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ORIGINAL ARTICLE

Retrospective Study

Procalcitionin as a diagnostic marker to distinguish upper and lower gastrointestinal perforation

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Abstract

AIM

To assess the accuracy of serum procalcitionin (PCT) as a diagnostic marker in verifying upper and lower gastrointestinal perforation (GIP).

METHODS

This retrospective study included 46 patients from the surgical intensive care unit (ICU) of the Second Affiliated Hospital of Harbin Medical University who were confirmed to have GIP between June 2013 and December 2016. Demographic and clinical patient data were recorded on admission to ICU. Patients were divided into upper (n = 19) and lower (n = 27) GIP groups according to the perforation site (above

or below Treitz ligament). PCT and WBC count was obtained before laparotomy and then compared between groups. Meanwhile, the diagnostic accuracy of PCT was analyzed.

RESULTS

Patients with lower GIP exhibited significantly higher APACHE II score, SOFA score and serum PCT level than patients with upper GIP (P = 0.017, 0.004, and 0.001, respectively). There was a significant positive correlation between serum PCT level and APACHE II score or SOFA score (r = 0.715 and r = 0.611, respectively), while there was a significant negative correlation between serum PCT level and prognosis (r = -0.414). WBC count was not significantly different between the two groups, and WBC count showed no significant correlation with serum PCT level, APACHE II score, SOFA score or prognosis. The area under the receiver operating characteristic curve of PCT level to distinguish upper or lower GIP was 0.778. Patients with a serum PCT level above 17.94 ng/dL had a high likelihood of lower GIP, with a sensitivity of 100% and a specificity of 42.1%.

CONCLUSION

Serum PCT level is a reliable and accurate diagnostic marker in identifying upper or lower GIP before laparotomy.

Key words: Procalcitionin; White blood cell count; Gastrointestinal perforation; Sepsis; APACHE II score; SOFA score

Core tip: Procalcitionin (PCT) is a rapid, reliable and accurate predictive marker and contributes to assisting the clinicians in identifying upper or lower gastrointestinal perforation (GIP) before laparotomy, and it can be used as a useful supplementary tool for early clinical judgment of perforation site. The results showed that patients with lower GIP exhibited significantly higher APACHE II score, SOFA score and serum PCT level than patients with upper GIP, which might be related to the differences in bacterial load and the severity of sepsis between upper and lower GIP.

Gao Y, Yu KJ, Kang K, Liu HT, Zhang X, Huang R, Qu JD, Wang SC, Liu RJ, Liu YS, Wang HL. Procalcitionin as a diagnostic marker to distinguish upper and lower gastrointestinal perforation. *World J Gastroenterol* 2017; 23(24): 4422-4427 Available from: URL: http://www.wjgnet.com/1007-9327/full/v23/i24/4422.htm DOI: http://dx.doi.org/10.3748/wjg.v23.i24.4422

INTRODUCTION

Gastrointestinal perforation (GIP) is one of the most common acute abdominal diseases in department of general surgery. As a life-threatening disease with a high mortality rate, especially for elderly people, GIP could easily lead to shock and usually needs active rescue in the intensive care unit (ICU) and emergency laparotomy[1]. In general, GIP is related to many factors such as older age, diabetes, antecedent diverticulitis, glucocorticoid therapy, usage of non-steroidal anti-inflammatory drugs (NSAIDs) and so on[2-4]. It is still a challenge to accurately predict upper or lower GIP before laparotomy, despite increased available clinical and biological variables. Early diagnosis of perforation site has beneficial effects on operative procedure, selection of antibiotics and even judgement of the severity of infection and prognosis.

