Where Are We Now?

Periprosthetic joint infection (PJI) is a devastating complication following THA, and it appears to be becoming more common [5]. In light of the morbidity and costs associated with treating PJI, accurate pre and perioperative tests to either confirm or to rule out infection are badly needed. In recent years, various biomarkers have been implemented into our clinical routine either to confirm or rule out PJI [16] with alpha defensin being one of the most-promising tests now available. The alpha-defensin test is market available as a lateral flow test and a laboratory-based immunoassay. Initial reports have shown outstanding sensitivity and specificity [6] even with prior administration of antibiotics [17]. But recently, we have seen inferior results for alpha-defensin tests concerning sensitivity and specificity [2, 3, 11, 18, 19].

In the current study, Eriksson and colleagues [7] performed a systematic review about alpha-defensin and PJI, and concluded that the alpha-defensin immunoassay (with its high sensitivity and specificity) might be a valuable complement to diagnostics of PJI, while the lateral flow test (which has lower sensitivity and high specificity) might be a useful tool to rule out PJI during surgery. Interestingly, all the studies evaluated in this systematic review used the Musculoskeletal Infection Society (MSIS) criteria for definition of PJI.

Where Do We Need To Go?

In a previous CORR Insights® article, Eoin Sheehan, MD, MCh, FRCS(Orth) stated that “the perfect test for PJI would have 100% sensitivity and 100% specificity” [19]. But will such a test ever exist? [10]. Before we can create one, we would first need to develop a consensus definition for PJI among the many already published [4, 13-15]. Generally, the MSIS criteria is the most commonly used [13], but this definition poorly diagnoses low-grade infections [13], which remains the most-challenging subgroup of PJI [4]. Indeed, causative bacteria are often low virulent normal skin commensals like cutibacteria (formerly propionibacteria) or coagulase-negative staphylococci and the clinical work-up generally lacks typical clinical features like fistula, reddening, or elevated laboratory parameters [14, 15]. We need studies focusing on this subset of PJIs.

It remains unclear whether sensitivity and specificity for alpha defensin would be the same or worse using different classification systems like the Infectious Diseases Society of America (ISDA) criteria for PJI, for example. Therefore, studies comparing the ISDA criteria [8] or other European classification systems [15] with the MSIS criteria in the same cohort of patients should be a priority. This is important because other definitions generally focus more on

**CORR Insights®**: Does the Alpha-defensin Immunoassay or the Lateral Flow Test Have Better Diagnostic Value for Periprosthetic Joint Infection? A Systematic Review

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low-grade infection, and the alpha-defensin test seems to have a weakness, particularly in this subset of PJI.

Studies investigating alpha defensin should not focus solely on hip and knee replacement. We also need studies that can determine whether different cut-off values (comparable to cell count and differential [15]) for ankle or shoulder arthroplasties are needed for alpha-defensin.

How Do We Get There?

We have seen a tremendous effort to bring more evidence to the treatment of PJI [12]. This summer’s consensus meeting (http://icm2018.squarespace.com/) will certainly include a discussion on the definition of PJI, and perhaps we will develop a new or more-refined definition that encompasses material from the existing classifications.

Beyond the definition, studies focusing on the performance of alpha defensin in low-grade and culture-negative PJI should examine bacteria like coagulase-negative staphylococci or cutibacteria. Among patients with shoulder or ankle PJI, there is no evidence of which I am aware that supports the use of alpha-defensin or any other biomarker, but gathering enough patients to perform a robust analysis on these diagnoses is difficult in single-center studies [1, 8], and so multicenter studies might shed light on this in the future. These studies might be coordinated by the international societies focusing on PJI like the European Bone and Joint Infection Society (EBJIS), the MSIS, or like a recent study focusing on streptococci by the European Society of Clinical Microbiology and Infectious Diseases Study Group on Implant-Associated Infections [9].

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