



PROCALCITONIN FOR DIAGNOSING POSTOPERATIVE INFECTION AFTER CARDIAC SURGERY POSTOPERATIVE INFECTION AND PROCALCITONIN

Paediatrics

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ABSTRACT

In cardiac surgery practice, systemic inflammatory response (SIRS) is a clinical condition that develops secondary to cardiopulmonary bypass (CPB) and increases mortality and morbidity. Postoperative infection among patients undergoing cardiac surgery, manifests itself in a way similar to SIRS and also increases mortality. Early diagnosis and treatment of infectious complications reduce mortality and morbidity. Procalcitonin, the precursor of calcitonin, is a specificity and sensitivity for early detection of bacterial sepsis have recently been confirmed by multiple studies Its serum level exceeds that level when postoperative infection or sepsis develops, depending on the severity of the either clinical condition. Despite being elevated in the event of bacterial and fungal infections; it is not affected by viral infections. Monitoring postoperative serum PCT kinetics is useful for making an early diagnosis of postoperative complications. Serum PCT should be routinely monitored in all patients undergoing cardiac surgery. PCT levels failing to drop by 24 hours postoperatively, or those exceeding 5 ng/ml, should be interpreted in favor of infection or any postoperative complication. Its marked superiority over CRP and WBC allows making a timely diagnosis of infectious complications and commencing antibiotic therapy without delay.

Serum PCT level is an important biomarker that offers promise for routine use to reduce postoperative morbidity and mortality after cardiac surgery.

KEYWORDS

Procalcitonin; sepsis; cardiac surgery.

INTRODUCTION:

In cardiac surgery practice, systemic inflammatory response is a clinical condition that develops secondary to cardiopulmonary bypass and increases mortality and morbidity. Serum levels of many biomarkers are naturally elevated during SIRS. However, they also tend to increase in case of infection, and this complicates differential diagnosis. Therefore, research efforts have been intensified to discover specific markers for postoperative infections that develop at intensive care units after cardiac surgery. Once the pioneering studies have pointed to an increased sensitivity of procalcitonin for early recognition of sepsis at intensive care units, many randomized controlled studies, particularly in the last decade, have been published on the role of serum procalcitonin in early detection of infection after cardiac surgery.

PROCALCITONIN

Procalcitonin, the precursor of calcitonin, is a polypeptide composed of 116 aminoacids [1]. In a healthy person, it is released into the thyroid tissue and is usually undetectable or below 0.1 ng/ml in blood [2]. Its specificity and sensitivity for early detection of bacterial sepsis have recently been confirmed by multiple studies [3,4].

PCT level starts to increase three to four hours after the entry of an endotoxin into the human body and reaches its maximum level by 24 hours. Its advantages over other biomarkers include a wide biological range, a rapid increase after a bacterial stimulus, and a long half-life [5]. It is still unclear why PCT is released during an inflammatory response, but it is thought to be synthesized in liver. It is converted by cytokines and lipopolysaccharides to peripheral mononuclear cells [6]. Sepsis is an bodily inflammatory response to infection, which usually results in organ dysfunction, and its early recognition is of paramount importance for reducing mortality. The major difficulty with detection of sepsis is delayed or false positive blood culture results. A delay in diagnosis increases both mortality and costs and duration of hospital stay [7,8]. Difficulty diagnosing sepsis in a timely manner is mainly related to unreliable clinical signs and laboratory tests [9]. Although the traditional markers C-reactive protein (CRP), sedimentation rate, and white blood cell count (WBC) are elevated in both sepsis and inflammation, they lack specificity [10,11]. Moreover, only 30% of patients with sepsis have detectable bacteremia due to recent antibiotic use [12,13]. A metaanalysis by Uzzan et al [14] revealed that PCT was superior to CRP at making the differential diagnosis of sepsis.

The possibility that procalcitonin may be a specific biomarker has been first theorized for sepsis and studies have been conducted. In a metaanalysis by Ren et al [15] PCT appeared to be significant predictor

of sepsis. That metaanalysis included studies conducted between 1998 and 2014, and although a significant proportion of the involved patients were adults, pediatric patients were also included. PCT's sensitivity and specificity were found 0.74 and 0.88, respectively. The authors concluded that PCT is an important biomarker for early diagnosis of sepsis but it should be combined with clinical parameters, physical examination findings, and other laboratory tests. Wacker et al [16] performed a metaanalysis containing 3244 patients, showing that PCT had a sensitivity of 0.77 and a specificity of 0.79. Although PCT is an important biomarker for recognition of sepsis at an early period, its standalone use is not recommended, and its use in combination with anemnesis, physical examination, and other parameters is encouraged. Another metaanalysis included studies on infective endocarditis and showed that PCT was more sensitive and specific than other biomarkers [17]. The increasing popularity of PCT over the last years has increased its routine use, particularly among intensive care patients. PCT is now routinely utilized for both detection and follow-up of infections. PCT measurement is currently performed with three different kits. The most commonly employed kit is the immunoluminetric LUMI-test. Q-test and Kryptor test are other testing methods [18].

Meissner et al. [19] reported that serum PCT level increased by 32% after minor aseptic surgery, 59% after aseptic cardiac and thoracic surgery, and as high as 95% after aseptic intestinal surgery.

