



Impact of white blood cell count on the development of contrast-induced acute kidney injury in patients receiving percutaneous coronary intervention

Chengxiao Fu^{1,2,*}, Chenxi Ouyang^{3,*}, Guoping Yang^{1,4}, Jingle Li⁵, Guiyang Chen^{1,5}, Yu Cao⁵ and Liying Gong^{1,6}

¹ Center of Clinical Pharmacology, the Third Xiangya Hospital, Central South University, Changsha, Hunan, China

² Department of Pharmacy, The First Affiliated Hospital of University Of South China, Hengyang, Hunan, China

³ College of Pharmacy, University Of South China, Hengyang, Hunan, China

⁴ Center of Clinical Drug Evaluation, the Third Xiangya Hospital, Central South University, Changsha, Hunan, China

⁵ Center of Cardiology, the Third Xiangya Hospital, Central South University, Changsha, Hunan, China

⁶ Center of Critical Care Medicine, the Third Xiangya Hospital, Central South University, Changsha, Hunan, China

* These authors contributed equally to this work.

ABSTRACT

This study aimed to investigate the efficacy of a pre-procedural white blood cell (WBC) count in the prediction of contrast-induced acute kidney injury (CI-AKI) risk in coronary artery disease patients receiving a percutaneous coronary intervention (PCI). This observational study comprises a sample of 1,013 coronary artery disease patients (including ACS and stable angina) receiving PCI, gathered from September 2015 to July 2017. CI-AKI incidence in the study population was 4.8% (49/1013). Patients in the CI-AKI group had significantly higher WBC counts than those in the non-CI-AKI group (10.41 ± 5.37 vs. 8.09 ± 3.10 , $p = 0.004$). Logistic analysis showed that WBC count (odds ratio [OR]: 1.12, 95% CI [1.03–1.21], $P = 0.006$) was a significant and independent predictor of CI-AKI risk in patients receiving PCI. Receiver-operating characteristic (ROC) curve analysis found that pre-procedural WBC count $\geq 11.03 \times 10^9/L$ was the optimal cut-off value in the prediction of CI-AKI risk with a sensitivity of 41.0% and a specificity of 86.5%. Patients with CI-AKI had a significantly worse 1-year survival rate than patients without CI-AKI (91.8% vs. 97.6%, $P = 0.012$). In summary, increased pre-procedural WBC count is associated with an increased risk of developing CI-AKI in patients receiving PCI.

Subjects Cardiology, Hematology, Internal Medicine, Nephrology, Radiology and Medical Imaging

Keywords White blood cell, Contrast-induced acute kidney injury, Coronary heart disease, Percutaneous coronary intervention

Submitted 24 October 2023

Accepted 9 May 2024

Published 28 June 2024

Corresponding authors

Yu Cao, caoyu0811@csu.edu.cn

Liying Gong, gongliying2016@outlook.com

Academic editor

Sonia Oliveira

Additional Information and
Declarations can be found on
page 12

DOI 10.7717/peerj.17493

© Copyright
2024 Fu et al.

Distributed under
Creative Commons CC-BY 4.0

OPEN ACCESS

INTRODUCTION

Contrast-induced acute kidney injury (CI-AKI) is a common complication arising among patients receiving percutaneous coronary intervention (PCI) and is associated with increased morbidity, mortality, and healthcare resource utilization (Davenport, Perazella & Nallamotheu, 2023; Davenport et al., 2020; Gupta et al., 2005; McCullough et al., 2006; Rihal et al., 2002). PCI often requires the administration of an iodinated contrast medium, which is often cited as the cause of CI-AKI. The incidence of CI-AKI is 2% for the general population (Demircelik et al., 2015); however, patients receiving PCI are at higher risk of developing CI-AKI, and patients who also suffer from chronic kidney disease and/or diabetes have a risk of almost 50% (Finn, 2006; Goldfarb et al., 2009).

The prognostic impact of CI-AKI depends on the persistence of renal function deterioration and the degree of kidney injury (James et al., 2011; Maioli et al., 2012). Currently, there is no effective medication used to treat CI-AKI emphasizes the need for clinical efforts to prevent its development prior to diagnosis (Toso et al., 2014). Several conditions and factors, including diabetes, chronic kidney disease, anemia, advanced age, congestive heart failure, and using a large amount of contrast media (CM) in procedures, can increase a patient's chances of developing CI-AKI (McCullough et al., 1997; Mehran et al., 2004; Wi et al., 2013).