Serum procalcitionin (PCT) concentration was discovered to be significantly higher in patients with bacterial and fungal infections, and sepsis first in 1993[5], which has been proved to be a rapid, reliable and accurate diagnostic marker and is used to identify infectious and non-infectious diseases now[6-8]. Sepsis could promote the secretion of PCT through stimulating various types of cells in a variety of tissues[9], which is typically produced by C cells of the thyroid. More importantly, PCT concentration is related to bacterial load[10], the severity of sepsis[11], and even prognosis[12,13]. Owing to different perforation sites and contents, the severity of sepsis and bacterial load are obviously different, especially when comparing upper and lower GIP. We hypothesized that, due to fewer bacteria, the severity of sepsis caused by upper GIP was lower than that caused by lower GIP, which could be reflected by serum PCT level. Thus, serum PCT level might be a useful supplementary tool for clinical judgment of perforation site.

So far, the evidence regarding the diagnostic validity and accuracy of PCT in predicting upper or lower GIP is lacking. To the best of our knowledge, few studies have formally assessed its role in this area. In this retrospective study, serum PCT level was evaluated as a diagnostic marker in distinguishing upper or lower GIP before laparotomy. To our knowledge, this study is the first to evaluate the role of PCT in predicting upper or lower GIP before laparotomy as a useful supplementary tool.

MATERIALS AND METHODS

Study design

The current study is a retrospective study performed in the surgical ICU of the Second Affiliated Hospital of Harbin Medical University (Harbin, China). Patients were enrolled from June 2013 to December 2016. The study protocol was approved by the ethics committee.

Study population

Patients who met the following criteria were included:

Table 1 Baseline data of patients

	Upper *n* = 19	Lower *n* = 27	*t* value	*P* value
Age	58.84	67.59	-2.280	0.028
Gender				
Male	7	14	1.013	0.314
Female	12	13		
Height	168.47	165.37	1.316	0.195
Weight	63.42	58.37	1.589	0.119
BMI	22.27	21.21	1.176	0.246
APACHEII	12.47	18.15	-2.477	0.017
SOFA	5.84	9.33	-3.041	0.004
PCT	33.26	40.73	-3.079	0.001
WBC	13.67	11.27	1.105	0.275

APACHE II: Acute physiology and chronic health evaluation II; SOFA: Sequential organ failure assessment score.

(1) ICU admission; (2) patients were definitely diagnosed with GIP by laparotomy; (3) serum PCT level and WBC count were detected before laparotomy; and (4) patients aged > 18 years. Patients who met following criteria were excluded: (1) uncertain perforation site; (2) pregnant or breast-feeding women; (3) being on blood purification treatment; and (4) those receiving antibiotic therapy before ICU admission. In addition, patients with incomplete medical records were also excluded. All enrolled patients were treated by same experienced physicians.

Diagnosis of GIP

GIP was defined as the destruction of integrity of the digestive tract, *i.e.*, a complete non-traumatic penetration of the wall of the esophagus, stomach, small or large bowel[2]. Patients were divided into upper and lower GIP groups according to the perforation site (above or below Treitz ligament). Owing to the complexity of GIP diagnosis, a careful and thorough clinical examination was necessary.

Serum PCT level and WBC count measurement

Serum PCT level and WBC count were measured following ICU admission immediately before laparotomy. Mini VIDAS (Hain Lifescience GmbH; Nehren, Germany) was applied to measure serum PCT level.

Data collection

Baseline data: Gender, age, height, weight, body mass index (BMI), prognosis, acute physiology and chronic health evaluation (APACHE) II score, sequential organ failure assessment (SOFA) score and perforation site were obtained from patient medical records.

Demographic and clinical data of selected patients were recorded on admission to SICU with blood samples taken for measurement of serum PCT level and WBC count immediately. APACHE II score and SOFA score were calculated using data collected from the first 24 h after admission.

Table 2 Correlation analysis

	APACHEII	SOFA	PCT	WBC	Prognosis
PCT	0.715	0.611	1.000	-0.143	-0.414
	< 0.001	< 0.001	< 0.001	0.342	0.004
WBC	-0.242	-0.033	-0.143	1.000	0.112
	0.105	0.829	0.342		0.457

PCT: Procalcitionin.

