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Procalcitonin cannot be used as a biomarker of infection in heart surgery patients with acute kidney injury

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ABSTRACT

Purpose: We intended to assess how acute kidney injuy impacts on procalcitonin levels in cardiac surgery patients, with or without infection, and whether procalcitonin might be used as a biomarker of infection in acute kidney injuy.

Material and Methods: A case–control study was designed which included patients that had had cardiac surgery between January 2011 and January 2015. Every patient developing severe sepsis or septic shock (n = 122; 5.5%) was enrolled. In addition, consecutive cardiac surgery patients during 2013 developing systemic inflammatory response syndrome (n = 318) were enrolled. Those recruited 440 patients were divided into 2 groups, according to renal function.

Results: Median procalcitonin levels were significantly higher during the 10 postoperative days in the acute kidney injury patients. Regression analysis showed that postoperatory day, creatinine, white blood cells and infection were significantly ($P < .0001$) associated to serum procalcitonin level. In patients with creatinine ≥2, median procalcitonin levels were similar in infected and non-infected patients. Only when creatinine was less than 2 mg/L, the median procalcitonin levels were significantly higher in patients with infection, as compared to those with no infection.

Conclusions: In acute kidney injuy patients, high procalcitonin levels are a marker of acute kidney injuy but will not be able to differentiate infected from non-infected patients.

1. Introduction

Cardiac surgery is an extended procedure in the developed world, with coronary artery bypass graft (CABG) and valve surgeries being the most common cardiac surgeries performed [1]. In Europe, 348,523 patients underwent cardiac surgery over a 2-year period (2006-2008) [1], with different proportions of CABG and valve surgeries depending on the specific country. In Spain, isolated CABG represents 30% of all cardiac surgeries and isolated valve procedures constitutes 32% [1].

Postoperative sepsis is one of the major complications following cardiac surgery, and an independent predictor of mortality [2,3]. Hospital-acquired infections are common, especially ventilator-associated pneumonia and surgical site infections, with both infections being associated to high morbidity and mortality, and also to longer hospital stay [4,5].

Procalcitonin (PCT) is used as a biomarker of infection [6] and has been successfully used as guidance for the initiation and duration of antibiotic therapy in patients with respiratory infections and to discontinue antibiotic therapy in intensive care unit (ICU) patients, being able to reduce antibiotic use as compared with standard therapy [7,8].

One major limitation of interpreting PCT levels in cardiac surgery patients is that PCT is also one of the inflammatory mediators involved in the inflammatory response elicited by this type of intervention [9,10],

Abbreviations: CABG, coronary artery bypass graft; PCT, procalcitonin; ICU, intensive care unit; CPB, cardiopulmonary bypass; AKI, acute kidney injury; NAKI, no acute kidney injury; CRP, C-reactive protein; WBC, white blood cells.

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leading to a systemic inflammatory response syndrome (SIRS) in most patients [11,12]. Thus, PCT elevations in cardiac surgery patients must be carefully interpreted.

In addition, cardiac surgery patients often develop kidney dysfunction [13], and patients with post-operative, as well as those with preoperative, acute kidney injuy (AKI) show higher rates of infection, which in turn are associated to higher mortality [14]. It would be of most importance, thus, closely monitoring these patients for the presence of infection. The value of PCT assessment in this situation is not clear. Renal dysfunction decreases PCT elimination [15], and while some studies observed no variation or just a small increase of PCT plasma levels in patients with AKI [15,16], a more recent study has shown a marked increase in PCT in 67 patients with postoperative renal dysfunction, either with or without infection [17]. Therefore, we intended to study how AKI impacts on PCT levels in a large series of patients, with or without infection, in the period following cardiac surgery, while assessing other putative variables that might influence in PCT levels, and determine whether PCT levels might still be used to assess infection in cardiac surgery patients presenting with renal dysfunction.