The inflammation response has been found to significantly impact the development of CI-AKI (Demircelik et al., 2015; Kocas et al., 2015; Kurtul et al., 2016; Kwasa, Vinayak & Armstrong, 2014; Liu et al., 2012). White blood cell (WBC) count, leukocyte count, platelet-to-lymphocyte ratio, and WBC differential are widely recognized as indications of inflammation (Kocas et al., 2015; Shah et al., 2017; Sun et al., 2018). Shah et al. (2017) discovered an independent association between increased major adverse cardiovascular events (MACE) and baseline WBC count in patients undergoing PCI for acute coronary syndrome (ACS) and stable coronary artery disease. Yet, to our knowledge, no studies have investigated using WBC count as a predictor of CI-AKI risk in PCI patients. Thus, this study aimed to investigate the relationships between pre-procedure WBC count and CI-AKI incidence in patients with coronary artery disease receiving PCI.

METHODS

The study protocol was approved by the ethics committee of the Third Xiangya Hospital of Central South University, and the approval number was R15006. Each of the subjects enrolled in this study provided informed consent to participate. We have received written informed consent from participants in our study. ClinicalTrials.gov identifier: NCT02888652. This study was performed according to the STROBE checklist.

Study design and subjects

The present study is a *post hoc* substudy to the research project entitled "A real-world study of P2Y12 receptor inhibitor therapy in patients with coronary heart disease undergoing PCI". Briefly, this study was a prospective observation study of consecutive patients who underwent PCI at 2 clinical centers in China between September 1, 2015, and September

1, 2017. Adult patients (18 years of age or older) with documented serum creatinine (SCr) records both pre- and post-PCI (within 72 hr after the procedure) were included. The exclusion criteria for the study included individuals who had failed PCI, those with hemodynamic instability or class IV heart failure (as defined by the NYHA functional classification system), stage 4 or higher chronic kidney disease (CKD), hypersensitivity to contrast medium, anyone who had been exposed to a second contrast medium within one week of the exposure to the first, and those who had received metformin or aminophylline within the 2 weeks prior to PCI.

All patients who were treated with drug-eluting stents and received dual antiplatelet therapy (aspirin associated with clopidogrel or ticagrelor) were recommended for 12 months. At the time of hospital admission, patients received a loading dose of 300 mg aspirin followed by 100 mg/day and either a loading dose of 300 mg clopidogrel followed by 75 mg/day or a loading dose of 180 mg ticagrelor followed by 90 mg/day as P2Y₁₂ inhibitor. PCI was performed according to standard clinical practice and PCI procedures were performed through the radial approach by experienced interventional cardiologists. Professional operators and radiologists can choose to use Visipaque or Iohexol for contrast-enhanced procedures. Procedural anticoagulation was performed by administering unfractionated heparin to target an activated clotting time of 250 to 300 s. At the decision of the professional operator's discretion, perioperative statin (rosuvastatin 20mg/day or atorvastatin 10mg/day), ACEI/ARB inhibitor, beta-blocker, proton pump inhibitor, and intra coronary or intravenous glycoprotein IIb/IIIa inhibitor was also administered during PCI.

ACS was defined as a group of clinical symptoms that can indicate acute myocardial ischemia. This includes ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), and unstable angina (UA) ([Kumar & Cannon, 2009](#)); hypertension is diagnosed when systolic blood pressure (SBP) >140 mmHg and/or diastolic blood pressure (DBP) >90 mmHg, or if the individual takes anti-hypertensive medication; low blood pressure (LBP) is defined as blood pressure <90/60 mmHg ([Murat, Kurtul & Yarlioglu, 2015](#)); diabetes is defined as having a fasting plasma glucose (FPG) level of ≥ 7.0 mmol/L, or a 2 h oral glucose tolerance test (OGTT) level of ≥ 11.1 mmol/L, or a history of diabetes, or requiring the use of glucose-lowering agents ([Collaboration NCDRF, 2015](#)).

All patients were given intravenous hydration. Standard hydration therapy, using saline or bicarbonate solution, was administered at the physician's discretion. All patients received pre- and post-procedural hydration with saline or bicarbonate solution at a rate of one mL/kg/h for 12 h. If a patient's ejection fraction (EF) was below 40% during PCI, hydration was initiated at a rate of 0.5 mL/kg/hr and continued for 18 to 24 h post-emergency PCI ([Levine et al., 2011](#); [Stacul et al., 2011](#)).

Endpoints and definitions

CI-AKI was defined as an increase in serum creatinine by ≥ 0.5 mg/dl or a relative $\geq 25\%$ within 72 h following the procedure without another clear cause for acute kidney injury ([Jarai et al., 2012](#); [Leoncini et al., 2014](#); [Thomsen, 2003](#)).

Samples and data collection

Blood samples were collected at admission and 48–72 h after CM administration to measure Scr concentrations. To define CI-AKI, the highest Scr value after the procedure was considered. Upon hospital admission, a specific clinical laboratory conducted a baseline measurement of the patient's WBC count in the Third Xiangya Hospital of Central South University. Serum glucose levels and lipid profiles were measured while patients were fasting in the morning after administration. The estimated glomerular filtration rate (eGFR) was calculated using the modification of diet in renal disease study equation (MDRD) (Levey *et al.*, 1999). All patients underwent a follow-up evaluation at the 1-year mark, either during a clinical visit or *via* telephone contact. An independent clinical events committee, unaware of the details of the study, evaluated all adverse events.

