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Article

The Postoperative Platelet to Creatinine Ratio as A Prognostic Index of In-Hospital Mortality in Patients with Acute Type A Aortic Dissection

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Abstract

Background: The purpose of the investigation was to assess the value of post-operation platelet to creatinine ratio (PCR) in predicting in-hospital mortality among patients with acute type A aortic dissection (TAAAD). **Methods**: A retrospective study was carried out from January 2017 to December 2019. The best cutoff value of post-operation PCR was assessed by receiver operating characteristic (ROC) curve. Patients were divided into survivors and nonsurvivors. Univariate and multivariate logistic analyses were carried out to identify independent risk factors influencing in-hospital mortality. **Results**: A total of 171 patients were included in this investigation, with an in-hospital mortality rate of 18.1%. The optimal cut-off value of post-operation PCR was 0.7242 (area under the ROC curve (AUC): 0.798, 95% confidence interval (CI) 0.730–0.856, $p < 0.001$), and the sensitivity and specificity were 74.2% and 74.3%. The levels of post-operation PCR were lower in nonsurvivors than in survivors (0.56 ± 0.33 *vs.* 1.50 ± 1.36, $p < 0.001$). Multivariate logistic regression analysis displayed that post-operation PCR was positively related to in-hospital survivors when confounding factors were adjusted (HR = 8.850, 95% CI = 2.611–30.303, $p < 0.001$). **Conclusions**: Post-operative PCR is a readily accessible and cost-effective biomarker that is independently associated with in-hospital mortality in TAAAD patients. Furthermore, it exhibits superior performance in predicting patient outcomes following surgery.

Keywords

creatinine; mortality; platelet; prognosis; type A aortic dissection

Introduction

Aortic dissection (AD) is a severe disease and 3–6 out of 100,000 people a year suffer from aortic dissection [1,2]. 75% of these patients are type A aortic dissection (AAD) [3]. Type A acute aortic dissection (AAAD) is a life-threatening cardiovascular emergency with an overall case-fatality rate estimated at 73% and a pre-hospital mortality rate of 49% [4]. It is defined by an intimal rip and propagation of the dissection between the media and intima layers of the ascending aorta [5]. Type A has a significant rate of early mortality over the first 48 hours and usually denotes the need for early surgical intervention. The prognosis for patients with acute type A aortic dissection (TAAAD) is significantly poor without proper treatment [6,7]. Studies are trying their best to identify risk factors for poor prognosis. However, the accuracy of prediction still can not meet clinical need.

Inflammation acts as a key part in the pathophysiology and prognosis of many diseases, including AAD [8–12]. Platelets (PLT) and creatinine (CREA) are two examples of simple, affordable, and readily available indicators of disease activities that are associated with inflammation. PLT can be used as an index to predict the outcome of infection-related and noninfectious diseases, such as ankylosing spondylitis, hepatitis, stroke and acute myocardial infarction [13–16]. Serum CREA has been associated with predictions of early changes of ischemic renal function and the occurrence of postoperative complications [17]. Previous studies have shown that ratio has better predictive performance than that of individual indicators, so we want to explore whether the ratio of the two (PLT and CREA) is better than that of a single indicator. As far as we know, there are no studies to evaluate the predictive value of PCR (platelet to creatinine ratio) and in-hospital mortality in TAAAD patients, especially to the post-operation patients. In this study, we investigated the relationship between the post-operation PCR and in-hospital mortality.

Methods

Study Design and Setting

A retrospective observational investigation was conducted between January 2017 and December 2019. A total of 171 TAAAD patients, confirmed with multidetector computed tomography (CT) scanning, were involved. The research was authorized by the institutional review board and in line with the Helsinki Declaration and as a retrospective study, a waiver of approval was permitted (2021-SR-529).

Selection of Participants

Patients (≥18 years older), who were initially diagnosed as TAAAD, treated with surgery, possessing complete information and alive 24 hours after the operations were included. Exclusion criteria as follows: (1) a trauma-related injury; (2) pregnancy; (3) hematologic diseases; (4) incomplete information; (5) patients with platelet transfusion during the surgery.

Methods of Measurement

The information as follows were collected: demographics (age, gender) and postoperative laboratory results (measured within 24 h after surgery) (Blood routine parameters, alanine aminotransferase (ALT), aspartate aminotransferase (AST), urea nitrogen (UREA), serum CREA, prothrombin time (PT), activated prothrombin time (APTT), fibrinogen (FIB), thrombin time (TT), D-dimer). PCR was calculated as the PLT divided by CREA.

Outcomes

The main outcome of this investigation was the relationship between PCR and in-hospital mortality (30-day mortality).

