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Significance of Serum Procalcitonin Measurement in Sepsis due to Peritonitis

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ABSTRACT

Procalcitonin is a useful marker for differentiating infection and inflammation and is a novel indicator of severity and prognosis in sepsis. Because diffuse peritonitis is a common cause of sepsis in surgery and emergency medicine, we evaluated the usefulness of the serum procalcitonin level in Japanese patients with peritonitis. In 27 patients with diffuse peritonitis, serum levels of procalcitonin and C-reactive protein (CRP) and the white blood cell count (WBC) were determined. The Sequential Organ Failure Assessment (SOFA) score and the Acute Physiology and Chronic Health Evaluation (APACHE) II score were calculated to evaluate the severity of sepsis. The serum procalcitonin correlated negatively with WBC but did not correlate with CRP. The serum procalcitonin correlated weakly with SOFA score ($R=0.384$, $p=0.008$) and moderately with the APACHE II score ($R=0.486$, $p=0.001$). On the other hand, CRP and WBC showed either no significant correlation with the severity scores or a weaker correlation than did procalcitonin. In conclusion, the present study demonstrates that the serum procalcitonin concentration is a better marker of the severity and prognosis of sepsis in Japanese patients with peritonitis than conventional infection markers, such as CRP and WBC. (Jikeikai Med J 2010 ; 57 : 5-10)

Key words : procalcitonin, sepsis, diffuse peritonitis, diagnostic marker

Introduction

Sepsis is often complicated by diffuse peritonitis. To reduce the mortality rate from multiple organ failure arising from sepsis due to diffuse peritonitis, early diagnosis and rapid and precise assessment of the severity of sepsis is needed, in combination with surgical elimination of the cause of sepsis[1,2]. The diagnosis of sepsis is usually based on infection with systemic inflammatory response syndrome. However, because this syndrome also has noninfectious causes, sepsis is often difficult to distinguish from other severe conditions. Conventional markers of inflammation, such as C-reactive protein (CRP) and the white blood cell (WBC) count, have low sensitivity and specificity for the diagnosis of bacterial infection and are, therefore, unlikely to reflect the severity of infection in sepsis[3,4].

Procalcitonin, a protein consisting of 116 amino acids with a molecular weight of approximately 13 kDa, is a precursor of calcitonin (a thyroid hormone). Usually, procalcitonin is produced in thyroid C cells and is secreted after processing into calcitonin, which is the hormonally active form. In healthy persons,

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procalcitonin is not released into blood. In patients with severe bacterial infection, on the other hand, procalcitonin is formed outside the thyroid gland and is secreted into blood in a stable form without undergoing degradation into calcitonin[5]. Synthesis of procalcitonin at various sites other than the thyroid gland in the presence of infection has been suggested, but such a concept has not yet been fully clarified[6–8]. Since Assicot et al. first reported the usefulness of procalcitonin in the diagnosis of bacterial infection in 1993, procalcitonin has been used as an important indicator for differentiating systemic infection from other forms of inflammation and for assessing the severity of infection[9–12]. However, few studies have evaluated the usefulness of procalcitonin in Japanese patients with peritonitis. The present study aimed to evaluate the usefulness of serum procalcitonin measurement in patients with sepsis due to peritonitis requiring surgical intervention in Japan.

Patients and Methods

The subjects of this study were 27 patients with diffuse peritonitis who underwent emergency surgical treatment at the Department of Emergency and Critical Medicine, Nippon Medical School Hospital, and were subsequently admitted to the intensive care unit from June 2002 through March 2009. Their ages ranged from 41 to 91 years (median, 67 years), and 10 of the patients were women. The causes of peritonitis were perforation of the upper gastrointestinal tract in 7 patients, perforation of the lower gastrointestinal tract in 17 patients, and intestinal necrosis due to strangulated bowel obstruction in 3 patients.

Serum concentrations of procalcitonin and CRP and the WBC count in peripheral blood were repeatedly determined as inflammation markers when the diagnosis of peritonitis was entertained and during the perioperative period. The Sequential Organ Failure Assessment (SOFA) score[13] and the Acute Physiology and Chronic Health Evaluation (APACHE) II score[14] were calculated daily as conventional indicators of disease severity and prognosis.

Procalcitonin levels were measured with immunoluminometric assay (LUMI test PCT ; B.R.A.H.M.S. Diagnostica, Berlin, Germany), which has been approved by the National Insurance System in Japan, as an indicator of sepsis and infection.

All patients gave their informed consent according to the regulations of the institutional review board of Nippon Medical School. Data collection was performed as part of the routine clinical work-up, the collected clinical and paraclinical data did not modify the patients' management, no interventions were performed for the patients, and statistical analyses were performed anonymously.

