01GM126062-05, 1R21AR080914-01, 1R21AR07908-01, 1R01AI173795-01), Department of Defense (W81XWH-18-1-0536), and Veterans Administration BLRD (1IO1 BX005062).

Background: Pediatric orthopedic surgeons must rapidly triage the severity of musculoskeletal infections (MSKI) to determine which children are at most risk for disease dissemination and adverse outcomes. Diagnostics, such as the Kocher criteria, are excellent at predicting the *likelihood* of an infection. However, there are few that predict the *severity* of an infection. There is a need for these diagnostics, as they not only predict adverse outcomes, but also allow for determining if a child is improving or declining through serial measurement. The gold standard diagnostic for determining severity is CRP. Alternatively, clinicians often use a serum white blood cell (WBC), because of its ubiquity. While useful for predicting infection, WBC is not sensitive for infection severity. The neutrophil-to-lymphocyte ratio (NLR) can be obtained readily from a complete blood cell count with differential and has been shown to be useful in COVID-19 and cancer. Thus, we hypothesized that, like CRP, the NLR is predictive of both infection and disease severity in pediatric MSKI.

Methods: A retrospective cohort study was conducted using a database of pediatric orthopedic consultations for MSKI between January 2013 and July 2022. Diagnoses were categorized as MSKI or no infection (e.g., transient synovitis) based on radiographic findings and review of medical records. The degree of infection was stratified based on previously published criteria as no infection, local, disseminated, or disseminated with complications infections. NLR was calculated as absolute neutrophil count divided by absolute lymphocyte count.

Results: 710 patients were included of which 260 had no infection, 254 had a local infection, 170 had a disseminated infection, and 26 had a disseminated infection with complications. Mean CRP, WBC count, and NLR in the infected group were significantly increased compared to the non-infected group (p<.0001). CRP upon admission was also stratified by disease severity with significant increases between patients with no infection, patients with local infection, patients with disseminated infections, and patients with disseminated infections and related complications (8.3 vs 39.25 vs 107.0 vs. 256.9, p<0.0001). In comparison, WBC count at admission was a poor predictor of infection severity with limited ability to discriminate between severity of infections (11.0 vs. 12.6 vs. 12.6 vs. 11.7, p<0.05). NLR was able to differentiate severity between no infection, local, and disseminated infections (p<.0001). NLR in the disseminated infections with complications group was higher than the NLR in the disseminated group despite the lack of statistical significance (4.368 vs. 8.282, p=.127),

Discussion: NLR is comparable to the gold standard of CRP and may be useful for assessing both the presence and the severity of MSKI in children. The lack of statistical significance in NLR between disseminated infection and disseminated infection with complications may be attributed to the low sample size of the complications cohort.

Significance/Clinical Relevance: Clinical tools to determine infection severity are needed for appropriate management. While commonly used, the WBC is shown to be a poor marker of severity of infection. Nonetheless, components of the WBC may still be useful, such as the neutrophil-to-lymphocyte ratio. NLR should be considered as a triage tool, in conjunction with CRP, for presence and severity of pediatric musculoskeletal infections.

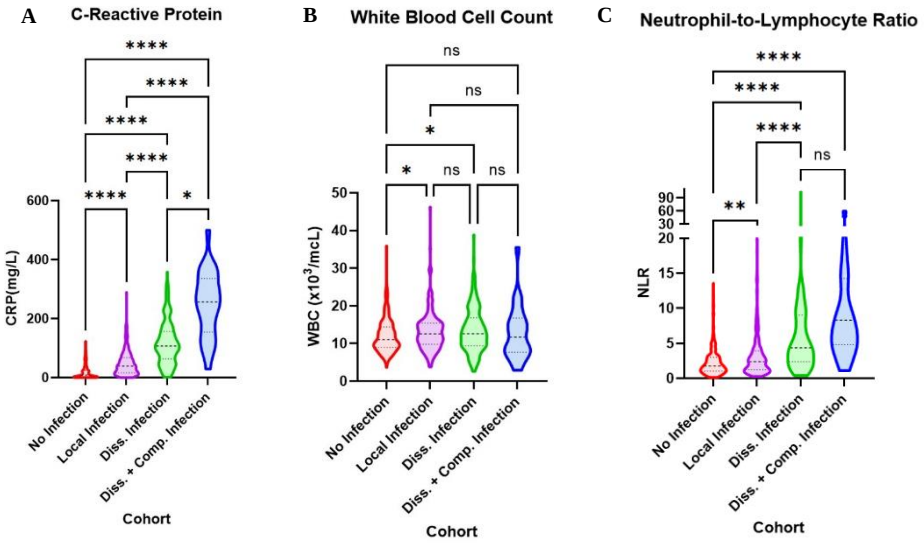

Figure 1. Mean Admission Laboratory Values. A) Mean values of admission C-Reactive Protein in the four levels of pediatric musculoskeletal infection severity. CRP significantly increases with more severe infections. B) Mean admission white blood cell count (WBC) between the four levels of infection severity. There is no distinguishable pattern or trend in WBC with infection severity. C) Mean admission neutrophil-to-lymphocyte ratio (NLR) in the four levels of pediatric musculoskeletal infection severity. The difference in NLR was significant in all comparisons except for between disseminated infection and disseminated infection with complications. Nonetheless, the NLR was highest in the complications cohort. ns>0.05, *<.05, **<.005, ****<.0001.