Association between procalcitonin and acute kidney injury in patients with septic shock: A case-control study

Ming Wu (boshiyy@126.com)
Shenzhen Second People's Hospital
Guang Fu
Central South University Third Xiangya Hospital
Hao-li Li
Shenzhen Second People's Hospital
Hai-chao Zhan
Shenzhen Second People's Hospital
Jun-fu Lu
Shenzhen Second People's Hospital
Yan-hong Chen
Shenzhen Second People's Hospital
Le-feng Wu
Shenzhen Second People's Hospital
Fan Zhang
Shenzhen Second People's Hospital
Zi-Long Yang
Shenzhen Second People's Hospital
Jia-jia Huang
Shenzhen Second People's Hospital
Yong-wen Feng
Shenzhen Second People's Hospital
Ying-yi Luan
Shenzhen Second People's Hospital

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Abstract

Objective

This study aims to assess the relationship between serum procalcitonin (PCT) and acute kidney injury (AKI) induced by sepsis shock.

Methods

A case-control study was designed which included patients that admitted in intensive care unit (ICU) between January 2015 and October 2018. The worst values of biochemical parameters in the first 48 hours from septic shock admission to ICU were evaluated. According to KDIGO guideline, these patients were divided into AKI and non-AKI groups.

Results

Of 1631 patients screened, 157 patients were included in the primary analysis in which 84 (53.5%) patients with AKI. Multiple logistic regression results showed that PCT (OR=1.017, 95% CI 1.009- 1.025, P<0.001) was associated with AKI induced by septic shock. The ROC analysis showed that the cutoff point for PCT to predict AKI development was 14 ng/ml, and with a sensitivity 63%, specificity 67%. Specifically, in multivariate piecewise linear regression, the occurrence of AKI decreased with the elevation of PCT when PCT was between 25mol/L and 120 mol/L (OR 0.963, 95% CI 0.929-0.999; P= 0.042). The AKI increased with the elevation of PCT when PCT was either less than 25mol/L (OR 1.077, 95% CI 1.022-1.136; P= 0.006) or more than 120mol/L (OR 1.042, 95% CI 1.009-1.076; P= 0.013). Moreover, the PCT level was significant higher in AKI group only in female patients with age under 75(P=0.001).

Conclusions

Our data revealed a nonlinear relationship between PCT in 48 hours admission to ICU and AKI in septic shock patients and PCT could be used as a biomarker of AKI only in female patients under 75 years with sepsis shock.

Introduction

Sepsis is commonly encountered in critical care conditions and has become the leading cause of mortality in ICU that affects approximately 30 millions people per year worldwide(1–3). Excessive and dysregulated immune response and systemic immune response syndrome (SIRS) followed by multiorgan dysfunction syndrome characterize sepsis and often cause massive secondary organ and cell injuries, which would then result in the high mortality of patients in ICU(4–6). Kidney is one the most commonly affected organ during sepsis or septic shock. Indeed, AKI is one of the common complications in patients with sepsis (up to 50%) and consequently result in up to 1/3 mortality (7, 8). Thus, early diagnosis of sepsis-associated AKI is critical for prevention of adverse outcomes.

Immune inflammatory response is the key pathophysiological signature of septic-AKI. Identifying potential physiological and biochemical indicators of the clinical routine reaction of immune inflammation to predict sepsis induced AKI is of enormous clinical significance. Procalcitonin (PCT) is a peptide precursor of the hormone calcitonin that has the molecular weight of ~13kD.It belongs to the acute phage proteins family that are released into blood in response to bacterial infection from a variety of cell sources(9). The serum level of PCT is nearly undetectable in healthy people and rises dramatically after systemic infection and sepsis(10, 11). Therefore, it has been widely employed as a biomarker for bacterial infection and promising diagnostic marker for sepsis (12, 13). Additionally, PCT-guided antibiotic therapy been shown to improve survival of sepsis patients (14). And data from previous clinical studies indicated that PCT could work as a marker for development of acute pancreatitis (15) and contrast induced AKI (16).

However, the validity of PCT as a predictor of sepsis-associated AKI development is still under debate and the result varied greatly across different studies (17). No consent has been reached regarding the relationship between PCT and AKI, especially under the diagnostic frame of sepsis 3.0 by far. Moreover, with the development of social economy, the aging of the population is more and more serious and age, as well as gender, is an important factors affecting procalcitonin. Thus, investigation the relationship between PCT and AKI in septic shock and the influence of age and gender on the relationship remain to be explored. Therefore, we intended to determine whether serum PCT level in 48 hours admission is associated with AKI in septic shock patients admitted to general adult ICU, and how PCT is affected by age and gender.