Statistical analysis

SPSS 25.0 (Armonk, NY, USA) was used to perform statistical calculations. Continuous variables were summarized by means \pm SD and median (interquartile range); categorical variables were summarized by percentages. The normality of continuous data was assessed using the Shapiro–Wilks test and the Kolmogorov–Smirnov test. Continuous variables normally distributed were compared using an unpaired student' *t*-test, while non-normal variables were compared using the Mann–Whitney U-test. The association between categorical variables and treatment groups was analyzed using Chi-squared or Fisher exact tests. In determining the factors independently associated with CI-AKI, we considered a comprehensive list of patient characteristics and treatment patterns as candidates. Using forward elimination, a multivariate logistic regression model in which all variables were associated with CI-AKI was developed. During the multivariable model-building process, variables with a *P* value ≤ 0.15 and those considered clinically important, biologically plausible, or supported by previously published data were included. Using variance inflation factors (VIF) to detect multicollinearity. The adjusted odds ratios were calculated for each of these variables. ROC curve analysis was utilized to assess the ability of baseline WBC count to differentiate between patients with and without CI-AKI. The optimal cut-off point was determined by identifying the baseline WBC count that maximized the sum of specificity and sensitivity. Kaplan–Meier survival charts were created to determine the difference in 1-year death rate between patients with CI-AKI and those without. To compare survival curves, we used the log-rank test. For all statistical tests carried out, two-tailed *P* values were used, with statistical significance being defined by a *P* value of ≤ 0.05 . We predict a sensitivity of 90% and specificity of 90%, while the prevalence rate of CI-AKI was 5%. the required sample size was finally calculated to be 728. The percentage of missing values was less than 1% for all variables in the study. Missing values of categorical variables were imputed to their most common value, and continuous variables to the median of the non-missing values.

RESULTS

Two centers enrolled 1300 patients for PCI between September 2015 and July 2017. Eleven patients did not complete hydration and were excluded. In total, 1,013 patients met the

study criteria (Fig. 1). In this study, all patients were given intravenous hydration. Of the total patients, 213 (21%) underwent emergency PCI and were treated with sodium bicarbonate for hydration.

All patients completed a follow-up evaluation at the one-year mark, either in person or *via* phone. Table 1 shows the baseline clinical characteristics stratified by CI-AKI, including patient demographics and clinical, biochemical, angiographic, and procedural variables. The incidence of CI-AKI was 4.8% (49/1013). Patients with CI-AKI (referred to as the “CI-AKI group” hereafter) had a significantly higher WBC count than those without CI-AKI (referred to as the “Non-CI-AKI group” hereafter) (10.41 ± 5.37 vs. 8.09 ± 3.10 10^3 mL, respectively; $P = 0.004$) and had a significantly lower chance of having used statins ($P = 0.022$) compared with patients in the Non-CI-AKI group. Female patients, low blood pressure, peripheral vascular disease (PVD), intra-aortic balloon pump (IABP), heart failure (I-III), lower hemoglobin, and higher fasting glucose were more likely to develop CI-AKI. There were no significant differences in age, hypertension incidence, and type of coronary artery disease between the patients with and without CI-AKI.

Univariate and multivariate logistic regression analyses were used to analyze the effects of multiple variables, as presented in Table 2. Based on the outcomes of the univariate analyses, age ≥ 75 years, Female, PVD, LBP, ACS, DM, fasting glucose, PVD, eGFR < 60 mL/min, heart failure (I-III), WBC count, P/L, Hb, IABP, EF, LDL, HDL, TC, use of Iohexol, and use of statins, were selected for multivariate logistic regression analyses. Apart from low Hb (OR 0.97, 95% CI [0.95–0.99]; $P = 0.002$), fasting glucose (OR 1.10, 95% CI [1.00–1.20]; $P = 0.043$), Iohexol (OR 4.55, 95% CI [1.37–15.14]; $P = 0.014$), WBC count (OR 1.12, 95% CI [1.03–1.21]; $P = 0.006$) remained significant and independent in predicting the occurrence of CI-AKI. The use of statins was identified as effective in preventing CI-AKI development (OR 0.24, 95% CI [0.05–1.21]; $P = 0.044$).

ROC curve analysis of pre-procedural WBC count found that pre-procedural WBC count could be used to predict CI-AKI incidence. [area under the curve = 0.684 (95% confidence interval 0.545–0.723), $P = 0.002$] (Fig. 2). A cut-off value of $\geq 11.03 \times 10^9/L$ was identified as optimal in predicting CI-AKI incidence, providing a sensitivity of 41.0% and specificity of 86.5%.

