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Authors: Georgios Komnos, Ronald Huang

QUESTION 3: What nutritional markers are the most sensitive and specific for surgical site infections and periprosthetic infections (SSIs/PJIs)? Does improvement in nutritional status reduce the risk of SSI/PJI?

RECOMMENDATION: Serum albumin < 3.5 g/dL has been demonstrated to be an independent risk factor for SSIs/PJIs following total joint arthroplasty in multiple, large-scale studies. However, other nutritional markers are poorly studied. Currently, there is insufficient evidence to prove that correction of preoperative nutritional markers reduces the risks of subsequent SSIs/PJIs. Despite the absence of such evidence, we recognize the importance of an optimized nutritional status before total joint arthroplasty (TJA) to reduce the risks of SSIs/PJIs.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 98%, Disagree: 1%, Abstain: 1% (Unanimous, Strongest Consensus)

RATIONALE

It is well established that malnutrition is associated with an increased risk of a number of adverse outcomes following TJA, including wound healing problems, longer hospital stays and PJIs [1–3]. The prevalence of malnutrition in patients undergoing orthopaedic procedures has been reported to be as high as 50% [4]. However, it is unclear which nutritional markers are most sensitive and specific for SSIs and PJIs. Serologic values and anthropometric measures have been utilized to determine nutritional status.

Serologic markers commonly used as markers of malnutrition include serum albumin concentration < 3.5 g/dL, serum total lymphocyte count (TLC) of <1500 cells/m^3 and serum transferrin < 200 mg/dL. Other serum markers, including serum prealbumin, have been discussed in nutritional literature but levels for malnutrition have been poorly defined in the orthopaedic literature.

Gherini et al. evaluated preoperative serum albumin and transferrin levels in patients undergoing primary total hip arthroplasty (THA) and found that delayed wound healing was associated with a lower preoperative serum transferrin (226 mg/dl in complicated cases vs. 262 mg/dl in those that did not have any complications) [5]. Alfargieny et al. found that serum albumin, but not serum TLC, was an independent predictor of SSIs following primary THA [6]. Other recent studies have also identified serum albumin as an independent predictor of SSIs and PJIs [2,6–12]. Studies of 37,173 patients undergoing total knee arthroplasty (TKA) and 49,475 patients undergoing THA in the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database found that albumin < 3.5 g/dL was a stronger independent predictor of SSI and mortality than obesity [8,13]. The superficial SSI rate was 2.14% in patients with hypoalbuminemia vs. 0.71% in patients with normal serum albumin following THA and 1.27 vs. 0.64% following TKA. The deep SSI rate was 0.38% in patient with serum albumin ≥ 3.5 g/dL vs. 0.12% in patients with hypoalbuminemia following TKA and 0.71 vs. 0.27% in THA [8,13].

In the revision TJA setting, low serum albumin has also been found to be an independent risk factor for postoperative SSIs and PJIs. Yi et al. evaluated the associations between malnutrition, septic failure and acute infection occurring after revision TJAs. The nutritional parameters used were serum albumin, TLC and transferrin. They found that in the presence of one or more altered parameters, suggestive of malnutrition, that these independently associated with both chronic PJIs and acute postoperative infections [2]. Bohl et al. found that patients undergoing revision TJA with hypoalbuminemia were more than twice as likely to develop PJIs within 30 days than those with serum albumin > 3.5 g/Dl [11].

Anthropometric measures such as calf circumference, arm muscle circumference and triceps skinfold have been utilized to identify undernutrition in orthopaedic patients, but cutoffs are poorly defined and correlations with SSIs and PJIs are not well studied [14–17].

Serum albumin is the most widely studied nutritional marker in patients undergoing TJA. Due to the correlations between nutritional status and postoperative complications, patients suspected of malnurishment should have nutritional parameters evaluated prior to elective arthroplasty. However, there is currently inadequate evidence to determine whether correction of preoperative nutritional markers results in decreased rates of SSIs and PJIs.