Materials And Methods

Study population

A case-control study was designed. we reviewed the medical records of 1631 patients admitted to general adult ICU in *the Second People's Hospital of Shenzhen* (A tertiary-care teaching Hospital) from January 2015 to October 2018. In which included 231(14.2%) patients with septic shock using the definition of Sepsis 3. Among them, 1 case is under age of 18, 21 cases were malignancies, 8 cases were chronic kidney diseases, 6 cases were transported to our ICU over 48 hours after diagnosis of septic shock, 28 cases were diagnosed septic shock after 48 hours admission into ICU, 8 cases were diagnosed with unknown shock, and 2 cases had missing data. Eventually, only 157 septic shock cases were included in our study. In a second step, the 157 patients were divided in two groups according to AKI criterion according KDIGO guideline: 84(53.5%) patients were included in the AKI and 73(46.5%) in the non-AKI groups. *(Figure 1)*

Including and Excluding Criteria

The septic shock was diagnosed based on the framework of Sepsis 3.0(1). The AKI was diagnosed using the criteria issued by issued by Kidney Disease: Improving Global Outcomes Clinical Practice Guidelines (KDIGO) after 48 hours of admission into ICU(18). Excluding criteria were listed following: 1 Chronic

kidney disease history; 2 Kidney transplantation history; 3 Under age of 18; 4 History of kidney trauma; 5 Death within 12 hours admitted to ICU; 6 Diagnosed AKI prior to admission to ICU.

Clinical variables

All clinical and laboratory data were acquired throughout the hospitalization time on daily basis and were recorded in standard data collection form. Data included, but were not limited to, demographic data (e.g. age, gender, work), biochemical parameters (e.g. blood cell count, liver function, kidney function, coagulation function, blood gas analysis), acute physiology and chronic health evaluation II (APACHE-II) score within first 48 hours of hospitalization, mechanic ventilation, heart rate, past history and infection source. The worst value of biochemical parameters within 48 hours admission to ICU was adopted for downstream analysis.

Statistical Analysis

Quantitative parameters are presented as the means±standard deviations or medians and interquartile ranges (25th, 75^{th} percentiles), and qualitative parameters are expressed as numbers and percentages. Continuous variables were compared using the independent two-sample t-test or Mann–Whitney U-test. Categorical variables were compared using the chi square test or Fisher's exact test. Univariate logistic regression analysis was performed to evaluate risk factors associated with AKI. All variables with P< 0.01 in univariate analysis were entered into a multivariate logistic regression with crude model and fully adjusted model: OR (odds ratio and 95% confidence interval levels (95% CI). the predictive ability of PCT for AKI was assessed using the AU-ROC curve method. The optimal cutoff value was determined using Youde's index. Then, we explored the relationship between PCT and AKI by smooth curve fitting after adjustment for potential confounders. Then, we further performed a multivariate piecewise linear regression model to assess the independent correlation between PCT and AKI according to smooth curve fitting. Lastly, we compared PCT and AKI in different age and sex group. All of the statistical analyses were performed with SPSS 23.0 (SPSS Inc., Chicago, IL, USA), Empower(R) (http://www.empowerstats.com, X&Y solutions, Inc., Boston, MA) software. *P* values (two-tailed) below 0.05 were considered statistically significant.

Results

Clinical Characteristics of the Patients

The detailed demographic and clinical profile data of all patients with septic shock on baseline were summarized in *Table 1.* Overall, 157 patients (95 were males and 62 (39.49%) were females) in total were enrolled in our study based on our including and excluding criteria, with age ranging from 19–89 years old and mean age being 61.86 ± 17.88 years old. Then patients were divided into AKI group (84 patients; 53.5%) and non-AKI group (73 patients; 46.5%). In terms of age, gender, infection sources, underlying diseases, mechanic ventilation and ICU time, there was no significant difference between those two

groups. Notably, the acute physiology and chronic health evaluation II (APACHE-II) score was significantly higher in AKI group compared to Non-AKI group (AKI 28.75±9.62 vs non-AKI 20.85±9.29, P<0.001).