Statistical analysis

Data are described as the mean ± SD and SPSS 13.0 (SPSS Inc., Chicago, IL, United States) was used for statistical analyses. To compare baseline data between groups, independent sample *t* test and χ^2 test were employed. Independent sample *t* test was used to compare APACHE II score, SOFA score and WBC count between groups. Owing to non-normality, serum PCT level between groups was analyzed by the Manny-Whitney rank sum test. Correlation between parameters was analyzed by Pearson or Spearman correlation. Area under the receiver operating characteristic (ROC) curve was calculated to evaluate the predictive value of PCT and to determine optimal cut-off value for distinguishing between upper and lower GIP before laparotomy. *P*-values < 0.05 were considered statistically significant.

RESULTS

Baseline data of patients

A total of 46 patients were enrolled in this retrospective study who underwent serum PCT level and WBC count measurement following ICU admission immediately before laparotomy. In all patients, GIP was proved by laparotomy. Nineteen patients were included into the upper GIP group, while the rest patients in the lower GIP group. As shown in Table 1, no significant differences were observed in baseline data with the exception of age ($P = 0.028$).

Diagnostic value of serum PCT level and WBC count

Patients with lower GIP exhibited significantly higher APACHE II score, SOFA score and serum PCT level than patients with upper GIP ($P = 0.017$, 0.004, and 0.001, respectively). However, WBC count showed no significant difference between the two groups, and WBC count showed no significant correlation with serum PCT level, APACHE II score, SOFA score or prognosis (Table 2). The area under the ROC curve of PCT level to distinguish upper and lower GIP was 0.778 (Figure 1). Patients with a serum PCT level above 17.94 ng/dL had a high likelihood of lower GIP, with a sensitivity of 100% and a specificity of 42.1% (Table 3).

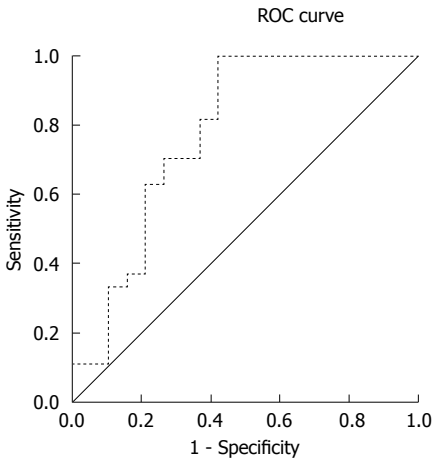

Figure 1 ROC curve shows that the area under the curve of procalcitionin level to distinguish upper or lower gastrointestinal perforation is 0.778.

DISCUSSION

PCT is a prepropeptide precursor of calcitonin, which had been proved to be a sensitive and specific predictive marker for bacterial infection[14,15], and thus was used to guide antibacterial therapy and reduce its length[16-19], which is not affected by hepatic or renal dysfunction[20-22]. PCT has many advantages of an ideal marker for routine clinical application, including simplicity, accuracy, specificity, stability and availability[23]. However, little is known on the predictive value of PCT in judging perforation site before laparotomy. We speculated that, when upper or lower GIP happens, they are different in bacterial load and the severity of sepsis owing to the leakage of different digestive tract contents, which could be reflected by serum PCT level. Antibiotic therapy might have an impact on bacterial load and even serum PCT level, therefore, patients who had used antibiotics before ICU admission were excluded[24].

APACHE II score and SOFA score are usually applied to evaluate the severity of disease[25], especially suitable for critically ill adult patients in ICU, which are closely related to mortality[25-29]. Therefore, in our study, they were chosen to assess the degree of illness. In particular, SOFA score was an important part of sepsis diagnosis in The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)[30].