Statistical Analysis

Continuous variables and categorical variables are showed as mean ± standard deviation (SD), as median (ranges), or as frequencies and percentages as appropriate. Mann-Whitney U test and chi-square test were adopted to make a comparison between groups. Univariate analysis and multivariate analysis were employed to select independent indexes. In the multivariate analysis continuous variable with $p < 0.05$ (age, red blood cell distribution width (RDW), PLT, APTT, FIB, D-dimer, ALT, UREA, CREA and post-operation PCR) were included to select independent factors. The optimal value of PCR was determined by receiver operating characteristic curve (ROC) with the highest Youden Index (Sensitivity + specificity – 1). Statistical analyses were carried out with SPSS version 21.0 (SPSS, Chicago, IL, USA) and MedCalc version 15.2.2 (MedCalc Software, Mariakerke, Belgium). $p \leq 0.05$ were considered statistically significant.

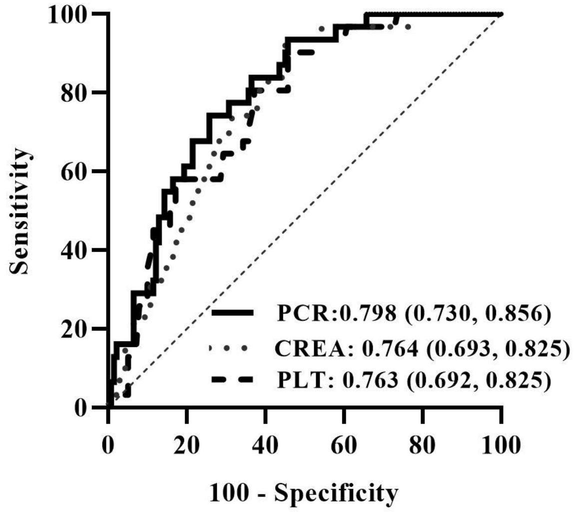

Fig. 1. Performance of biomarkers on the prediction of acute type A aortic dissection (TAAAD) patients in in-hospital mortality.

Results

Characteristics of study subjects

Table 1 presented the basic characteristics of included patients. The age of the nonsurvivors was elder than that in the survivors (61.10 ± 13.49 *vs.* 51.66 ± 11.33, $p < 0.001$). Compared with the survivors, the levels of red blood cell distribution width (RDW), PT, APTT, D-dimer, AST, UREA and CREA were higher than that in the non-survivors, while the levels of PLT and FIB were lower than that in the nonsurvivors (all $p < 0.05$). Gender, lymphocytes, neutrophils, hemoglobin (HB), TT, and ALT did not differ significantly (all $p > 0.05$). In addition, significant decreased post-operation PCR was discovered in the non-survivors (0.56 ± 0.33 *vs.* 1.50 ± 1.36; $p < 0.001$).

Multivariate Analysis

Univariate analysis suggested that age, RDW, PLT, APTT, FIB, D-dimer, ALT, BUN, CREA and post-operation PCR were related to in-hospital mortality. Then multivariate logistic regression, including the above indicators with a p-value < 0.05, was conducted to select independent factors. the results suggested that age (odds ratio (OR) = 1.055, 95% confidence interval (CI) = 1.014–1.097, $p = 0.007$) and post-operation PCR (OR = 8.850, 95% CI = 2.611–30.303, $p < 0.001$) were independent factors (Table 2).

Table 1. Characteristics of patients according to outcome.

Characteristics	Cohort	Survivors	Nonsurvivors	*p*-value
	N = 171	N = 140	N = 31	
Gender (male), %	131 (76.6%)	111 (79.3%)	20 (64.5%)	0.080
Median age (range), y	53.37 ± 12.26	51.66 ± 11.33	61.10 ± 13.49	<0.001
Hypertension, n (%)	147 (85.96)	121 (86.43)	26 (83.87)	0.713
Diabetes mellitus, n (%)	6 (3.51)	4 (2.86)	2 (6.45)	0.328
Ischemic complications (%)	13 (7.60)	8 (5.71)	5 (16.13)	0.048
Renal dysfunction (%)	1 (0.58)	1 (0.71)	0 (0)	0.639
Time to operating room from diagnosis (hour)	4 (0–14)	5 (0–14)	2 (0–14)	0.113
Intervals from symptom onset to hospital (hour)	9 (1–75)	9 (2–75)	8 (1–46)	0.092
Lymphocyte ($\times 10^9$/L)	0.53 (0.08–6.24)	0.52 (0.18–2.47)	0.62 (0.08–6.24)	0.400
Neutrophils ($\times 10^9$/L)	10.30 ±3.07	10.43 ± 3.06	9.70 ± 3.07	0.229
HB (g/L)	115.09 ± 15.61	115.90 ±15.07	111.42 ±17.62	0.149
RDW (%)	14.30 ± 1.58	14.17 ± 1.64	14.90 ± 1.13	0.020
Platelet ($\times 10^9$/L)	118.25 ± 65.00	127.23 ± 67.05	77.71 ± 27.45	<0.001
PT (s)	13.91 ±6.60	13.09 ± 2.53	17.56 ± 14.10	0.001
APTT (s)	37.84 ± 15.08	36.34 ± 14.60	44.59 ± 15.60	0.006
FIB (g/L)	3.20 ± 1.25	3.34 ± 1.25	2.57 ± 1.08	0.002
TT (s)	31.24 ± 25.91	29.56 ± 25.00	38.64 ± 28.82	0.078
D–dimer (mg/L)	6.19 ±3.17	10.80 ± 1.05	11.45 ± 1.27	0.254
ALT (U/L)	38 (15–8429.9)	37 (15, 2729.6)	44.9 (21.9, 8429.9)	0.186
AST (U/L)	74.6 (11.6–7500)	70.4 (11.6, 3411.3)	108.1 (35, 7500)	0.001
UREA (mmol/L)	11.39 ± 4.34	10.97 ± 3.87	13.31 ± 5.71	0.006
CREA (μmol/L)	125.92 ± 69.51	116.13 ± 64.17	170.13 ± 76.37	<0.001
PCR	1.33 ± 1.29	1.50 ± 1.36	0.56 ± 0.33	<0.001