Correlations between PCT and AKI in septic shock patients

To explore the risk factors associated with AKI induced by septic shock, we choose PCT, Platelet counts, Lymphocyte counts, Platelet/Lymphocyte ratio, Alanine aminotransferase (ALT), Aspartate aminotransferase (AST) and APACHE-II score as variables. As the results shown in *Table 2,* only PCT and APACHE-II score were identified as risk factors for AKI development in both univariant (PCT OR:1.009(1.005, 1.014), P<0.001; APACHE OR:1.089(1.050, 1.130), P<0.001) and multivariant(PCT OR: 1.017(1.009, 1.025), P<0.001; APACHE OR: 1.116(1.052, 1.184), P<0.001) regression analysis. However, the APACHE score includes variables (e.g. creatinine and urea nitrogen) that are associated with kidney dysfunction.Receiver operation characteristic (ROC) curve was applied to evaluate the predictive performance of serum PCT level within 48 hours admission to ICU. As the ROC curve shows (*Figure 2A)*,, the area under curve (AUC) was 0.686(95%CI 0.6–0.77, P<0.001). The cutoff value of PCT was 14.0 ng/ml (*Figure 2B)*,, with a sensitivity of 63%, specificity 67%, positive likelihood ratio 1.8, negative likelihood ratio 0.53, positive predictive value 67%, negative predictive 62%.

Nonlinear association between PCT level and AKI

In line with a previous study, Platelet/Lymphocyte ratio was shown to a protective prognostic factor for AKI(19). Additionally, in order to specifically depict relationship between PCT level and AKI induced by septic shock, we employed multivariate piecewise linear regression. Interestingly, the results, as shown in *Figure 3 and Table 3,* demonstrated a nonlinear association between PCT level and AKI development. Specifically, PCT level was negatively associated with AKI development within a certain range (25mol/L~120mol/L, OR: 0.963 (0.929,0.999), P = 0.042) while positively associated with AKI outside this range (<25mol/L, OR 1.077, 95% CI 1.022–1.136; P = 0.006 or >120mol/L, OR 1.042, 95% CI 1.009–1.076; P = 0.013).).

Comparisons of age and gender between AKI and Non-AKI patients and its effects on PCT

Considering that the age and gender of patients might be confound factors in our study(20), in order to further explore the effects from age and gender we decided to further divide the patients into four subgroups based on previous study(21), namely *<75 male, <75 female, ≥75 male, ≥75 female.* Regardless of age, as shown in *Table 4,* the AKI development showed no difference between male and female patients. Our data show that PCT level was higher in AKI than Non-AKI (84.80±85.86 vs 36.22±54.18, P<0.001) group regardless of age and gender (*Table 5)*..Interestingly, we found that regardless of age, no difference of PCT level was observed in male patients between AKI patients and Non-AKI patients (*Table 5,* P = 0.06 in <75 subgroup, P = 0.097 in ≥75 subgroup). However, we did observe that PCT level was significant higher in AKI patients only in female patients with age <75(*Table 5,* P = 0.001).

Discussion

Renal failure is associated with high mortality in septic shock patients. To clarify the mechanism of septic kidney injury is the cornerstone of early prediction and treatment. Sepsis is characterized by excessive and persistently dysregulated systemic inflammatory response, which eventually cause end organ damage(22–24). During the progression of sepsis, AKI is one the common complications in clinical settings(7, 8). The pathophysiology of AKI development is not well understood. It is widely accepted that microcirculatory dysfunction(6, 25, 26) and excessive inflammation both contributed to epithelial and tubular cell damage(27–29). AKI is defined by abnormalities of series of biomarkers of kidney function, such as creatinine, urea nitrogen, urine volume, and even some clinical biomarkers, such as cystine, neutrophils gelatinase-associated lipid delivery protein (NGAL), kidney injury molecule–1(KIM–1), etc. However, as for creatinine, urea nitrogen, urine, they are often influenced by other known and unknown factors. Moreover, such biomarkers of kidney function are not being tested routinely in developing countries. therefore, there is an urgent need for early detection biomarkers of renal function simply and routinely.

Inflammatory response dysfunction is the key pathophysiological mechanism of septic-AKI. There are some inflammatory markers (IL1, IL16, TNF-a, PCT, CRP, WBC, PLT, lymphocytes, platelets, platelets/lymphocytes, etc.) that have been used to monitor the inflammatory response in clinical practices. In our study, those clinical parameters were used to detect the relationships of AKI with univariant and multivariant regression analysis. Particularly, considering the very limited approaches to monitor the systemic inflammation in septic shock patients, serum PCT level outweighs other inflammatory biomarkers (e.g. IL6, TNF alpha) due to its convenient accessibility in developing country. Our data showed that only PCT and APACHE-II score were identified as risk factors for AKI development, especially PCT which adds up to the clinical significance of our findings.

