Editorial Commentary: Are Serum Inflammatory Markers Useful Diagnostic Tools in the Shoulder?

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Abstract: Serum inflammatory markers are commonly used to evaluate for the presence of surgical-site infection or periprosthetic joint infections following orthopaedic surgery. However, data on the utility of these tests following shoulder surgery are more limited. Worse diagnostic performance is seen in the shoulder when compared with use of these tests in the evaluation of hip and knee infections, likely due to the low virulence of the commonly cultured shoulder organisms, and the normalization of these serum markers following shoulder surgery is less well defined when compared with the hip and knee literature. A better understanding of the behavior of these serum inflammatory markers in the shoulder may enhance the utility of these tests in the diagnosis and management of infection following elective shoulder surgery.

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Surgical-site infections (SSI) or periprosthetic joint infections (PJI) are some of the most serious complications associated with orthopaedic and arthroplasty surgery, leading to poor outcomes, increased cost, and technically difficult revision surgery. In particular, SSI and PJI of the shoulder can be a diagnostic and therapeutic challenge due to the low virulence of the commonly causative organisms. *Cutibacterium acnes* (*C. acnes*) is the most frequently cultured organism at the time of revision shoulder arthroplasty and is the most common organism associated with clinically relevant shoulder SSI and PJI.[1-5] Although a number of perioperative diagnostic tests are currently available to evaluate for the presence of SSI or PJI, many of these tests have more limited data on their efficacy in the shoulder, including serum inflammatory markers such white blood cell (WBC) count, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP), with worse diagnostic performance in the shoulder when compared with the evaluation of hip and knee SSI or PJI.[4,6] We have noted the poor diagnostic performance of serum inflammatory markers in our own work on shoulder PJI,[2,3,7-9] and these limitations can impact treatment decision-making in both the acute or chronic setting.

SSI or PJI of the shoulder in the acute setting often initially manifests itself with wound drainage and/or cellulitis at the incision site in the early postoperative period. Serum WBC, ESR, and/or CRP are commonly used diagnostic tests in this clinical scenario to help determine if such clinical signs represent a developing superficial or deep infection and what further treatment is warranted, including the need for joint aspiration and possible repeat surgical intervention. However, these serum markers normally elevate immediately following surgery before normalizing over the subsequent weeks to months. While these normalization curves have been well studied in the hip and knee literature, there are few studies evaluating this following shoulder surgery.[10-13] A better understanding of the normal period of elevation of these inflammatory markers would help in determining when an elevated test is abnormal and concerning for infection during the early postoperative period, particularly when these elevations may be more subtle in the setting of the less-virulent bacteria that are commonly seen in the shoulder.

In the article, "Hematologic Expression After Shoulder Surgery: Normalization Curve of Serum Inflammatory Markers," by Rhee, Kim, Kim, Ro, Ko, and Rhee,[14] the authors evaluate a series of 205 patients undergoing open (n = 44) or arthroscopic (n = 77)

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rotator cuff repair (RCR) or shoulder arthroplasty (n = 84) to determine the normalization curves of serum WBC count, WBC differential for segmented neutrophils, ESR, and CRP after elective shoulder surgery. Baseline values of each marker were taken 12 hours before surgery, and subsequent blood tests to measure each marker were performed 1 day, 2 days, 1 week, 2 weeks, 1 month, 2 months, 3 months, 6 months, and 1 year after surgery. The authors found that mean WBC count and mean WBC differential peaked 1 day after surgery, with mean WBC count returning to normal beyond 2 days after surgery and mean WBC differential decreasing to normal values 1 month after surgery in patients who underwent RCR and 2 months after surgery in patients who underwent shoulder arthroplasty. Mean ESR peaked at 2 weeks postoperatively and normalized after 1 month in patients who underwent RCR and after 3 months in patients who underwent shoulder arthroplasty. Mean CRP levels peaked 2 days after surgery in all patients but normalized within 2 weeks of surgery in patients who underwent RCR and 1 month after surgery in patients who underwent shoulder arthroplasty. Mean serum ESR and CRP values at peak time were significantly greater in patients who underwent shoulder arthroplasty compared with patients who underwent RCR ($P = .001$). The authors concluded that peak levels of the serum inflammatory markers after elective shoulder surgery were greater and normalized slower following more invasive surgery.

Rhee et al.[14] should be commended for the methodologic approach and rigor used in this study. A well-defined cohort of patients undergoing either RCR or shoulder arthroplasty was evaluated to determine how serum inflammatory markers normalize after the 2 most common elective shoulder surgeries, with extensive blood testing performed in the early postoperative period and continued until 1 year after surgery to provide a complete picture of the normalization process with each of these markers. This study design provides a unique contribution to the shoulder literature, with both patients undergoing RCR and shoulder arthroplasty able to be compared in a single study. The authors importantly exclude patients from the study with comorbidities that could independently elevate inflammatory markers, including patients with active inflammatory disease, autoimmune disorders, infectious disease, liver cirrhosis, neoplasia, or those receiving blood transfusions after surgery. However, a substantial number of patients (n = 143, 35% of the initial 414 patients) also were excluded from the cohort due to lost to follow-up (n = 53) or missing serum marker data (n = 90). The authors appropriately acknowledge this as a possible source of selection bias in the study limitations.

Although the results of the study demonstrate how peak levels of both serum ESR and CRP are greater and normalize slower after more invasive shoulder arthroplasty surgery compared with RCR, the characteristics of CRP seen in the study results are potentially the most important findings. The authors highlight how these traits make CRP the most attractive marker of those studied as a clinical test in helping to diagnose the presence and severity of infection in the early postoperative period after shoulder surgery. In contrast to WBC count, WBC differential, and ESR, which all varied widely with regards to their normalized values, CRP showed consistent undetectable median, upper and lower quartile values less than 0.5 after normalization. Mean CRP levels were also normalized within 2 weeks of surgery in patients who underwent RCR and nearly normalized within 2 weeks of surgery in shoulder arthroplasty patients, in contrast to ESR levels, which did not normalize until 1 month after surgery in patients who underwent RCR and 3 months after surgery in patients who underwent shoulder arthroplasty. These characteristics demonstrate that CRP can be used to help distinguish the significance of clinical findings concerning for infection in the early postoperative period, such as wound drainage or cellulitis. For example, the presence of wound drainage or cellulitis more than 2 weeks after surgery in combination with a normalized CRP may be more suggestive of a superficial wound infection that can be successfully treated with a period of oral antibiotics, whereas these same findings in the presence of a persistently elevated CRP should raise suspicion for a deeper wound infection and trigger further evaluation to confirm or rule out this concern, including joint aspiration with the fluid sample sent for culture and synovial analysis. I have commonly used CRP in this algorithmic manner, and the results of this study lend further support to this approach. If suspicion for deep infection is high upon further workup, repeat surgical intervention may be warranted, with the ability to perform open irrigation and debridement with implant retention if deep infection is identified in the early postoperative period.

Future studies are needed to continue to evaluate these serum markers and other diagnostic tests, as well as the optimal treatment approach in patients who develop SSI or PJI following shoulder surgery. Data are still limited in many instances in defining management of infection following shoulder surgery,[15] both in the acute and chronic setting, with the goal of future work to develop more well-defined algorithms that lead to improve clinical outcomes in the treatment of infection following shoulder surgery.

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