ALT, alanine aminotransferase; APTT, activated prothrombin time; AST, aspartate aminotransferase; CREA, creatinine; FIB, fibrinogen; HB, hemoglobin; PT, prothrombin time; RDW, red blood cell distribution width; TT, thrombin time; UREA, urea nitrogen; PCR, platelet to CREA ratio.

Table 2. Multivariable logistic regression of in-hospital mortality for patients with type A acute aortic dissection.

Variables	HR	95% CI	*p*-value
Age	1.055	1.014–1.097	0.007
PCR	8.850	2.611–30.303	<0.001

CI, confidence interval; HR, hazard ratio; PCR, platelet to CREA ratio.

Performance of Post-Operation PCR

ROC presented that the area under the ROC curve (AUC) of post–operation PCR (AUC: 0.798, 95% CI 0.730–0.856, $p < 0.001$) was best, followed by CREA (AUC: 0.764, 95% CI 0.693–0.825, $p < 0.001$) and PLT (AUC: 0.763, 95% CI 0.692–0.825, $p < 0.001$) (Fig. 1). When 0.7242 was selected as the optimal value of PCR, the sensitivity and specificity were 74.2% and 74.3%, respectively. In addition, the mortality of patients with post-operation PCR >0.7242 was 7.14% while the mortality of patients with post-operation PCR >0.7242 was 38.98%.

Discussion

The findings of this study indicate that post-operative platelet to creatinine ratio (PCR) is an independent predictive factor associated with in-hospital mortality among patients with acute type A aortic dissection (TAAAD). Compared to platelet count (PLT) and serum creatinine (CREA) alone, post-operation PCR showed superior predictive value.

Previous studies have focused on admission biomarkers for TAAAD prognosis, such as decreased PLT count and platelet to hemoglobin ratio at admission, which were associated with poor outcomes [18,19]. However few investigations focus on the predictive value of post-operation indexes in in-hospital mortality to postoperative patients. Inflammation played a key role in the development of TAAAD and PLT has been identified as a biomarker to predict the outcome of TAAAD [20]. PLT is an inexpensive indicator and can be easily obtained from a complete blood count test. To TAAAD patients, PLT and dynamic monitoring of PLT were also associated with in-hospital mortality, and patient's renal function changed due to cardiovascular surgery [21–23]. In the current study, we included 171 patients. We firstly made a comparison between the two groups, and a significant difference in the levels of post-operation PCR was found. After adjusting for factors with a p-value $<$ 0.05, post-operation PCR was an independent factor. At last, ROC were employed to analyse the performance of post-operation PCR, the results showed that the recognition ability of PCR was the best. The results suggested that post-operation PCR could be used to identify the patients at higher risks.

In this study, we have found that the levels of post-operation PCR are closely related to the in-hospital death, but the exact mechanism is unknown. One possible explanation is that TAAAD is an inflammatory disease, while PLT is associated with inflammatory and can be used as an index of disease severity. It is well known that when the platelet is activated, many pro-inflammatory (platelet activating factor, interleukin (IL)-6 and IL-1) are released, leading to a series of chain reactions [24,25]. Another possible explanation is that the surgical treatment would cause a large consumption of platelets, resulting in a decrease in platelets; at the same time, surgery will also affect the patient's renal function, influence the synthesize and secrete thrombopoietin (TPO), thereby reducing the production of platelets.

As it is a retrospective study, defects are inevitable. First, this is a single-center, small sample cohort investigation, some variables may have been missed or unmeasured in the medical records. Second, we do not dynamically monitor changes in platelets and kidney function. Third, due to lacking internal and external verification of this study, larger multi-center prospective studies are needed.

Conclusions

In conclusion, this investigation suggests that post-operation PCR is a readily accessible and cost-effective biomarker that independently predicts in-hospital mortality in TAAAD patients. Post-operation PCR performs better than PLT and CREA in predicting patient outcomes.

Availability of Data and Materials

The datasets are available from the corresponding author on reasonable request.

Author Contributions

JZ, SQ and XC designed the research study. XC, YC and YW performed the research. JZ and SQ analyzed the data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study was performed to conform with the Declaration of Helsinki and was approved by the local ethics committee of the first affiliated hospital of nanjing medical university (2021-SR-529). Due to the retrospective design of the study, a waiver of participant informed consent was granted.

Acknowledgment

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

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