Rationale for recommendation

The primary utility of CRP on admission is as a baseline for serial measurements during the treatment course. The existing literature regarding CRP as a diagnostic test for ABA is limited by small sample sizes, suboptimal methodology, varied populations of interest (i.e., wide range of pre-test probabilities) and control groups, varied reference standards, use of different numeric cut-offs, and verification bias. Results suggest limited accuracy in discriminating ABA caused by any bacterial pathogen from other infectious or non-infectious processes. Despite these limitations, in a child with suspected ABA, we suggest performing a CRP on initial evaluation. CRP is offered in most hospital settings, can be obtained simultaneously with blood being drawn for culture and other tests, is relatively inexpensive, and produces results that usually are quickly available. When taken in context of the clinical presentation and other testing modalities, CRP may add benefit for multidisciplinary clinical decision making for children with clinically suspected ABA. Although not specifically analyzed in published studies (particularly those prior to widespread routine use of molecular tests for diagnosis of ABA), children with a low initial CRP are likely to include many with *K. kingae* infections, for whom long-term outcomes are excellent [24, 94]. Normal or minimally elevated concentrations of serum CRP do not exclude ABA but should prompt investigation of additional non-infectious etiologies.

Procalcitonin

Summary of evidence

Procalcitonin (PCT) is an acute phase reactant that increases during infection. It is purported to rise more rapidly and be more specific for bacterial infection compared with other markers of inflammation. The diagnostic accuracy of procalcitonin for ABA has been evaluated in three prospective, cross-sectional studies [80, 81, 100] in which children with ABA or osteomyelitis were included. These studies used varying combinations of clinical, microbiological, and radiographic criteria to classify patients as having ABA or osteomyelitis. Clinicians were blinded to PCT results in two of the included studies [81, 100]. The studies had different disease prevalence as a result of differences in inclusion criteria. One included only patients with fever along with musculoskeletal complaints (ABA prevalence 52.2%) [81], whereas two included both febrile and afebrile patients (ABA prevalence 14.2% [100] and 21.1% [80], respectively). A PCT cut-off value ≥ 0.5 ng/mL was considered a priori as positive in two of these studies [81, 100], while the other derived the optimal cut-off value from their studied cohort [80].

At a PCT cut-off value of 0.5 ng/mL, the two included studies reported a high specificity (96.9% [100] and 100.0% [81]) of PCT when used to discriminate confirmed and presumed osteoarticular infections vs. non-infected patients, while reporting a very low sensitivity (12.5% [100] and 43.5% [81],. In the third study, the optimal cut-off was determined to be 0.1 ng/mL, and the authors reported that patients with a PCT value over 0.1 ng/mL were 2.5 times more likely to have acute musculoskeletal infections than those with a PCT value below this cut-off [80]. Nevertheless, this same study showed that CRP performed better than PCT [80].

In addition to these studies, a recent meta-analysis assessing the diagnostic test accuracy of serum PCT for bone and joint infections in children and adolescents also confirmed the paucity of published data, precluding any formal conclusion [83]. Another meta-analysis [101] of 10 studies of PCT in osteoarticular infection not restricted to ABA, concluded superior positive and negative likelihood ratios and improved area under a receiver operating characteristic curve (AUC) for PCT compared with CRP; however, the results of this meta-analysis were primarily based on adult populations, thus not considered generalizable to the pediatric population.

Rationale for recommendation

PCT has utility in risk stratification among bacterial versus nonbacterial etiologies of some clinical scenarios. However, currently available data regarding accuracy of PCT in the diagnosis of children with ABA have limitations of relatively small sample sizes of children with ABA or osteomyelitis. Validity is uncertain and the sensitivity appears suboptimal. Also, no prospective evaluation of PCT to distinguish successful from unsuccessful antimicrobial/surgical therapy of ABA has been conducted. In addition, PCT is not routinely available in many hospitals and is more expensive than CRP.

Complete blood count (CBC)

Background

A complete blood cell count (CBC) with differential generally should be performed on initial evaluation of children with suspected ABA (see Table 1 for definitions) to assess the severity of infectious processes as well as to provide useful information regarding alternative diagnoses (e.g., leukemia). The peripheral white blood cell (WBC) count is often but not always elevated in children with ABA [59, 72, 74, 80, 102–104].

The WBC is higher on average with adjacent osteomyelitis infection than without [86, 88] and may be higher when ABA is caused by *S. aureus* or streptococcal species than *K. kingae* [95, 105]; however, substantial overlap precludes the use of a specific diagnostic cut-off value. WBC does not differ on average, between confirmed and presumed ABA cases (see Table 1 for definitions) [24, 106]. WBC on admission also is not useful in distinguishing ABA from Lyme arthritis [96].

The WBC is often higher in children with ABA than transient nonbacterial synovitis, a clinically defined syndrome traditionally often referred to as toxic synovitis (see Table 1 for definitions), but the substantial overlap precludes diagnostic value in distinguishing these entities [74–77, 107, 108]. There is