PCT is a precursor of calcitonin which is undetectable in physiological state and could be significantly induced by bacteria infection(30). Thus, PCT has been widely used as a biomarker for infection and sepsis(12, 13). Higher PCT level has also been shown to be associated with increased AKI development in patients with suspected infection(31) and reduced recovery from AKI in critically ill patients(32). However, the mechanism of how PCT contributed to AKI development was not fully understood. More aspects of PCT in AKI development have been revealed. Indeed, in the setting of sepsis, previous study has shown that PCT could be induced by bacterial toxins and can mediate direct cytotoxicity on mesangial cells by increasing synthesis of proinflammatory cytokines(33). Moreover, PCT has also been shown act as a chemoattractant for monocytes at inflammation site and higher PCT level would recruit more monocytes and contribute to the inflammation-mediated cell injury(34). Apart from cytotoxicity and inflammation, increased PCT level has also been reported to be associated with increased creatinine and decreased glomerular filtration rate(35–37). And higher level of PCT was observed in AKI patients compared to non-AKI patients (38, 39). Based on those findings, PCT level is expected to exhibit an approximately linear relationship with AKI development and increased PCT level in blood is expected to be associated with higher risk of AKI in patients.

However, our data demonstrated a nonlinear relationship between PCT level within 48 hours admission to ICU and AKI development in septic shock patients, which suggested that increased PCT may not always indicate higher risk of AKI in septic shock patients. Specifically, within a certain range, increased PCT level is associated with decreased AKI development in septic shock patients. The mechanism behind this non-linear association is largely unknown. It is reasonable to speculate that at the early time of infection, the PCT level was associated with extent of host inflammatory response and the AKI was possibly caused by toxins from invaded pathogens. Therefore, more invaded pathogens lead to severer inflammatory response and higher PCT level. Afterwards, appropriate inflammatory response was necessary to combat invaded pathogens, which could explain why increased PCT level was associated with decreased AKI development. Eventually, excessive inflammatory response with extremely high PCT level would inevitably add up risk to AKI development. On the side, the discrepancies may be attributed to the usage of different timepoint PCT values. In previous studies, the authors used the PCT values on admission to ICU while we used the highest value of PCT level within 48 hours admission. The former is a static value that does not reflect the effect of treatment on PCT and organ function. The latter is a dynamic value that reflects the effect of treatment on PCT and organ function.

Previous studies on PCT and AKI have not considered the influence of confounding factors. As a biomarker of inflammation, PCT is also influenced by age and gender. We notice that age and gender might be a confounder factor in our study. So, we did subgroup analysis based the age and gender, which have been shown to be associated with AKI development. Actually, young age and female gender has been reported to be two protective factors in AKI(40–43). Older patients (≥75 years) have significantly higher in-hospital ICU mortality than younger patients in sepsis(21). In this study, we used this cutoff point of age and further divided our patients into four group based on age and gender. We found that serum AKI exhibited significantly higher level in AKI group based on the data from the entire cohort. However, after we did stratification analysis based on age and gender, we found serum AKI level was actually significantly higher in AKI group only for female septic shock patients who were less than 75 years old (*<75 female)*.. Moreover, we did observe a trend of higher of serum PCT level in AKI patients of other three groups (*< = 75 male, ≥ 75 male, ≥ 75 female),*, though not statistically significant.

Our study has following limitations. Firstly, this is a retrospective study of relatively small sample size in a single center. And the study may be confounded and biased by other unknown factors. Thus, the evidence grade of this study is compromised to some extent. Secondly, we identified PCT as an early predictive biomarker of AKI development in septic shock patients in ICU. However, our AOC curve analysis did not show a robust sensitivity (63%) or specificity (67%) probably due to small sample size. Thirdly, though we looked age and gender, other unknown confounding factors may bias our results. More large-scale randomized clinical trials are needed to validate our results.

In conclusion, we found a nonlinear relationship between PCT level within 48 hours admission to ICU and AKI with septic shock patients and PCT could be used as a biomarker of AKI in female patients under 75 years with septic shock. Based on our study, elevated PCT within 48 hours admission to ICU may suggest a better prognostic factor of AKI with septic shock.

Declarations

Acknowledgement

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Ethics approval and consent to participate

The ethics committee of the Second People's Hospital of Shenzhen approved this study (Ethical Number: 20180515001), and the consent was obtained from all patients or their families by telephone. All information of patient's privacies was protected under the confidentiality policy.

Disclosure Statement

The authors have no conflicts of interest to declare

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Author Contributions

Ming Wu, contributed to the study conception and design. All authors performed the research. Hai-chao Zhan and Hao-li Li collected and analyzed the data, Guang Fu, Ying-yi Luan and Ming Wu wrote the manuscript.

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Tables

Table1.