The follow-up period ended in September 2018, with complete 12-month follow-up data for all patients. One-year mortality occurred in 27 patients (2.7%). The CI-AKI group had a significantly higher incidence of mortality (8.2% vs. 2.4% $P = 0.037$). In the multivariate analysis, one-year mortality was associated with CI-AKI (OR 3.47, 95% CI [1.12–10.74]; $P = 0.031$). The Kaplan–Meier cumulative survival curves of CI-AKI are shown in Fig. 3. Patients who developed CI-AKI had a significantly lower 1-year survival rate than those who did not (91.8% vs. 97.6%, $P = 0.012$).

DISCUSSION

The result of our study suggests that an increase in pre-procedure WBC count at the time of treatment may be related to the development of CI-AKI. In addition, the predictive power of pre-procedural WBC count was independent of other known clinical and laboratory-based

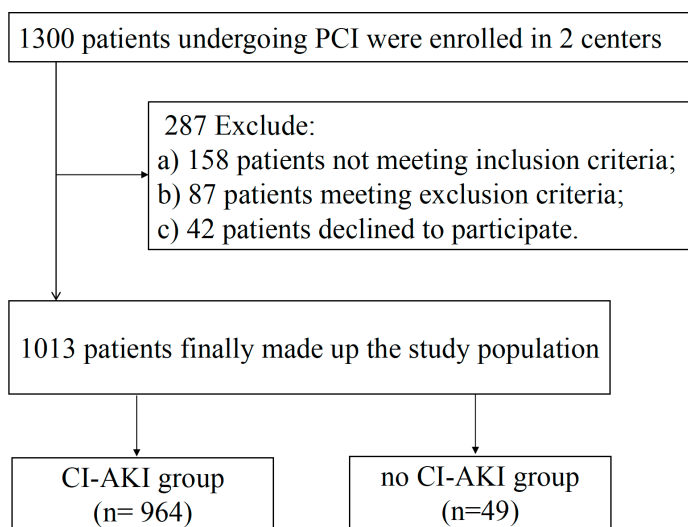


Figure 1 Flowchart depicting the inclusion and exclusion of the patients in the present study. PCI indicates percutaneous coronary intervention; CI-AKI indicates contrast-induced acute kidney injury.

Full-size DOI: [10.7717/peerj.17493/fig-1](https://doi.org/10.7717/peerj.17493/fig-1)

predictors of CI-AKI. A count value of $\geq 11.03 \times 10^9/L$ was identified as the optimal cut-off value in the prediction of CI-AKI incidence, with a sensitivity of 41.0% and a specificity of 86.5%.

Some associated conditions and qualities, such as advanced age, anemia, congestive heart failure, diabetes, chronic kidney disease, and large amounts of CM in treatments, have been identified as essential factors predisposing patients to develop CI-AKI (McCullough *et al.*, 1997; Mehran *et al.*, 2004; Wi *et al.*, 2013). Moreover, a number of popularized risk score models, such as the Bartholomew and Mehran scoring systems, have been developed to evaluate a patient's risk of developing CI-AKI (Bartholomew *et al.*, 2004; Mehran *et al.*, 2004). However, these systems do not consider inflammatory factors and require a patient's entire medical history to assess the risk, making them inconvenient for clinical practice. Clinicians need a sensitive, inexpensive, easily obtainable clinical indicator to assess a patient's risk of CI-AKI prior to PCI.

Thus far, no adjunctive pharmaceutical has been found to effectively treat CI-AKI, which emphasizes the need for accurate clinical assessment methods to prevent CI-AKI development in patients. Evidence from both clinical and experimental studies supports the idea that statins can effectively prevent the development of CI-AKI (Han *et al.*, 2014; Jia *et al.*, 2009; Leoncini *et al.*, 2014). Statins (including rosuvastatin and simvastatin) may be renoprotective *via* several mechanisms, including anti-inflammation, attenuation of endothelial dysfunction, anti-proliferation of mesangial cells, protection of podocytes, and inhibition of the uptake of contrast media into renal tubular cells (McCullough *et al.*, 2016). The anti-inflammatory properties of statins are well-documented. Our study also demonstrates that standard dose statins administered in addition to standard hydration can reduce the incidence of renal injury. Statins can reduce the concentrations of pro-inflammatory cytokines and circulating C-reactive protein (CRP) and inhibit vascular

Table 1 Baseline biochemical and procedural characteristics and medications and lifestyle of the study participants.

