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Original article

Potential use of procalcitonin as biomarker for bacterial sepsis in patients with or without acute kidney injury

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ABSTRACT

Introduction: There are few investigations regarding the relationships between procalcitonin (PCT) and the acute kidney injury (AKI) in the diagnosis of sepsis. The purpose of this study was to clarify the diagnostic accuracy of the use of PCT levels in patients with or without AKI.
Methods: This study was conducted as a single-center retrospective study. We enrolled 393 patients in whom PCT were measured on admission. We grouped the patients into non-AKI and AKI, and those with AKI were classified according to the RIFLE criteria (Risk, Injury, Failure). The patients in each group were further classified into the sepsis and the non-sepsis group. We subsequently investigated the diagnostic accuracy of the PCT for detecting sepsis in these groups.
Results: The levels of PCT were significantly higher in the sepsis group than in the non-sepsis group among the non-AKI and each AKI patients ($p < 0.0001$). The diagnostic accuracy of the PCT for detecting sepsis was determined according to a ROC analysis; AUC value was 0.958 in the non-AKI group, in the Risk, Injury and Failure groups were 0.888 and 0.917, 0.857, respectively. AUC value for non-AKI group was significantly different from that of Failure group ($p < 0.05$).
Conclusions: In Failure AKI patients, the diagnostic accuracy of the PCT level is significantly lower than non-AKI patients. It is therefore suggested that we should be careful in using PCT value to diagnose sepsis in patients with Failure under RIFLE criteria.

1. Introduction

Sepsis caused by bacteria is the major cause of death in intensive care unit (ICU) patients. Rapid initiation of the correct treatment is crucial important for improving sepsis condition [1,2]. Additionally, the most recent international sepsis guidelines entitled “Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012” recommend early diagnosis and treatment of sepsis to avoid multiple organ failure and other adverse outcomes [3]. In treatment of sepsis antibiotics have already clear benefits, however potential complications from their inappropriate or prolonged using are also well known. Inappropriate or prolonged using of antibiotics lead to multidrug-resistant bacterial strains, allergic reactions, antibiotic-related colitis, and other adverse events [4–6]. From such situations it is emphasized that the early and accurate detection of sepsis are very important.

Since the definition of systemic inflammatory response syndrome (SIRS) was proposed by the American College of Chest Physicians/Society of Critical Care Medicine (ACCP/SCCM) in 1991 [7], many clinical trials on sepsis diagnosis and treatment have been conducted. And sepsis was defined when patients met the criteria for SIRS and an infectious source was documented or strongly suspected based on clinical presentation. Blood culture is frequently used as the “gold standard” diagnostic method for sepsis. However, it usually takes 3–7 days to obtain blood culture results and frequently yields low positive results or low sensitivity [8]. Therefore, the general practical medical treatment used for sepsis is based on the doctor's own experience (empiric therapy).

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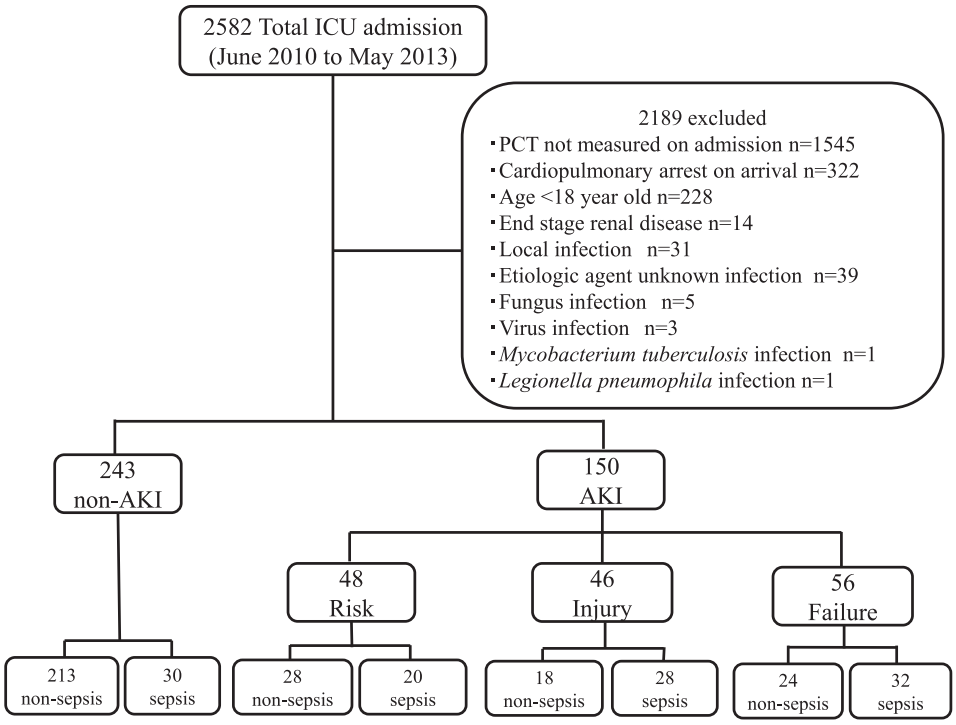