The data were retrospectively collected and analyzed statistically by means of Spearman's rank-correlation test using Dr. SPSS II for Windows (SPSS Japan Inc, Tokyo, Japan). Statistical significance was indicated by a p value < 0.05.

Results

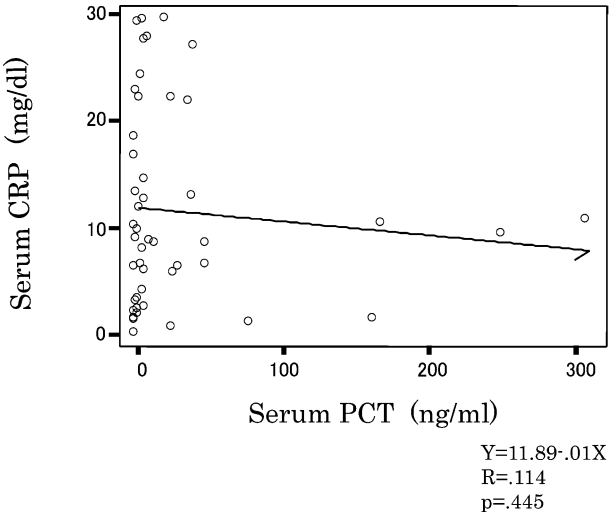
Serum procalcitonin levels negatively correlated with the WBC count ($R = -0.393$, $p = 0.007$), whereas no correlation was found between serum procalcitonin and serum CRP levels ($R = 0.114$, $p = 0.445$; Fig. 1). Serum procalcitonin correlated weakly with the SOFA score ($R = 0.384$, $p = 0.008$) and moderately with the APACHE II score ($R = 0.486$, $p = 0.001$; Fig. 2). A conventional infection marker, CRP, had a weaker correlation with the SOFA score ($R = 0.293$, $p = 0.048$) than did procalcitonin and had no significant correlation with the APACHE II score ($R = 0.229$, $p = 0.125$; Fig. 3).

The WBC count, another conventional infection marker, showed no significant correlation with either the SOFA score ($R = -0.006$, $p = 0.969$) or the APACHE II score ($R = -0.157$, $p = 0.299$; Fig. 4).

It is noteworthy that the patients with a serum procalcitonin concentrations greater than 50 ng/ml showed a SOFA score greater 5 points and an APACHE II score greater than 8 points (Fig. 2). This tendency was not observed for the other inflammatory markers (Fig. 3, 4).

Discussion

In the present study, because serum procalcitonin



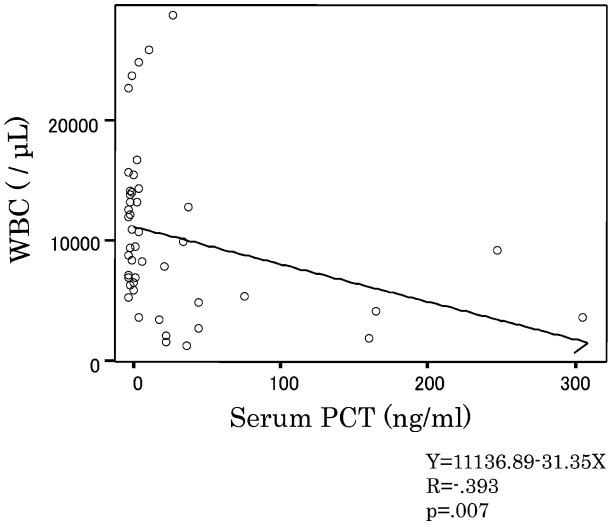
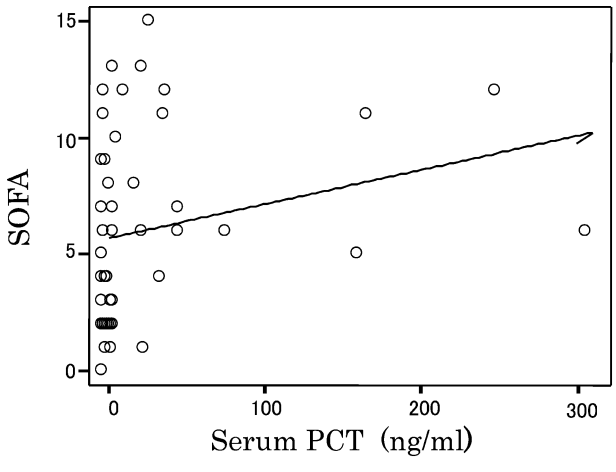


Fig. 1. Relationships between serum levels of procalcitonin and CRP and the WBC count in patients with peritonitis. A weak negative correlation was found between the calcitonin level and the WBC count ($R=-0.393$, $p=0.007$).