Variable	Total (n = 1013)	Non-CI-AKI Group (n = 964)	CI-AKI Group (n = 49)	P Value
Age, y	62.70 ± 10.46	62.67 ± 10.48	63.39 ± 10.19	0.637
Female	284 (28.0%)	263 (27.3%)	21 (42.9%)	0.018
BMI, kg/m ²	24.31 ± 3.27	24.33 ± 3.24	23.93 ± 3.87	0.415
SBP, mmHg	132.17 ± 22.07	132.30 ± 21.72	129.67 ± 28.27	0.525
DBP, mmHg	78.13 ± 12.52	78.09 ± 12.29	78.98 ± 16.55	0.711
Clinical presentation				
ACS	873 (86.2%)	829 (86.0%)	44 (89.8%)	0.452
Stable angina	140 (13.8%)	135 (14.0%)	5 (10.2%)	0.452
Risk factor				
Age >75	101 (10%)	97 (10.1%)	4 (8.2%)	0.810
LBP	57 (5.6%)	50 (5.2%)	7 (14.3%)	0.016
DM	464 (45.8%)	444 (46.1%)	20 (40.8%)	0.473
PVD	379 (37.4%)	368 (38.2%)	11 (22.4%)	0.026
Hb <60, mg/dl	12 (1.2%)	12 (1.2%)	0 (0%)	>0.99
IABP	15 (1.5%)	11 (1.1%)	4 (8.2%)	0.004
Heart failure (I-III)	20 (2.0%)	16 (1.7%)	4 (8.2%)	0.013
Kidney transplantation	0 (0%)	0 (0%)	0 (0%)	>0.99
eGFR base line (ml/min/1.73m ²)	74.88 ± 28.38	74.19 ± 25.21	88.78 ± 64.08	0.001
eGFR <60mL/min (ml/min/1.73m ²)	319 (31.5%)	311 (31.4%)	8 (33.3%)	0.844
eGFR after PCI (ml/min/1.73m ²)	80.05 ± 27.96	81.11 ± 27.66	58.65 ± 25.44	<0.01
Smokers				
Current smoker	383 (37.8%)	366 (38.0%)	17 (34.7%)	0.645
Former smoker	169 (16.7%)	165 (17.1%)	4 (8.2%)	0.101
Hypertension	662 (65.4%)	629 (65.2%)	33 (67.3%)	0.763
TIA/Stroke	118 (11.6%)	113 (11.7%)	5 (10.2%)	0.747
Previous PCI	134 (13.2%)	129 (13.4%)	5 (10.2%)	0.522
Previous CABG	6 (0.6%)	6 (0.6%)	0 (0%)	>0.99
Angiographic data and treatment				
Multivessel disease	829 (81.8%)	787 (81.6%)	42 (85.7%)	0.571
Multivessel PCI	657 (64.9%)	629 (65.2%)	28 (57.1%)	0.283
LCA	67 (6.6%)	60 (6.2%)	7 (14.3%)	0.037
LAD	945 (93.3%)	899 (93.3%)	46 (93.9%)	>0.99
Contrast media dose, mL	87.97 ± 9.80	87.96 ± 9.77	88.27 ± 10.49	0.830
Iohexol	735 (72.6%)	691 (71.7%)	44 (89.8%)	0.037
Laboratory				
WBC,10 ⁹ /L	8.21 ± 3.28	8.09 ± 3.10	10.41 ± 5.37	0.004
N,10 ⁹ /L	6.30 ± 5.89	6.24 ± 5.87	8.74 ± 6.37	0.027
L,10 ⁹ /L	1.70 ± 1.21	1.70 ± 1.22	1.46 ± 0.76	0.255
Hb, g/L	133.15 ± 17.27	133.41 ± 17.16	127.94 ± 18.55	0.030
Platelet	212.40 ± 60.54	211.99 ± 60.49	220.55 ± 61.48	0.334

(continued on next page)

Table 1 (continued)

Variable	Total (n = 1013)	Non-CI-AKI Group (n = 964)	CI-AKI Group (n = 49)	P Value
P/L	152.52 ± 83.45	151.56 ± 83.58	171.20 ± 79.35	0.108
LDL cholesterol	2.34 ± 0.89	2.32 ± 0.88	2.58 ± 0.99	0.056
HDL cholesterol	1.14 ± 0.28	1.14 ± 0.28	1.21 ± 0.22	0.089
Triglycerides, mmol/L	1.81 ± 1.43	1.82 ± 1.45	1.72 ± 1.08	0.661
Total cholesterol, mmol/L	4.47 ± 1.28	4.45 ± 1.28	4.80 ± 1.24	0.072
Fasting glucose, mmol/L	6.32 ± 2.54	6.25 ± 2.38	7.66 ± 4.64	0.050
Baseline LVEF, %	58.09 ± 11.91	58.35 ± 11.77	53.04 ± 13.56	0.004
Medications				
ACEI	689 (68.0%)	659 (68.4%)	30 (61.2%)	0.296
ARB	135 (13.3%)	129 (13.4%)	6 (12.2%)	0.819
Beta-blocker	826 (81.5%)	786 (81.5%)	40 (81.6%)	0.986
Calcium antagonist	298 (29.4%)	287 (29.8%)	11 (22.4%)	0.272
Statins	1000 (98.7%)	954 (99.0%)	46 (93.9%)	0.022
GPIIb/IIIa inhibitors	415 (41.0%)	391 (40.6%)	24 (49.0%)	0.242
Nitrates	495 (48.9%)	467 (48.4%)	28 (57.1%)	0.235
Proton pump inhibitor	823 (81.2%)	779 (80.8%)	44 (89.8%)	0.116

Notes.