Baseline characteristics of septic shock patients with non-AKI and AKI. APACHE-II, Acute Physiology and Chronic Health Evaluation score; LOS, Length of stay

Characteristics	Total（n=157）	Non-AKI（n=73）	AKI（n=84）	P value
Age (years), mean (S.D.)	61.9±17.9	60.3±18.0	63.3±17.8	0.29
Gender				0.48
Female N (%)	62	31 (50.0)	31(50.0)	
male N (%)	95	42 (44.2)	53 (55.8)	
Infection sources				0.68
Lungs N (%)	57	31 (54.4)	26 (45.6)	
Urinary tract N (%)	20	7 (35.0)	13 (65.0)	
Biliary/ digestive tract N (%)	12	4 (33.3)	8 (66.7)	
Abdominal cavity N (%)	27	13(48.1)	14 (51.9)	
Skin and soft tissue N (%)	6	2 (33.3)	4 (66.7)	
Two or more N (%)	31	14(45.2)	17(54.8)	
The catheter N (%)	1	0 (0)	1 (100.0)	
Other N (%)	3	2 (66.7)	1 (33.3)	
Underlying diseases				**0.49**
Diabetes N (%)	16	10(62.5)	6(37.5)	
High blood pressure N (%)	14	3(21.4)	11(78.6)	
Coronary heart disease (N (%)	9	5(55.6)	4(44.4)	
Chronic lung disease N (%)	5	2(40.0)	3(60.0)	
Cerebrovascular accident N(%)	10	6(60.0)	4(40.0)	
Non basic diseases N (%)	54	24(44.4)	30(55.60)	
Two basic diseases N (%)	26	12(46.2)	14(53.8)	
Three or more N (%)	23	11(47.8)	12(52.2)	
Mechanical Ventilation				0.09
yes N (%)	95(60.5)	39 (53.4)	56(66.7)	

no N (%)	62(39.5)	34 (46.6)	28 (33.3)	
APACHII score	25.1±10.2	20.9±9.3	28.8±9.6	<0.001
LOS ICU, median (IQR) (d)	7.0(2.5,17.0)	8.0(2.0,16.0)	7.0(3.0,19.8)	0.78
Biochemical parameters				
PCT(ng/ml)	20.7(5.0,132.0)	10.6(2.3,49.2)	30.8(7.6,200.0)	<0.001
CRP(mg/dl)	131.3±75.9	134.1±75.7	128.8±76.5	0.66
WBC(1×10^9/L)	16.4±11.2	15.7±11.2	17.0±11.3	0.47
Neutrophil(1×10^9/L)	14.4±10.4	14.3±10.8	14.5±10.1	0.90
Lymphocyte(1×10^9/L)	0.6(0.4,1.3)	0.6(0.3,1.0)	0.7(0.4,1.9)	0.07
RBC (1×10^{12}/L)	3.8±0.9	3.7±0.8	3.8±0.9	0.60
HGB(g/l)	110.0(93.0,123.0)	107(91.5,122.0)	110.0(95.3,123.0)	0.42
NLR	18.4(6.5,34.6)	20.8(10.5,39.6)	15.0(5.0,31.1)	0.04
Platelets(1×10^9/L)	151.5±96.2	165.5±98.4	139.3±93.2	0.09
PLR	183.0 (90.5,394.4)	253.7(137.9,476.3)	150.5(62.6,303.1)	0.002
Albumin (g/l)	24.2(20.6,27.9)	24.2(20.8,27.0)	24.2(20.4,28.7)	0.88
TBiL(umol/L)	16.4(10.7,28.0)	14.6(9.6,21.5)	19.3(11.8,31.2)	0.10
ALT(U/L)	51.0(28.0,120.5)	51.0(27.5,123.5)	50.0(28.0,117.3)	0.80
AST(U/L)	70.0(35.0,243.0)	76.0(36.5,193.0)	59(31.8,268.3)	0.53
Creatinine (umol/L)	134.2(79.0,226.2)	76.1(50.7,96.5)	217.4(158.9,271.4)	<0.001
BUN(mmol/l)	10.2(6.4,15.2)	6.2(4.4,8.7)	13.8(10.4,17.5)	<0.001
PO_2/FiO_2	228.2±97.7	225.2±95.5	230.8±100.0	0.72
PT(s)	15.5(13.6,20.3)	15.5(13.3,19.0)	15.8(13.9,22.2)	0.40
APTT(s)	45.3(37.5,63.3)	43.4(36.9,58.6)	46.9(38.5,65.2)	0.26
INR	1.4(1.2,1.8)	1.3(1.2,1.6)	1.4(1.2,2.0)	0.27
TT(s)	19.8(17.6,22.4)	20.1(18.0,23.0)	19.5(17.1,21.8)	0.14
D-Dimer (mg/L)	7.7(3.3,22.9)	4.9(2.5,11.6)	11.0(4.8,28.8)	<0.001
FIB (g/L)	3.2(2.2,4.4)	3.1(2.1,4.3)	3.3(2.3,4.5)	0.53