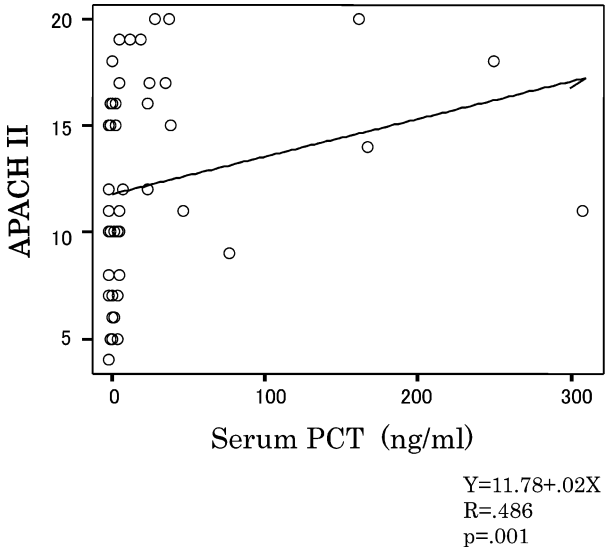
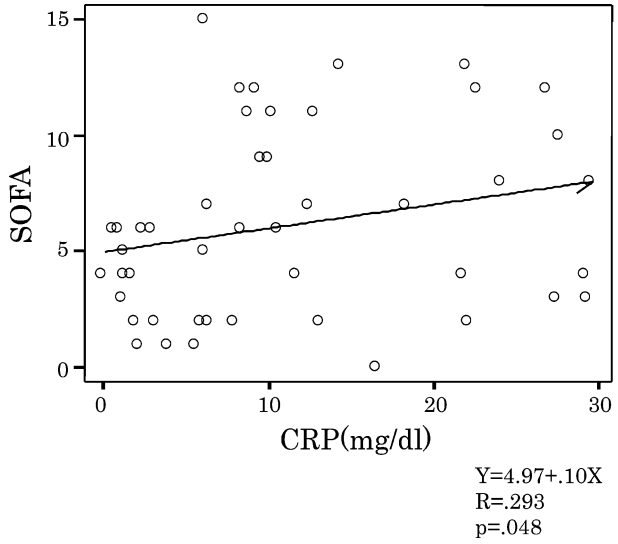
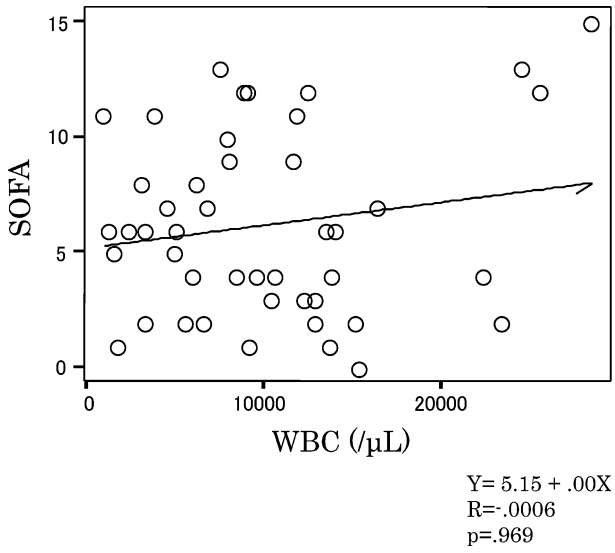
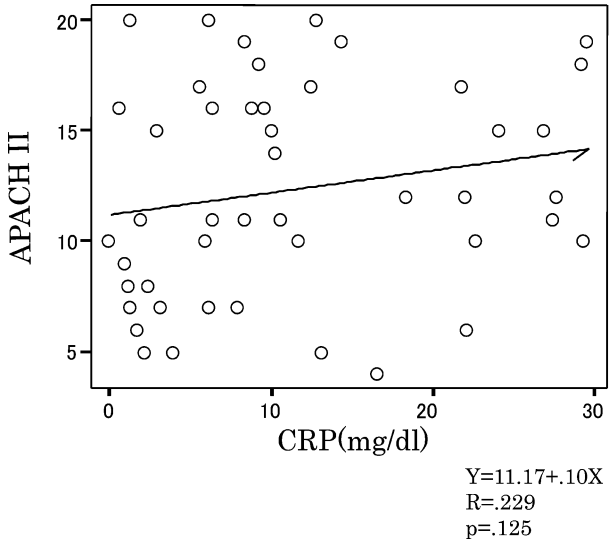


