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CORR Insights®: Plasma D-dimer Does Not Anticipate the Fate of Reimplantation in Two-stage Exchange Arthroplasty for Periprosthetic Joint Infection: A Preliminary Investigation

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Where Are We Now?

Two-stage revision is the main treatment option for chronically infected total joint arthroplasties. The first stage seeks to eradicate the infection. It consists of removing the components, placing an antibiotic-impregnated spacer, and administering postoperative intravenous antibiotics (usually for 6 weeks or so). Once the infection is eradicated, the surgeon can remove the spacer and reconstruct the joint with revision arthroplasty components. The problem is, it is difficult to know with certainty that the infection indeed has been eradicated prior to proceeding with second-stage revision surgery.

Although serum and synovial fluid biomarkers are reasonably effective in diagnosing periprosthetic joint infection (PJI) after TKA and THA [5-7], their accuracy in the setting of two-stage revision total joint arthroplasty is unclear. The erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are sensitive but not specific. Their values usually decrease over time following a well-performed first-stage procedure, but we lack useful cutoff values that can help us to proceed with confidence to the reconstructive stage.

The current study Pannu et al. [3] identifies an important and still-unsolved problem: the lack of a biomarker that confirms for a surgeon that the infection has been eradicated, and so it is reasonable to perform the second-stage reconstruction. In their study, the authors determined that not even a promising new serum biomarker—plasma D-dimer—was effective in predicting the outcome of two-stage revision total joint arthroplasty.

The search continues for an effective serum biomarker that can identify PJI and indicate efficacy of treatment in two-stage revision total joint arthroplasty.

Where Do We Need To Go?

Synovial fluid biomarkers have been shown to be more reliable than serum biomarkers in diagnosing PJI after TKA and THA [8]. However, it appears that the good diagnostic accuracy of synovial fluid biomarkers like synovial alpha defensin or combined synovial alpha defensin and synovial CRP, in the context of diagnosing PJI, does not make them equally good at determining whether a PJI has been eradicated in the context of two-stage revision [2, 5, 8]. The effect of surgical debridement during the first stage, presence of antibiotics in the spacer cement, and serum levels of intravenous or oral antibiotics may all affect the results of synovial fluid analysis for culture and biomarkers. Future studies should evaluate a range of synovial biomarkers obtained after first-stage treatment of infected TKA in predicting the outcome of second-stage revision for infection.

In two-stage revision for infection, joint aspiration generally is recommended following completion of antibiotic therapy prior to the second-stage revision arthroplasty. Fluid is typically obtained for culture, but depending on the volume of fluid obtained, synovial

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biomarkers can also be measured. While small single-cohort studies have evaluated the diagnostic accuracy of synovial fluid analysis in revision total joint arthroplasty [2, 5, 7], large well-controlled studies are still needed to determine whether synovial fluid biomarkers alone or in combination with serum biomarkers and other tests improve the accuracy of establishing the efficacy of first-stage surgery for infection and appropriate timing of second-stage revision total joint arthroplasty.

How Do We Get There?

Serum biomarkers including interleukin (IL)-4, IL-6, tumor necrosis factor (TNF)-α, procalcitonin, soluble intercellular adhesion molecule 1 (sICAM-1), and a number of synovial fluid biomarkers including human β-defensin (HBD)-2, human β-defensin (HBD)-3, cathelicidin LL-37, IL-1β, IL-6, IL-8, IL-17, TNF- α, interferon-δ, and vascular endothelial growth factor have been identified, which may be helpful in diagnosing PJI [1]. Combined synovial fluid alpha defensin and synovial fluid CRP has been found to have greater sensitivity than synovial fluid alpha defensin alone in diagnosing PJI [8]. Combined serum IL-6 and synovial fluid IL-6 improves the accuracy of establishing the diagnosis of periprosthetic infections [4]. These studies suggest that combined biomarkers in serum and synovial fluid may be helpful in establishing the efficacy of first-stage treatment of infected total joint arthroplasty in controlling infection and appropriate timing of second-stage revision total joint arthroplasty. Future studies therefore should evaluate multiple serum and synovial fluid biomarkers simultaneously to determine whether a specific combination of biomarkers can be identified after first-stage revision for infection, which predicts the outcome of second-stage revision surgery.

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