Data are expressed as mean ± SD or number of patients or percent (%).

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; LBP, low blood pressure; DM, diabetes mellitus; PVD, peripheral vascular disease; LCA, left coronary artery; LAD, left anterior descending artery; TIA, transient ischemic attack; ACS, acute coronary syndromes; PCI, percutaneous Coronary Intervention; CABG, coronary artery bypass grafting; WBC, white blood cell; Hb, hemoglobin; N, neutrophil; L, lymphocytes; LDL, low-density lipoprotein cholesterol; HDL, high-density lipoprotein cholesterol; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; P/L, platelet/lymphocytes; IABP, intra-aortic balloon pump; LVEF, left Ventricular Ejection Fraction.

reactive oxygen species (ROS) generation ([Antoniades et al., 2011](#); [Antoniades et al., 2010](#); [Ascer et al., 2004](#); [Bulcao et al., 2007](#); [Van de Ree et al., 2003](#)). The development of CI-AKI is said to be significantly influenced by inflammation. [Gao et al. \(2011\)](#) and [Shacham et al. \(2015\)](#) both found that CRP can increase CI-AKI incidence in patients receiving PCI. Test of WBC count, leukocyte count, and WBC differential are widely used as inexpensive indicators of inflammation. Our study supports the idea that these measures of inflammation are useful predictors of CI-AKI risk.

Inflammation is considered an independent risk factor in the development of CI-AKI. One of the most cost-effective markers used in detecting inflammation is WBC count. This study provides additional evidence of the clinical usefulness of a cost-effective and standard measure for potential risk stratification in patients undergoing PCI-related CI-AKI. Emerging evidence suggests that a more robust inflammatory and oxidative response is crucial in the development and progression of CI-AKI. Numerous studies have been conducted to evaluate the link between inflammation and the incidence of CI-AKI ([Akin et al., 2015](#); [Gao et al., 2011](#); [Kurtul et al., 2016](#); [Yuan et al., 2017](#)). [Yuan et al. \(2017\)](#) found an association between various clinical measures (WBC count, N count, and CRP levels) and CI-AKI incidence in ACS patients who undergo PCI. Similarly, [Gao et al. \(2011\)](#) also found an association between CRP level and the incidence of CI-AKI in patients who underwent PCI. In accordance with these studies, we found that a higher pre-procedure WBC count was independently associated with the development of CI-AKI. Our findings

Table 2 Univariate and multivariate analysis of the risk factors related to CI-AKI in patients receiving PCI.

Variable	Univariate Analysis			Multivariate Analysis		
	OR	95%CI	P value	OR	95%CI	P value
Female	2.00	(1.12–3.58)	0.020	1.51	(0.65–3.54)	0.342
Age \geq 75 years	0.80	(0.28–2.26)	0.666	0.42	(0.09–2.01)	0.277
LBP	3.05	(1.31–7.12)	0.01	0.95	(0.27–3.35)	0.941
DM	0.81	(0.45–1.45)	0.473	0.65	(0.29–1.44)	0.289
Heart failure (I-III)	5.27	(1.69–16.40)	0.004	1.53	(0.31–7.56)	0.602
ACS	1.43	(0.56–3.68)	0.454	0.78	(0.27–2.21)	0.635
PVD	0.47	(0.24–0.93)	0.030	0.70	(0.32–1.52)	0.369
eGFR $<$ 60	0.96	(0.51–1.79)	0.892	1.08	(0.49–2.38)	0.852
Previous smoker	0.43	(0.15–1.21)	0.111	0.92	(0.28–3.01)	0.892
IABP	7.70	(2.36–25.13)	0.001	2.29	(0.47–11.22)	0.305
Multivessel PCI	0.71	(0.40–1.27)	0.248	0.56	(0.29–1.10)	0.092
Multivessel disease	1.35	(0.60–3.05)	0.472			
LAD	1.11	(0.34–3.66)	0.866			
LCA	2.51	(1.08–5.83)	0.032	2.27	(0.79–6.56)	0.129
WBC count	1.15	(1.08–1.22)	$<$ 0.001	1.12	(1.03–1.21)	0.006
Hb	0.98	(0.97–1.00)	0.031	0.97	(0.95–0.99)	0.002
P/L	1.00	(1.00–1.01)	0.110	1.00	(0.99–1.01)	0.438
Fasting glucose	1.15	(1.06–1.25)	0.001	1.10	(1.00–1.20)	0.043
Statin	0.16	(0.04–0.60)	0.007	0.24	(0.05–1.21)	0.044
Contrast media dose	1.00	(0.97–1.03)	0.829			
Iohexol	3.48	(1.36–8.86)	0.009	4.55	(1.37–15.14)	0.014
LDL cholesterol	1.33	(0.99–1.78)	0.056	1.97	(0.86–4.49)	0.109
HDL cholesterol	2.38	(0.88–6.46)	0.089	1.99	(0.53–7.51)	0.308
Total cholesterol	1.20	(0.98–1.47)	0.072	0.69	(0.37–1.31)	0.258
Baseline LVEF, %	0.97	(0.94–0.99)	0.004	0.98	(0.95–1.00)	0.059

Notes.