Fig. 1. Study design.

Many trials have identified potential biomarkers. More than 170 biomarkers have been studied for use in evaluation of sepsis [9]. In 1993, procalcitonin (PCT) was first described as a marker elevated in bacterial infections [10]. In infectious conditions, PCT is released from nearly all tissues including lung, liver, kidney, pancreas, spleen, colon, and adipose tissues [11]. Currently, PCT is recognized as one of the suitable markers for diagnosis of sepsis or severe sepsis. In comparison to other markers which have traditionally been reported, PCT gives a high rate of specificity for sepsis diagnosis [12]. However, the concentration of PCT in the human blood is elevated in various conditions, such as in severe trauma, surgical invasive procedures, and critical burn injury, which leads to SIRS. So it is necessary to be aware of false-positive results [13]. In addition, it has been reported that renal function is a major determinant of PCT levels and thus different thresholds should be applied according to renal function impairment [14]. To the best of our knowledge, there are few studies investigating the relationship between PCT and acute kidney injury (AKI). So, the purpose of this study is to clarify the accuracy of diagnosing sepsis using the PCT levels according to AKI severity.

2. Materials and methods

This is a retrospective study conducted at Fukuoka University Hospital, which is a 915-bed academic center with 34-bed ICU. The ICU has an average admission of about 800 patients per year. The ICU admissions typically include 60% outpatients (including those transferred from the emergency department), 30% transferred from other hospitals, and 10% in-house patients (not including post-operated and newborn patients). The ratio of adult and pediatric (<16 years) patients was 93:7. The study was approved by the institutional review board of Fukuoka University Hospital according to the Declaration of Helsinki. The informed consent was waived in view of the retrospective and anonymous nature of the study.

2.1. Study population

All the 2582 patients admitted to the ICU during the 3 years period (June 2010 through May 2013) were enrolled. Exclusion criteria were lack of PCT measurement on admission, cardiopulmonary arrest on arrival, age < 18, end-stage renal disease, local infection (excluded by sepsis criteria [7]), etiologic agent unknown, and patients with *Mycobacterium tuberculosis*, virus, fungus, *Legionella pneumophila* infection. In this study, we excluded patients with non-bacterial infection and those whose etiologic agent unknown, because PCT is known to be a specific biomarker for bacterial infection only. Moreover we classified the patients' condition of acute renal injury (AKI) using the RIFLE (Risk Injury Failure

Table 1
RIFLE criteria [11].

	GFR criteria	Urine output criteria
Risk	Increased serum creatinine × 1.5 or GFR decrease >25%	Urine output <0.5 ml/kg/h × 6 h
Injury	Increased serum creatinine × 2 or GFR decrease >50%	Urine output <0.5 ml/kg/h × 12 h
Failure	Increased serum creatinine × 3 or GFR decrease >75%, serum creatinine ≧4 mg/dL (acute rise >0.5 mg/dL)	Urine output <0.3 ml/kg/h × 24hr or Anuria × 12 h
Loss	Persistent ARF = complete loss of kidney function > 4 weeks	
ESKD	End stage kidney disease (>3 months)	

RIFLE, Risk of renal dysfunction, Injury to the kidney, Failure of kidney function, Loss of kidney function and End-stage kidney disease; GFR, Glomerular Filtration Rate; ARF Acute Renal Failure.