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1.2. PREVENTION: RISK MITIGATION

Authors: Matthew Austin, Mark Spangehl, Max Greenky

QUESTION 1: What preoperative screening for infections should be performed in patients undergoing revision hip or knee arthroplasty because of presumed aseptic failure?

RECOMMENDATION: In addition to taking a thorough history, obtaining radiographic imaging and performing a physical examination, all patients with a failed hip or knee arthroplasty awaiting revision surgery should have their serum erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) measured. Patients with high index of suspicion for infection should be considered for further workup.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 96%, Disagree: 4%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

While there are many etiologies that can cause pain and failure following total joint arthroplasty (TJA), infection is the most common cause of failure in total knee arthroplasty (TKA) and the third most common cause of failure in total hip arthroplasty (THA) [1,2]. The evaluation of patients with a painful TJA begins with a thorough history, physical examination and joint-specific radiographic imaging.

Patients with recent bacteremia, prolonged drainage after surgery, multiple surgeries on the same joint, history of prior periprosthetic joint infections (PJIs), history of surgical site infections of the same joint, comorbidities resulting in an immunocompromised state (i.e., diabetes mellitus, inflammatory arthropathy, etc.) or patients with increased risks of skin barrier penetrations (i.e., intravenous drug abuse, skin ulceration, chronic venous stasis, etc.) should be considered at higher risk for PJIs [3]. Physical exam findings suggestive of PJIs include joint erythema, warmth or large atraumatic effusion.

Plain radiographs should be obtained for all patients presenting with a painful TJA. It is useful to compare serial radiographs. Plain radiographic findings that should increase suspicions of PJIs include signs of early loosening, early osteolysis, periosteal elevation and transcortical sinus tract [4,5]. However, it is important to note that radiographs are rarely diagnostic of PJIs, and can often be normal in the setting of infection.

Infection can be an occult cause of pain following TJA. Therefore, screening for PJIs should be performed in every patient with a painful hip or knee arthroplasty. A successful screening test should have high sensitivity, be widely available and cost-effective. Serum inflammatory markers have been a cornerstone for screening for PJIs in the painful TJA [3–9]. Obtaining an ESR and CRP have proven to be effective screening tools for PJIs due to their high sensitivity, wide availability and cost-effectiveness [10–18]. Using ESR and CRP in combination improves sensitivity and negative predictive values [10,13,14,17–20].

It is important to note that ESR and CRP levels below established thresholds do not definitively exclude the possibility of PJIs [10,13,20]. This is especially true of patients with slow growing organisms such as *Cutibacterium acnes* (*C. acnes*) [21]. It is also true that patients with elevated serological markers do not definitely have PJIs. It is recommended that in the presence of elevated serology and/or high, clinical suspicion for PJIs, even in the presence of normal serology, joint aspiration be performed [3,5,7].

There are some additional limitations to screening using inflammatory markers. ESR, especially, and CRP are normally elevated in the early postoperative periods. Patients with elevated metal ion levels can also present with elevated ESR and CRP levels creating a clouded diagnostic picture [9]. In an effort to overcome these shortcomings, other serum biomarkers have been studied for the diagnosis of PJIs. Interleukin-6 (IL-6) is a cytokine produced by activated monocytes, macrophages and T-cells and has been shown to be a highly-sensitive and specific biomarker for PJIs. However, selection bias, cofounding variables and small study sizes have limited its wide spread adoption [11,22–24]. In a recent study, Shahi et al. evaluated serum D-dimer (fibrinolytic by-product) as a marker of PJIs. In their study, D-Dimer outperformed both ESR and CRP individually and when combined in terms of sensitivity and specificity for diagnosis of PJIs [20]. While promising, this was the first study to analyze the role of D-dimer in diagnosing PJIs.

It is clear that there is a need for more specific and accurate serological screening tests in order to diagnose PJIs. The future holds