THE RELATIONSHIP BETWEEN THE RISK FACTORS OF CI-AKI AND MACE AND THE CYS C LEVEL IN ELDERLY PATIENTS AFTER PCI

Airong Fu, Jun Liao*, Wei Wang
Department of Cardiology, The first people's hospital of Huzhou (the first affiliated hospital of Huzhou teacher's college), Huzhou, 313000, PR China

ABSTRACT

Objective: *To investigate the risk factors of contrast-induced acute kidney injury (CI-AKI) and major adverse cardiovascular events (MACE) in follow-up period in elderly patients after percutaneous coronary intervention (PCI) and the relationship between these risk factors and cystatin C(CysC) level.*

Methods: *A total of 424 elderly patients who received PCI in our hospital from January 2017 to May 2020 were included in this study, and they were divided into groups according to the level of CysC. Univariate and multivariate methods were used to analyze the independent influencing factors of CI-AKI and MACE risk during follow-up, and ROC curve was drawn to evaluate the effectiveness of CysC level in predicting CI-AKI risk.*

Results: *The incidence of CI-AKI during hospitalization, age, proportion of patients with hy-pertension, type 2 diabetes mellitus (T2DM), old myocardial infarction, left ventricular ejection fraction (LVEF)<40%, myocardial infarction, perioperative diuretic, preoperative levels of CysC and SCr in the group with CysC>1.5 mg/L were significantly higher than those in the group with CysC≤1.5mg/L (P<0.05). The level of estimated glomerular filtration rate (eGFR) in the group with CysC >1.5 mg/L was significantly lower than that in the group with CysC≤1.5mg/L (P < 0.05). Multivariate analysis showed that the level of CysC was an independent influencing factors of CI-AKI (OR=1.72, 95% CI: 1.30~2.83, P=0.00). ROC curve analysis showed that CysC could be used to predict the risk of CI-AKI, AUC=0.81 (95% ci: 0.69~0.93), the best cut-off value was 1.5mg/L, and the sensitivity and specificity were 79.84% and 72.66% respectively (p<0.05). The total incidence of MACE and the incidence of target vessel revascularization in CysC>1.5 mg/L group were significantly higher than those in CysC≤1.5mg/L group (P<0.05). Cox regression analysis showed that CysC>1.5 mg/L was an independent influencing factor of MACE risk during follow-up period (RR=18.24, 95% CI: 2.12-39.67, P=0.00).*

Conclusion: *CI-AKI and MACE in follow-up period are closely related to high CysC level in elderly patients after PCI.*

Keywords: *Percutaneous coronary intervention, old age, CI-AKI, MACE, risk, cystatin C.*

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Introduction

CysC belongs to protease inhibitor, and its reabsorption and metabolism process is mainly completed by proximal renal tubule in human body[1]. At present, it is considered that the level of CysC has nothing to do with age, sex, race, muscle mass and other factors, but the slight change of glomerular filtration rate can have a significant impact on the level of serum CysC, so CysC is considered as a sensitive biomarker of renal filtration function[2-3]. The change of CysC level can be used as one of the diagnostic criteria of CI-AKI, but the relationship be-tween CI-AKI and prognosis of elderly ACS patients after interventional therapy and serum CysC level remains controversial[5]. Based on the above evidence, this study included 510 STEMI patients who underwent arteriography in our hospital from January 2012 to December 2020. The patients were divided into groups according to whether

there was spontaneous recanalization of diseased arteries, in order to explore the influencing factors of spontaneous recanali-zation of diseased arteries in STEMI patients and the relationship between the factors and FAR, which is reported as follows.

Materials and methods

General information

This study included 424 elderly patients who received PCI in our hospital from January 2017 to May 2020, and divided them into groups according to the level of CysC.

Inclusion criteria:

- Patients who meet ACS diagnostic criteria[5];
- Patients who successfully completed PCI;
- Age ≥18 years old;
- Serum CysC level was detected before operation.

Exclusion criteria:

- Hypotension;
- Cardiogenic shock;
- Allergy history of iodine or iodine contrast agent;
- Maintenance hemodialysis or peritoneal dialysis;
- Previous history of acute kidney injury (AKI);
- Received nephrotoxic drugs in recent 2 weeks;
- Systemic infection, autoimmune diseases or endocrine diseases;
- Malignant tumor;
- Incomplete clinical data.

The research design conforms to the Helsinki Declaration, and the patients and their families have signed the informed consent.