Abbreviation: PCT: Procalcitonin; CRP: C-reactionprotein; WBC: white blood cell; RBC: red blood cell HGB: Haemoglobin; NLR: Neutrophil/Lymphocyte ratio; PLT: platelets; PLR: platelets/ Lymphocyte ratio; TBIL: total bilirubin; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; BUN: blood urea nitrogen; PT: Prothrombin time; APTT: activated partial thromboplastin time; TT: thrombin time; FIB :fibrinogen

Table 2

Risk factors associated with AKI induced by septic shock in univariable and multivariable regression model. APACHE-II, Acute Physiology and Chronic Health Evaluation score .

Variable	Univariable		Multivariable fully adjusted model	
	OR (95%CI)	P value	OR (95%CI)	P value
PCT (ng/ml)	1.009 (1.005, 1.014)	<0.001	1.017 (1.009, 1.025)	<0.001
Platelet counts(10^9/L)	0.997 (0.994, 1.001)	0.095	0.998 (0.993, 1.003)	0.491
Lymphocyte(g/L)	1.506 (1.060, 2.142)	0.023	1.301 (0.931, 1.818)	0.123
Platelet/lymphocyte ratio	0.999 (0.998, 1.000)	0.036	0.999 (0.999, 1.000)	0.045
Alanine aminotransferase(U/L)	1.003 (1.000, 1.005)	0.052	1.002 (0.998, 1.007)	0.324
Aspartate transaminase(U/L)	1.001 (1.000, 1.002)	0.026	1.000 (0.998, 1.001)	0.787
APACHII score	1.089 (1.050, 1.130)	<0.001	1.116 (1.052, 1.184)	<0.001

Table 3

Nonlinear association between PCT level and AKI

Inflection point of PCT(ng/ml	Effect size (OR)	95%CI	P value
<25	1.077	1.022 , 1.136	0.006
≤25 ≥120	0.963	0.929 , 0.999	0.042
120	1.042	1.009 ,1.076	0.013

Table 4

Comparisons of age and gender between AKI and Non-AKI patients

Age	Gender	Non-AKI (N)	AKI (N)	P
≤75	M	28	38	0.244
	F	25	20	
>75	M	14	15	0.583
	F	6	11	
Total	M	42	53	0.477
	F	31	31	

Table 5

The effects of age and gender on PCT(ng/ml) between AKI and Non-AKI patients

Age	Gender	Non-AKI	AKI	P
≤75	M	42.16±55.56	78.09±86.85	0.060
	F	32.02±53.38	104.54±88.37	0.001
>75	M	21.55±44.26	64.85±85.14	0.097
	F	60.22±72.50	99.30±81.29	0.324
Total	all	36.22±54.18	84.80±85.86	<0.001