Fig. 2. Relationships between the serum procalcitonin level, the SOFA score, and the APACHE II score. The serum procalcitonin concentration correlated weakly with the SOFA score ($R=0.384$, $p=0.008$) and correlated moderately with the APACHE II score ($R=0.486$, $p=0.001$).

correlated with the SOFA and APACHE II scores, procalcitonin reflected the severity of peritonitis more sensitively than did the serum CRP level or the WBC count, which are conventional indicators of infection in nonimmunocompromised hosts. Recent reports have shown that, in the presence of sepsis, procalcitonin is produced in various cells and organs, such as leukocytes, the liver, lung, and spleen[6–9]. The serum procalcitonin level rises rapidly during the initial 2 to 3 hours after the onset of infection and peaks at 12 to 24 hours. The half-life of serum procalcitonin is 20 to 24 hours and is not prolonged even in the presence of renal dysfunction[9,15,16]. The rise in the procalcitonin level in the presence of fungal or viral infection is limited; thus, procalcitonin is useful for distinguishing bacterial infection from fungal or viral infection[17–20]. In patients with severe bacterial infection, elevation of the serum procalcitonin level is a more







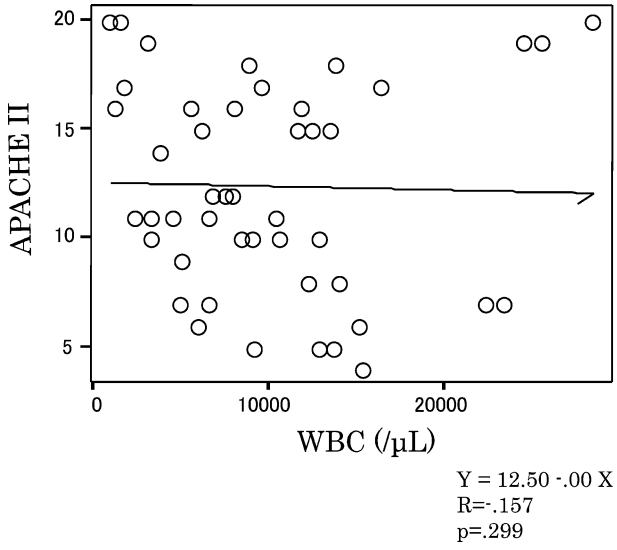


Fig. 3. Relationships between the serum CRP level, the SOFA score, and the APACHE II score. The serum CRP level correlated only weakly with the SOFA score ($R=0.293$, $p=0.048$)

Fig. 4. Relationships between the WBC count, the SOFA score, and the APACHE II score. The WBC count did not correlate with either the SOFA score ($R=-0.0006$, $p=0.969$) or the APACHE II score ($R=0.157$, $p=0.299$).

reliable diagnostic marker and a more useful prognostic factor than are such markers of inflammation as serum levels of CRP, interleukins 6 and 8, and lactate and the WBC count[21–23]. Alexander et al. have reported that the measurement of serum procalcitonin over time is useful for determining the optimum timing of re-operation in patients with peritonitis[24]. The serum CRP level has been reported to rise owing to operative stress 6 to 8 hours following surgery and to peak at 48 hours[25,26]. For this reason, the CRP level serves as a nonspecific indicator of the severity of infection during the early postoperative period. According to a meta-analysis by Uzzan et al., the serum procalcitonin level is more useful than is the CRP level for the differential diagnosis of sepsis[27]. However, Tang et al. have reported that the diagnostic odds ratio for the serum procalcitonin level was only 7.79 when used for the diagnosis of sepsis and concluded that procalcitonin was not useful for this

purpose[28]. Thus, procalcitonin is more useful than is CRP, but it seems reasonable to make a judgment on the basis of the procalcitonin level in combination with conventional markers of infection and the general condition of the patient. In the early stages of upper gastrointestinal perforation, chemical peritonitis rather than bacterial peritonitis prevails. For this reason, evaluation based on serum procalcitonin measurement in patients with perforation of upper gastrointestinal tract, may not be as valuable as the evaluation in lower gastrointestinal perforation.

A limitation of this study is that the number of subjects was small and did not allow multivariate analysis. A larger follow-up study is desirable.

In conclusion, the present study has demonstrated the superiority of the serum procalcitonin level over the CRP level and the WBC count as an indicator of the severity and prognosis of sepsis in patients with diffuse peritonitis requiring surgical intervention in Japan.

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