Method

The patients' sex, age, height, weight, complicated basic diseases, heart func-tion, smoking, drug use and laboratory examination indexes were recorded. EGFR was calculated according to the modified MDRD formula, and the for-mula was 175×SCr-1.234× age -0.179×[0.79 (female)][5]. The diagnosis of ACS depends on the typical symptoms, ECG changes and detection of biomarkers of myocardial injury.

Hydration method

Isotensive crystalloid solution was infused 3~12 hours before operation and 6~24 hours after operation, and the infusion rate was 1.0~1.5 ml/(kg·h). Follow-up was completed by telephone or outpatient review, and the follow-up time was >12 months.

CI-AKI was diagnosed according to "KDIG0 clinical practice guide for acute kidney injury (2012)". Follow-up recorded the occurrence of MACE.

Statistical processing

Chose SPSS20.0 software for data analysis. Kolmogorov-Smirnov test was used for the evaluation of normality, and T-test was used for the comparison of measurement data conforming to normal distribution, and the result was expressed as ($\bar{x}\pm s$). χ^2 test was used to compare the counting data, which was expressed as %.

A logistic regression model was used to evaluate the independent influencing factors of CI-AKI risk after PCI. Cox model was used to evaluate the independent influencing factors of MACE risk in follow-up after PCI. ROC curve was drawn to evaluate the clinical efficacy of CysC in predicting the risk of CI-AKI. $P<0.05$ is statistically significant.

Result

Univariate analysis of influencing factors of CI-AKI

The incidence of CI-AKI during hospitalization, age, proportion of pa-tients with hypertension, type 2 diabetes mellitus (T2DM), old myocardial infarc-tion, left ventricular ejection fraction (LVEF) <40%, myocardial infarction, perioperative diuretic, preoperative levels of CysC and SCr in the group with CysC>1.5 mg/L were significantly higher than those in the group with CysC≤1.5mg/L ($P<0.05$).

The level of estimated glomerular filtration rate (eGFR) in the group with CysC >1.5 mg/L was significantly lower than that in the group with CysC≤1.5mg/L ($P<0.05$). See Table 1.

Multivariate analysis of influencing factors of CI-AKI

Multivariate analysis showed that the level of CysC was an independent influencing factors of CI-AKI (OR=1.72, 95% CI: 1.30~2.83, P=0.00).

ROC curve analysis of clinical efficacy of CysC level in the prediction of CI-AKI

ROC curve analysis showed that CysC could be used to predict the risk of CI-AKI, AUC=0.81 (95% ci: 0.69~0.93), the best cut-off value was 1.5mg/L, and the sensitivity and specificity were 79.84% and 72.66% respectively ($p<0.05$).

Indicators	CysC>1.5mg/L group (n=89)	CysC≤1.5mg/L group (n=335)	*P*
Age (years)	72.49±9.18	61.84±8.37	0.00
Male (case)	70	253	0.54
BMI (kg/m^2)	24.61±3.36	24.20±3.54	0.97
Smoking (case)	39	126	0.21
Complicated with hypertension (case)	74	233	0.00
Combined with T2DM (case)	30	62	0.00
Complicated with hyperlipidemia (case)	34	111	0.32
Complicated with old myocardial infarction (case)	14	29	0.00
LVEF <40% (case)	21	50	0.01
Dosage of contrast agent (ml)	143.38±18.02	136.74±17.66	0.35
CI-AKI (case)	20	21	0.00
Diagnosis type (case)			0.00
UA	45	212	
STEMI	12	32	
NSTEMI	32	92	
Perioperative medication (cases)			
β-blockers	65	247	0.81
ACAI	17	73	0.47
ARB	22	77	0.68
Statins	75	272	0.42
Diuretics	33	93	0.02
Laboratory indicators (case)			
Hb (g/L)	125.40±24.24	130.79±25.33	0.21
WBC count (×10^9/L)	8.69±2.18	8.34±2.37	0.76
CysC (mg/L)	1.96±2.47	0.92±2.79	0.00
SUA (mmol/L)	455.19±93.92	439.88±90.23	0.27
Preoperative SCr (μmol/L)	98.62±14.80	86.89±11.47	0.00
Preoperative eGFR [ml/ (min·1.73m^2)]	57.14±8.60	77.91±10.96	0.00
Hydration (case)	61	218	0.45

Table 1: Univariate analysis of influencing factors of CI-AKI.