LBP, low blood pressure; DM, diabetes mellitus; PVD, peripheral vascular disease; ACS, acute coronary syndromes; IABP, intra-aortic balloon pump; LCA, left coronary artery; LAD, left anterior descending artery; WBC, white blood cell; P/L, platelet/lymphocytes; PCI, percutaneous coronary intervention; LDL, low-density lipoprotein cholesterol; HDL, high-density lipoprotein cholesterol; LVEF, left Ventricular Ejection Fraction.

align with the results of *Yuan et al. (2017)* but extend to the patients not diagnosed with ACS.

To date, the exact mechanism of CI-AKI development is poorly understood. Iodinated contrast media may cause AKI due to direct toxicity, endothelial dysfunction, oxidative stress, and hemodynamic changes (*Sendeski, 2011*). Although our study cannot fully clarify the plausible mechanism behind the association between higher pre-procedure WBC count and CI-AKI risk, we posit a hypothesis. After administering contrast media during PCI, the highly concentrated contrast media can restrict fluid flow through the medullary vessels and tubules, thus prolonging its contact with the vascular endothelium and the tubular epithelial cells (*Akcaý, Nguyen & Edelstein, 2009; Seeliger et al., 2012*). As contrast media are commonly cytotoxic, this process causes damage to the tubular and endothelial cells, which as a result, the injured kidneys triggers the transport of various leukocytes, such as

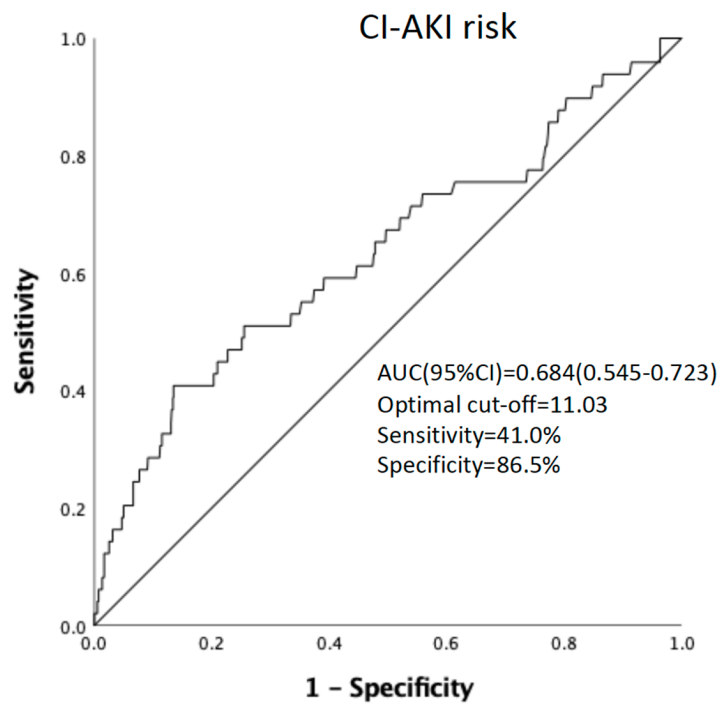


Figure 2 ROC curve analysis of the pro-procedure WBC count in predicting CI-AKI incidence in PCI patients.

Full-size DOI: 10.7717/peerj.17493/fig-2

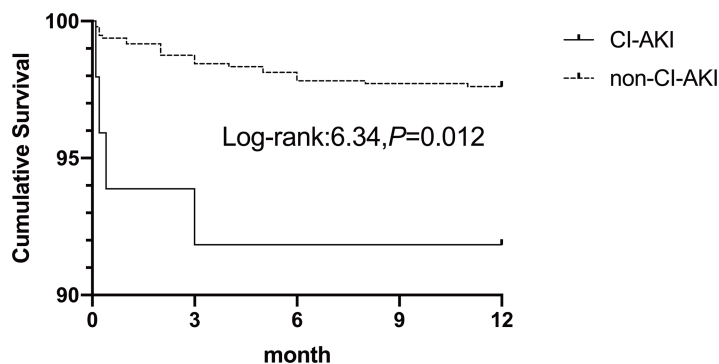


Figure 3 Kaplan–Meier cumulative survival between patients with CI-AKI and non-CI-AKI.