The results of the present study showed that patients with lower GIP exhibited significantly higher APACHE II score, SOFA score and serum PCT level than patients with upper GIP, which might be related to the differences in bacterial load and the severity of sepsis between upper and lower GIP. In contrast, our findings did not show a significant difference between the two groups regarding WBC count. In other words, WBC count did not have a predictive value for sepsis, which is in accordance with previous studies[31]. Further correlation analysis showed that there was a significant positive correlation between serum PCT level and APACHE II score or SOFA score, and a significant negative correlation between serum PCT level and prognosis. By analyzing the ROC curve, an optimal cut-off value was selected as a predictive value to distinguish between upper and lower GIP before laparotomy.

Table 3 Area under the receiver operating characteristic curve

Area	Std. Error	Asymptotic Sig.	Asymptotic 95%CI	
			Lower bound	Upper bound
0.778	0.077	0.001	0.628	0.928

There were several limitations in the present study. First, patients were selected from a single center, which made the evidence level for this study relatively low. Second, the sample size was relatively small. Thus, experiments with larger sample size are needed to verify our findings in the future. At last, this study only concerned serum PCT level measured immediately after ICU admission and before laparotomy, but lacked of dynamic observation of changes in serum PCT level after laparotomy.

In conclusion, PCT is a rapid, reliable and accurate predictive marker and contributes to assisting clinicians toward identifying upper or lower GIP before laparotomy, which can be used as a useful supplementary tool for early clinical judgment of perforation site.

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COMMENTS

Background

Gastrointestinal perforation (GIP) is one of the most common acute abdominal diseases in department of general surgery with high mortality rates, which could easily lead to shock and needs rescue therapy in the intensive care unit. It is still a challenge to accurately predict upper or lower GIP before laparotomy, despite increased available clinical and biological variables. Serum procalcitionin (PCT) concentration is related to bacterial load as well as the severity of sepsis, and even prognosis. Thus, the authors hypothesized that, due to fewer bacteria, the severity of sepsis caused by upper GIP is lower than that caused by lower GIP, which could be reflected by serum PCT level.

Research frontiers

At present, the research on PCT has mainly focused on the following aspects: being used as a predictive marker for bacterial infection, distinguishing between bacterial and non-bacterial infections, guiding antibacterial therapy and reducing its length and so on. But so far the evidence regarding the diagnostic validity and accuracy of PCT in predicting upper or lower GIPs is lacking. To the best of our knowledge, few studies have formally assessed its role in this area.

Innovations and breakthroughs

This study is the first to evaluate the role of PCT in predicting upper or

lower GIP before laparotomy as a useful supplementary tool. This study has confirmed that PCT is a rapid, reliable and accurate predictive marker and can be used for early clinical judgment of perforation site.

Applications

When upper or lower GIP happens, they are different in bacterial load and the severity of sepsis owing to leakage of different digestive tract contents, which could be reflected by serum PCT level. Therefore, PCT contributes to assisting clinicians toward identifying upper or lower GIP before laparotomy, which has beneficial effects on operative procedure, selection of antibiotics and even judgement of the severity of infection and prognosis.

Terminology

PCT is a prepropeptide precursor of calcitonin, and its level was discovered to be significantly higher in patients with bacterial and fungal infections, and sepsis first in 1993. GIP was defined as the destruction of integrity of the digestive tract, *i.e.*, a complete non-traumatic penetration of the wall of the esophagus, stomach, small or large bowel. Patients were divided into upper and lower GIP groups according to the perforation site (above or below Treitz ligament).

Peer-review

This is an interesting study about the procalcitionin as a diagnostic marker to distinguish upper and lower gastrointestinal perforation. In this retrospective study, the authors included 46 patients from the SICU of the Second Affiliated Hospital of Harbin Medical University who were confirmed to have GIP between June 2013 and December 2016. There was a significant positive correlation between serum PCT level and APACHE II score or SOFA score, while there was a significant negative correlation between serum PCT level and Prognosis. Patients with a serum PCT level above 17.94 ng/dL had a high likelihood of lower GIP, with a sensitivity of 100% and a specificity of 42.1%.

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