Univariate analysis of the influence of CysC on the risk of MACE in follow-up period

The total incidence of MACE and the incidence of target vessel revascular-iza-tion in CysC>1.5 mg/L group were sig-nificantly higher than those in CysC≤1.5mg/L group (P<0.05). There was no significant difference in all-cause mortality between the two groups (P>0.05). See Table 2.

Indicators	CysC>1.5mg/L group (n=89)	CysC≤1.5mg/L group (n=335)	*P*
Total cases of MACE	17	31	0.01
All-cause mortality	4	11	0.52
Revascularization of target vessel	12	21	0.03

Table 2: Multivariate analysis of influencing factors of MACE risk in follow-up period.

Multivariate analysis of the influence of CysC on the risk of MACE in follow-up period

Cox regression analysis showed that CysC>1.5 mg/L was an independent in-fluencing factor of MACE risk during follow-up period (RR=18.24, 95% CI: 2.12-39.67, P=0.00).

Discussion

A total of 424 elderly patients who received PCI in our hospital from January 2017 to May 2020 were included in this study, and they were divided into groups according to the level of CysC. The results showed that the level of CysC was an independent influencing factor of CI-AKI and MACE in follow-up period. Meanwhile, the AUC of CysC for predicting the risk of CI-AKI was 0.81 (95% CI: 0.69-0.93), the best cut-off value was 1.5mg/L, and the sensitivity and specificity were 79.84% and 72.66% respectively (P<0.05). It is suggested that serum CysC level ≥1.5mg/L can be used to pre-dict CI-AKI and MACE during 12 months follow-up in elderly patients after PCI.

Among the 424 patients included in this study, 41 patients had CI-AKI after PCI, with an incidence of 9.67, which further showed the importance of early prevention and treatment of CI-AKI. At present, CysC is recognized as an en-dogenous biomarker of glomerular filtration rate change. Compared with serum SCr, CysC can reflect the early changes of renal function more sensitively and accurately. At the same time, the level of CysC in serum changes more rapidly after injection of iodine contrast agent, suggesting that cysc level is more sensitive for CI-AKI prediction[6-7]. Other studies suggest that the baseline CysC level before PCI can be used to predict the risk of CI-AKI and the cardiac death in a follow-up period of more than 10 years[8-9].

ROC curve analysis in this study confirmed that CysC could predict CI-AKI more accurately than SCr by AUC results, and the sensitivity and specificity were satisfactory when 1.5mg/L was taken as cutoff value. The results of this study

also confirmed that the baseline CysC level can be used as an independent factor to predict the risk of MACE in elderly patients within 12 months after PCI. Some scholars have reported that patients with CysC≥2.0mg/L often have a higher inci-dence of MACE within 12 months after PCI, which is basically consistent with the results of this study[10]. Previous studies have confirmed that, compared with SCr and eGFR, serum CysC level can reflect the renal function of patients more accurately, and the higher the baseline CysC level, the worse the basic renal function[11-12].

It is also reported that the level of serum CysC is positively correlated with the degree of myocardial ischemia in patients with coronary heart disease, and the increase of CysC level can also lead to the increase of left ventricular weight and left ventricular hypertrophy[13-15]. In addition, the linear relationship between CysC level and the risk of heart failure was also confirmed. Meta-analysis suggests that the level of CysC is an independent influencing factor of cardiovascular death risk in elderly people, so CysC may also be an overall evaluation index reflecting human pathophysiological abnormalities based on kidney diseases, rather than a simple evaluation marker of renal func-tion[16-17].

This study has some limitations: this study is a single-center retrospective report, and it is difficult to completely eliminate the influence of confounding factors. Due to the lack of some data, the measured CysC level may be affected by hyperthyroidism, inflammation and rheumatoid factors.

Micro inflammation in patients with T2DM and chronic renal insufficiency can often induce the in-crease of CysC level, so the conclusion of this paper needs further confirmation in the follow-up study. To sum up, CI-AKI and MACE in the follow-up period of elderly patients after PCI are closely related to the high level of CysC.

Clinicians can take early preventive intervention for patients with high risk of CI-AKI according to the baseline CysC level, and minimize the risk of MACE through close follow-up intervention, thus improving the clinical prognosis.

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Corresponding Author:
Jun Liao
Department of Cardiology, The first people's hospital of Huzhou (the first affiliated hospital of Huzhou teacher's college), Huzhou, 313000, PR China
Email: lj360154784@163.com
(China)