

Editorial

Preoperative Serum Inflammation Markers Should be Routinely Assessed in Patients Undergoing Primary Total Knee Arthroplasty

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The authors review their experiences with perioperative infection markers.

Total knee arthroplasty (TKA) is one of the most commonly performed elective surgeries in the United States (US) (Singh et al. 2019). Periprosthetic joint infection (PJI), occurring in 1-2% of TKA patients (Jin, Gallego Luxan,

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Hanly, et al. 2022), is one of the most serious complications of TKA and can result in significant morbidity (e.g., TKA failure), mortality and healthcare costs (Aggarwal, Rasouli, and Parvizi 2013; Beam and Osmon 2018; Premkumar, Kolin, Farley, et al. 2021). A number of risk factors for PJI have been identified, including demographic, clinical, and perioperative variables (Lucenti, Testa, Caldaci, et al. 2024), but there are no validated predictive models for early detection of PJI after TKA. Clinicians routinely assess TKA patients for biomarkers of inflammation, serum C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), after surgery to help screen for and diagnose PJI (Parvizi and Della Valle 2010), but CRP and ESR are not routinely captured prior to surgery. We believe that preoperative CRP and ESR levels should be routinely assessed prior to TKA to help physicians interpret postoperative elevations in these markers and determine which patients should receive additional workup for PJI (e.g., aspiration and culture of synovial fluid) after surgery.

Approximately 4% of primary TKA patients have elevated CRP and ESR levels before surgery and patients with both elevated markers have an 18-fold higher risk for developing PJI than patients with normal levels (Xu et al. 2018). Despite this apparent strong association between CRP/ESR levels and risk for PJI, elevations in these biomarkers may be due to factors other than infection, including demographics, smoking, alcohol abuse, obesity, and comorbidities (Barretto, Campos, and Ooka 2022). Thus, if CRP and ESR are elevated after TKA, but are not significantly higher than preoperative levels, they may not be indicative of infection and warrant additional work-up. Additionally, all TKA patients will experience an increase in CRP and ESR after surgery as a normal response to acute injury. In patients with uninfected knees, CRP and ESR do not normalize until, respectively, 3-6 weeks and 3 months after TKA (Choi et al. 2023). By establishing a baseline reference, physicians should be better able to determine whether postoperative elevations in CRP and ESR are most likely due to a normal acute response to surgery, pre-existing factors, or infection to guide decision making about further testing with radiographs, blood tests, and joint aspiration.

In my clinical practice, we routinely assess CRP and ESR before surgery in patients undergoing primary TKA. Postoperatively, CRP and ESR are assessed in patients who exhibit clinical signs of infection, such as warmth, swelling, pain, and/or erythema, when presenting to the emergency department or surgeon's office. Patients with elevated postoperative CRP and ESR levels that are at least 20% higher than their baseline levels, are considered at high risk for infection and usually undergo additional work-up for PJI unless they show signs of clinical improvement.

In my clinical practice, among 337 patients who underwent primary TKA between January 1, 2016, and December 31, 2022, 19.3% had elevated preoperative CRP (>8.2 mg/L), 24.8% had elevated preoperative ESR (>36 mm/hr), and 10.2% had both elevated preoperative CRP and ESR. Postoperative CRP and/or ESR were assessed in approximately 23 patients (6.8% of all TKA patients). Postoperative CRP,

ESR, and both CRP and ESR were elevated in, respectively, 69.6% (16/23), 77.3% (17/22), and 63.6% (14/22) of patients. Among the 14 patients with both elevated CRP and ESR levels postoperatively, 7.1% (1/14) did not have elevations $\geq 20\%$ above baseline/preoperative levels, while the remaining 92.9% (13/14) had elevations of both biomarkers that were $\geq 20\%$ greater than their preoperative levels.

To illustrate our approach, I will describe cases in which preoperative CRP/ESR values influenced decision making in primary TKA patients treated in my practice. An 89-year-old female patient with diabetes presented with extreme postoperative pain 9 years after TKA. The patient had elevated postoperative CRP (11 mg/L) and ESR (52 mm/hr) levels suggestive of infection; however, because their preoperative values were also elevated (CRP: 21.1 mg/L; ESR: 21 mm/hr), and the postoperative values were not 20% or higher than preoperative values, the patient did not meet criteria for further infection workup. The patient's symptoms improved over subsequent weeks, confirming that her symptoms were not due to PJI. Had the patient not have baseline preoperative inflammatory labs, an unnecessary aspiration would likely have been done. Furthermore, a 66-year-old male patient with a body mass index > 40 kg/m² presented with severe knee pain two weeks after primary TKA. Inflammatory markers were elevated postoperatively (CRP: 20 mg/L; ESR: 25 mm/hr) relative to baseline levels (CRP: 4.1 mg/L; ESR: 23 mm/hr), but both markers were not increased by 20% and, thus, did not warrant additional workup for PJI. This patient had returned to his baseline and simply needed more time to recover. These cases demonstrate the utility of routinely assessing preoperative CRP/ESR to inform clinical decisions that may reduce unnecessary testing.

The interpretation of inflammatory markers requires a comprehensive assessment of patient demographics and medical history and a thorough clinical examination. Relying solely on laboratory values may result in diagnostic errors, as they do not have 100% sensitivity and specificity for detecting PJI. Integrating laboratory findings with a complete clinical picture of the patient is the key to clinical signs of infection such as swelling, pain, or drainage, clinicians can develop a comprehensive understanding of the patient's current condition, enabling precise diagnosis and treatment strategies. To illustrate possible exceptions to this algorithm, one of my primary TKA patients, a 67-year-old male, presented 3 months after TKA due to stiffness, swelling, and pain. He had normal preoperative ESR (24 mm/hr) and CRP (5.4 mg/L) values, and elevated postoperative ESR (91 mm/hr) and CRP (111 mg/L) values, but did not undergo infection workup because of improving pain symptoms.

While I have found knowledge of preoperative CRP/ESR to have utility in my practice, research should be conducted to determine the accuracy of the proposed algorithm and the cost effectiveness of routine collection of preoperative inflammatory markers in primary TKA patients. Exploration of this topic may help guide the development of clinical guidelines, facilitate optimal healthcare resource utilization, enhance patient outcomes by limiting unnecessary

invasive joint aspiration, and improve the quality of care. Research could lead to the broader implementation of a comprehensive and highly accurate PJI risk assessment algorithm applicable to different patient populations within subspecialties of orthopedic surgery.

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