Figures

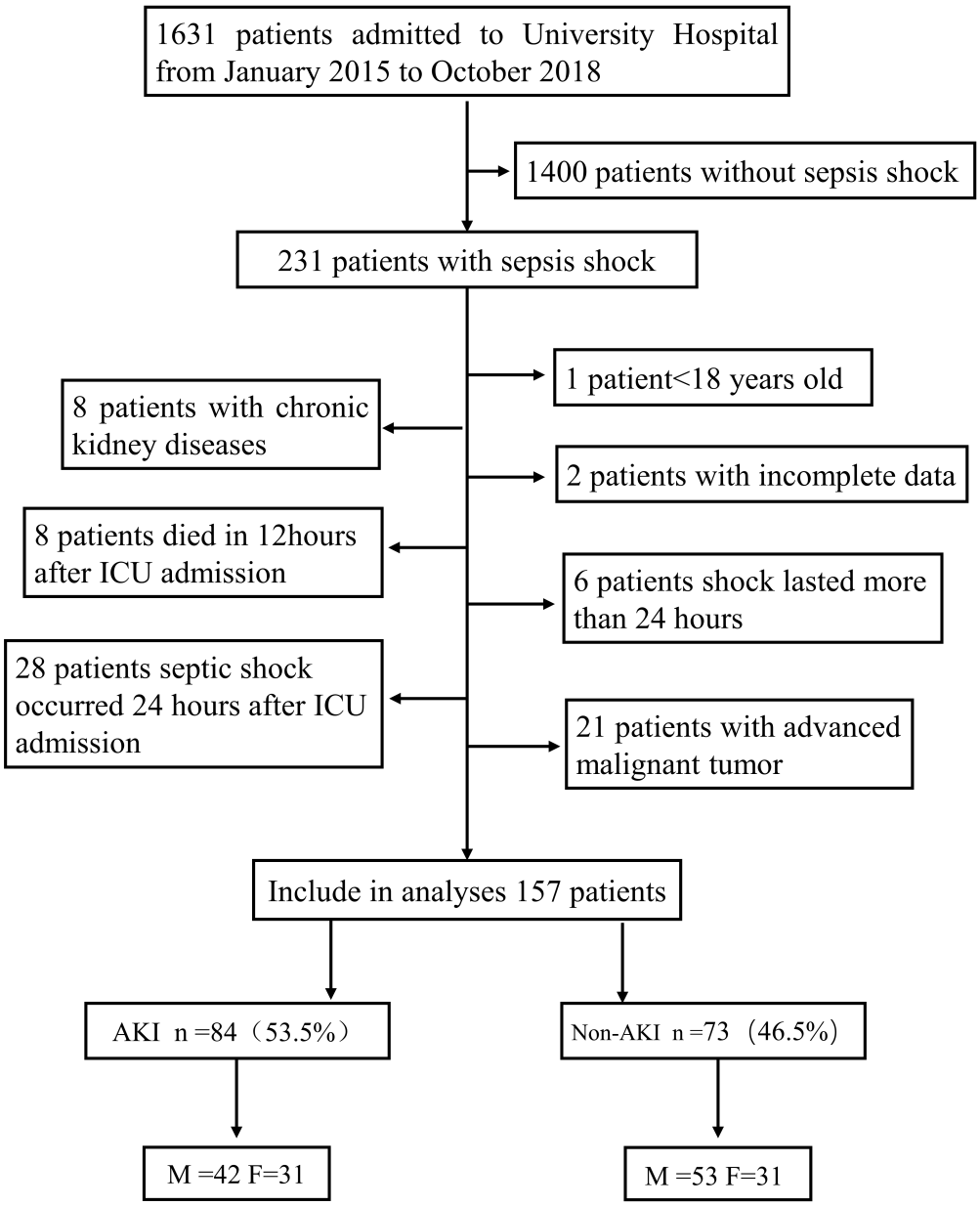

Figure 1

Flow diagram of study subjects. From January 2015 to October 2018, 231 septic shock patients in the ICU were assessed for possible enrollment according to inclusion and exclusion criteria, and 157 patients were included in the final analysis.