2. Material and methods

2.1. Study population

A case-control study was designed, which included 440 patients that had had cardiac surgery with cardiopulmonary bypass (CPB) at the Hospital Clínico Universitario de Valladolid (Spain) in the period between January 2011 and January 2015. The case group consisted of all patients that developed severe sepsis or septic shock (n = 122, infection rate 5.5%; 94 with pneumonia and 28 with surgical site infection); in the control group, patients from 2014 that did not develop these conditions were included consecutively (n = 318). All patients that began receiving antibiotic treatment for suspected infection whose germ culture results were negative were excluded from the study. In a second step, the 440 patients (122 with severe sepsis or septic shock plus 318 with SIRS) were divided in 2 groups according to renal function during the postoperative period: 92 patients were included in the AKI and 348 in the no acute kidney injury (NAKI) arm (Fig. 1).

Blood samples for biologic measurements (PCT, C-reactive protein [CRP], white blood cells [WBC], creatinine, glucose and lactate) were drawn on the first day in the ICU and daily in the morning until the tenth postoperative day. Procalcitonin was measured by an immunoluminometric assay (LUMItest Procalcitonin; Brahms Diagnostica) adapted to the analyzer Cobas 6000 (Roche Diagnostics) with detection limit 0.2 to 100 ng/ml. C-reactive protein was measured by automatic laser nephelometry (BN II analyzer; Siemens Dade Behring); normal values were less than 6 mg/L, and the coefficient of variation of the measurement was less than 5%.

The study was conducted according to the Helsinki Declaration and Good Clinical Practice and was approved by the Institutional Review Board (IRB) of Hospital Clínico Universitario de Valladolid. Waived informed consent was authorized because routine care of the patient was not modified.

2.2. Patients' management in the ICU

The surgical and anesthetic techniques and the treatments received by the patients in the ICU were the ordinary procedures routinely conducted at the hospital. After admission to the ICU and verification of hemodynamic stability, the patients were placed at a 45° position. Gastric protection was routinely carried out with ranitidine (50 mg intravenously per 12 hours) during the first 24 hours of admission in the ICU; if it continued to be required, ranitidine was replaced by sucralfate (1 g orally or through nasogastric tube every 8 hours). All patients were extubated in the ICU when hemodynamically stable. Mouthwashes with chlorhexidine were carried out twice a day. Antibiotic therapy was administered in patients with infection, according to the bacterial pathogens isolated from these patients, as well as following international guidelines.

2.3. Definitions

Diagnosis of infection: clinical assessment of the patient was performed daily in the ICU for infection diagnosis. Severe sepsis and septic

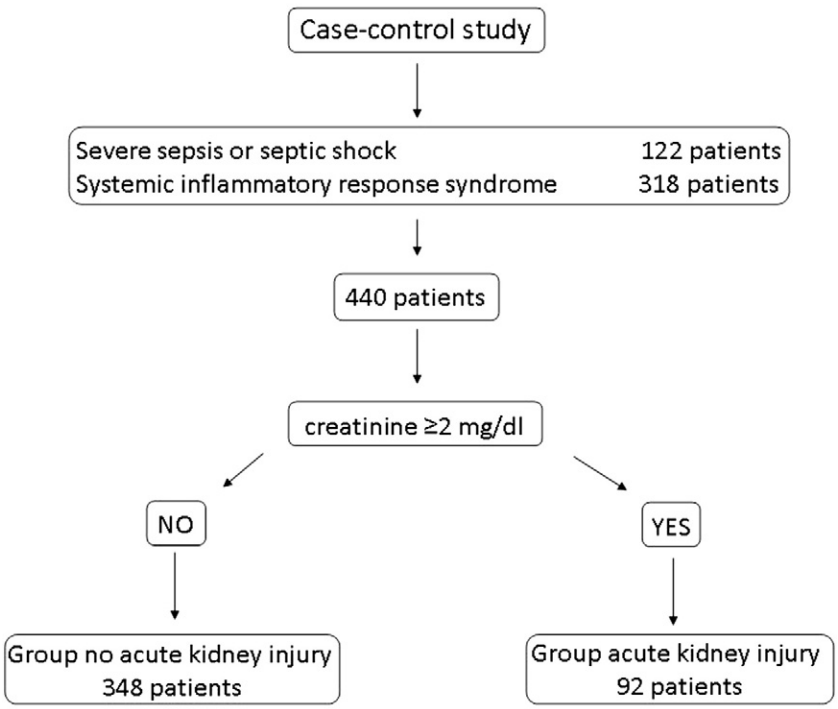

Fig. 1. Study flow diagram.