Serum PCT level peaks at 24 hours after uncomplicated cardiac surgery. Many studies to date have reported PCT at a range of 0.5-7.0 ng/ml by immunoluminometric study [20-25]. The type of surgical procedure is closely linked to serum PCT increase. Serum PCT level was higher among patients who underwent on-pump cardiopulmonary bypass compared to those who underwent off-pump surgery [26]. Similarly, PCT levels were lower in patients who underwent minimally invasive bypass surgery compared to those operated with the classical technique [20]. Serum PCT increase was more prominent in patients who underwent valve surgery [21]. PCT level increased to a greater extent among patients who underwent ventriculotomy than those operated with atriotomy [27]. Serum PCT level was found higher among pediatric cardiac patients operated for tetralogy of fallot than those who were operated for ventricular or atrial septal defect [28].

Intraoperative factors also influence serum PCT concentration. Longer aortic clamp, CPB, and operative times lead to increased serum PCT level [29]. Meissner et al [30], in a study comparing PCT with other inflammatory markers, noticed that PCT elevation as a result of non-infectious causes (trauma, tissue injury) occurred to a lesser degree than other markers (CRP, WBC). The amount of increase was

significantly greater among patients who were infected after cardiac surgery. Sponholz et al [31] performed a metaanalysis of studies conducted between 1990 and 2006. Monitoring dynamic PCT

levels showed that they were significantly greater in patients with postoperative infection, sepsis, and organ failure. PCT increase was significantly more common in systemic infections than the local ones, but it was not clinically relevant in viral infections. PCT elevation in fungal and bacterial infections has been corroborated by many similar studies [32,33]. Çapcı et al [34] showed that PCT was more sensitive than other biomarkers (sedimentation rate, WBC, CRP) for postoperative infection among patients undergoing pediatric cardiac surgery. Mean PCT level among uncomplicated patients after cardiac surgery is 4 ng/ml whereas it climbs to as high as 30 ng/ml in infected patients. PCT level is dramatically lowers after a 5-day course of antibiotics [35].

Sharma et al [36] quantified PCT levels for postoperative infections. Among patients with a PCT level of 2 ng/ml, they reported a sensitivity of 58% and a specificity of 42%; on the other hand, when levels exceeded 7 ng/ml, the corresponding figures were 95% and 80%, respectively. A mean serum PCT level of 51.97 ng/ml was detected for patients with positive blood cultures.

Elevated levels of CRP and WBC are not as helpful as other infectious parameters for diagnosing infection after cardiac surgery. Multiple studies have indicated a parallel postoperative increase in CRP and WBC count independent of infectious status [37,38]. Two studies reported a correlation between elevated serum Interleukin-6 (IL-6) and PCT levels [39,40]. Multiple studies reported correlation between sepsis and PCT after cardiac surgery [41,42]. While patients with sepsis had a mean serum PCT level of 20 ng/dl, it reached 97 ng/dl in septic shock [43]. Several attempts have been made to standardize serum PCT levels to diagnose postoperative infection and sepsis, but this topic remains debated [44,45]. Dörge et al [46] suggested that a PCT level exceeding 10 ng/dl in the first 24 hours is a poor prognostic sign. Fritz et al [47] demonstrated a PCT level of 2.8 ng/dl among patients with a low postoperative risk. Daily measurement of PCT level is useful for determining the prognosis of sepsis and organ dysfunction. Significant correlations have been found between serum PCT level and APACHE II and SAPS scores. Meissner also showed a correlation between PCT level and SOFA, an indicator of the severity of organ dysfunction. Other studies pointed to a correlation between other complications of cardiac surgery and PCT level [48,49]. Lechamy et al [25] demonstrated a significant increase in PCT level in patients with postoperative myocardial infarction. Meissner et al [30] reported a significant correlation between PCT level and respiratory failure and need for positive inotropic support. Adamik et al [49] reported that a PCT cut-off level of 2 ng/ml could significantly predict prognosis.

There appears a significant correlation between postoperative complication rates and PCT levels after cardiac transplantation. PCT level markedly increases in case of acute rejection or bacterial/fungal infections. Hammer et al [50] reported that PCT level was increased among patients who developed systemic or local infection after heart lung transplantation.

CONCLUSION:

Infection is one of the major factors leading to excess mortality and morbidity after cardiac surgery. Infections should be addressed at once, well before sepsis or multi-organ failure ensues. Systemic inflammatory response is an expected clinical manifestation among patients undergoing cardiac surgery. However, its distinction from infectious complications is difficult most of the time. Whereas CRP, WBC, and sedimentation rate are largely inadequate for an accurate differential diagnosis, PCT level provides an opportunity for a timely diagnosis. After an uncomplicated cardiac surgery serum PCT level peaks in the first 24 hours and returns to normal at a mean of 1 week. PCT level varies by the type and duration of surgical procedure. It usually does not exceed 5 ng/ml. Its serum level exceeds that level when postoperative infection or sepsis develops, depending on the severity of the either clinical condition. Despite being elevated in the event of bacterial and fungal infections; it is not affected by viral infections. Monitoring postoperative serum PCT kinetics is useful for making an early diagnosis of postoperative complications. Serum PCT should be routinely monitored in all patients undergoing cardiac surgery. PCT levels failing to drop by 24 hours postoperatively, or

those exceeding 5 ng/ml, should be interpreted in favor of infection or any postoperative complication. Its marked superiority over CRP and WBC allows making a timely diagnosis of infectious complications and commencing antibiotic therapy without delay. Serum PCT level is an important biomarker that offers promise for routine use to reduce postoperative morbidity and mortality after cardiac surgery.

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