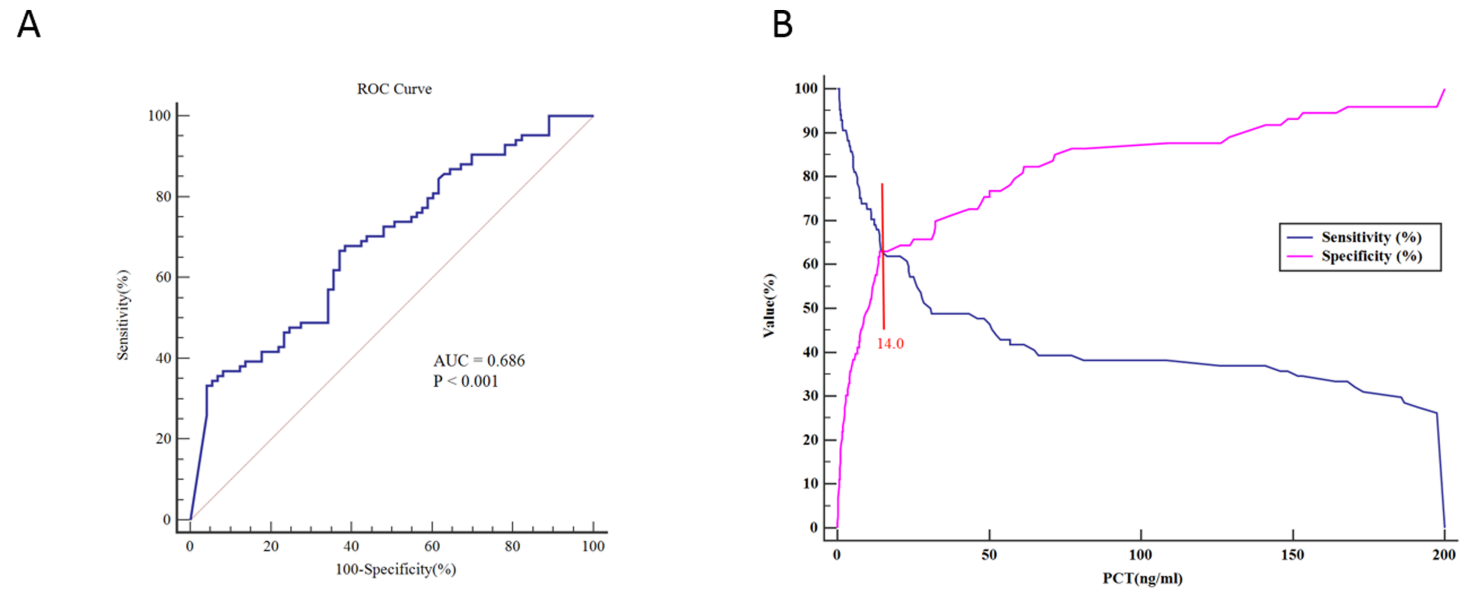

Figure 2

ROC curve of PCT predicting AKI in septic shock patients

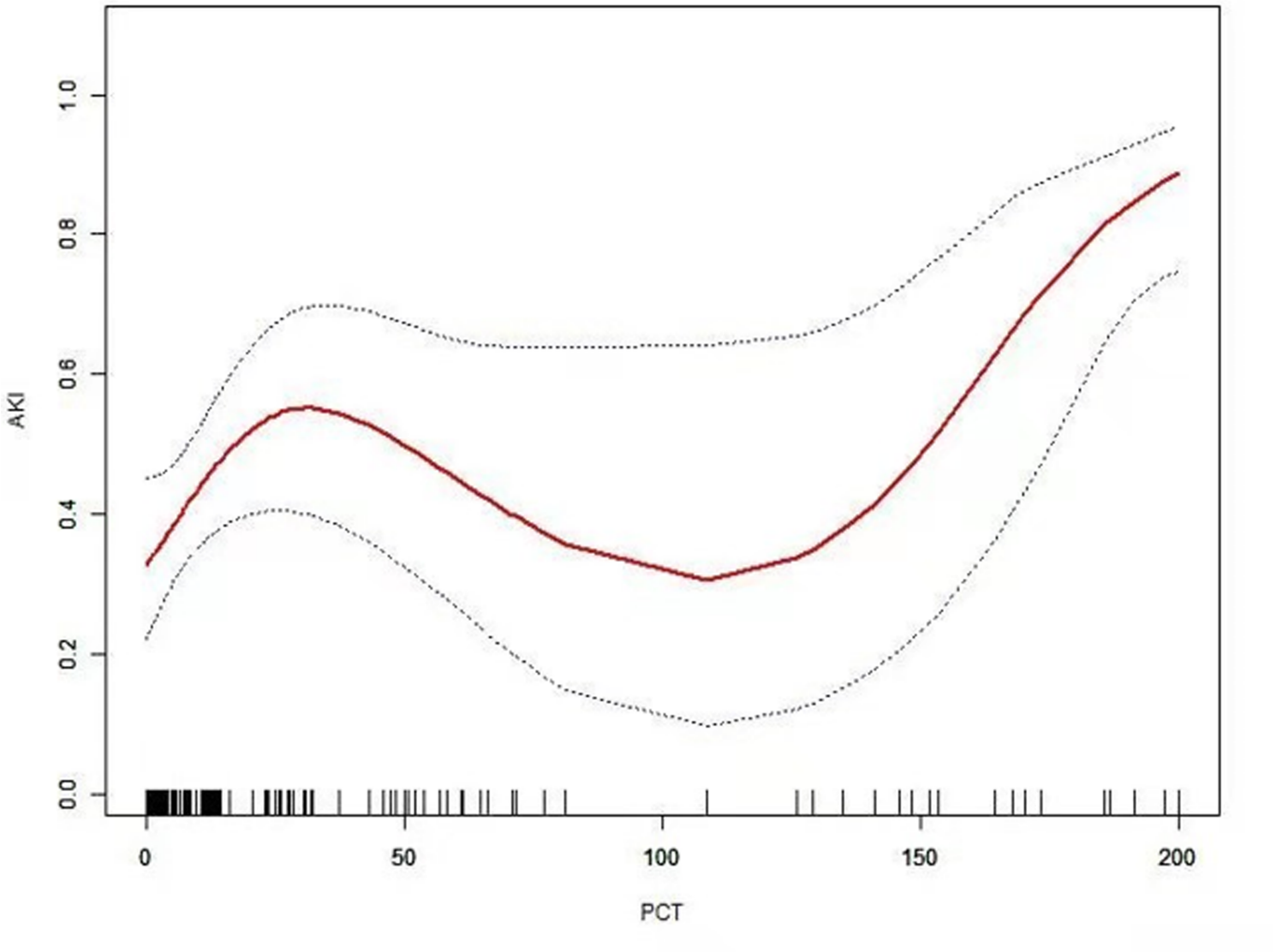

Figure 3

The relationship between PCT and AKI by smooth curve fitting.