Full-size DOI: 10.7717/peerj.17493/fig-3

neutrophils, lymphocytes, macrophages, and natural killer cells. Such high concentrations of white blood cells can further enhance the generation of inflammatory mediators such as chemokines and cytokines in endothelial cells and tubular cells, contributing to the recruitment of more leukocytes in the kidneys (Akca, Nguyen & Edelstein, 2009). There is a possibility that a higher pre-procedure WBC count combined with contrast media exposure during PCI could significantly increase the risk of CI-AKI.

The development of CI-AKI following PCI can affect both short- and long-term mortality, and morbidity and is an expensive complication (Caixeta & Mehran, 2010;

Liu et al., 2023; McCullough et al., 2006; Rihal et al., 2002). Considering the prognostic implications of CI-AKI, the early identification of at-risk patients is extremely important. Emerging strategies such as minimalizing contrast media volume, intravascular volume repletion, intra-aortic balloon pump use, and statins use can significantly reduce CI-AKI risk in patients receiving emergency or elective PCI. ROC curve analysis showed that the baseline WBC count was effective in differentiating between patients who developed CI-AKI and those who did not, however, and so this may not be a significant issue. Using WBC counts to identify patients at higher risk would significantly reduce the number of patients developing CI-AKI and is a technique whose utilization should be strongly considered in clinical practice.

CONCLUSIONS

Our study confirmed that WBC count is an independent and powerful predictor of risk for CI-AKI in patients undergoing PCI. ROC curve analysis showed that a baseline WBC count of 11.03 was a fair preliminary indicator of creatinine increases, and patients who experienced CI-AKI had a notably lower 1-year survival rate compared to those who did not suffer from CI-AKI. There is mounting evidence supporting the use of WBC count as a prognostic marker for determining CI-AKI risk in patients who receive PCI (*Shah et al., 2017*). To effectively use this marker in clinical settings, further studies are needed to establish treatment options, identify anti-inflammatory medications, and compare its utility with other known inflammatory markers.

LIMITATIONS

This study is not without limitations. First, it is important to note, however, that this study was merely observational and was conducted in two medical centers with a small sample size which may have affected our results. Second, we excluded patients without measured plasma creatinine upon admission or 24–72 h after PCI procedure, which may introduce selection bias. Third, C-reactive protein (CRP) is the important of inflammatory factor, However, we just test CRP levels in some high-risk patients. This study would be more convincing with a detailed analysis of cytokines, for example, TNF- α , IL1, and IL6 in the plasma. However, this is just an observation study, so we did not test TNF- α , IL1, and IL6 in patients. Finally, Some variables such as age, kidney disease, and diabetes mellitus in previous studies had no statistical significance in our study, which was perhaps because of the strict definition of CI-AKI we used. Patients who developed CI-AKI showed significant differences in their baseline as compared to those who did not. Despite controlling for potential confounding factors related to known comorbidities and drug use, we cannot completely eliminate the possibility of unmeasured confounders affecting our results. Therefore, our findings should be considered as a hypothesis for further confirmation through additional studies.

ACKNOWLEDGEMENTS

The authors are indebted to the lab staff and the CCU nurses for their precious help in collecting and processing blood samples. They are also very grateful to Manhui Hu and Feng Zheng for their secretarial assistance.

ADDITIONAL INFORMATION AND DECLARATIONS

Funding

This work was supported by the National Natural Science Foundation of China (No. 81803639). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Grant Disclosures

The following grant information was disclosed by the authors:
National Natural Science Foundation of China: 81803639.

Competing Interests

The authors declare there are no competing interests.

Author Contributions

- Chengxiao Fu performed the experiments, analyzed the data, authored or reviewed drafts of the article, and approved the final draft.
- Chenxi Ouyang performed the experiments, analyzed the data, authored or reviewed drafts of the article, and approved the final draft.
- Guoping Yang conceived and designed the experiments, prepared figures and/or tables, authored or reviewed drafts of the article, and approved the final draft.
- Jingle Li conceived and designed the experiments, analyzed the data, prepared figures and/or tables, and approved the final draft.
- Guiyang Chen conceived and designed the experiments, prepared figures and/or tables, and approved the final draft.
- Yu Cao conceived and designed the experiments, analyzed the data, prepared figures and/or tables, and approved the final draft.
- Liying Gong conceived and designed the experiments, analyzed the data, authored or reviewed drafts of the article, and approved the final draft.

Human Ethics

The following information was supplied relating to ethical approvals (*i.e.*, approving body and any reference numbers):

Approval Letter of IRB the Third Xiangya Hospital of Central South University

Clinical Trial Ethics

The following information was supplied relating to ethical approvals (*i.e.*, approving body and any reference numbers):

The ethics committee of the Third Xiangya Hospital of Central South University

Clinical Trial Registration

The following information was supplied regarding Clinical Trial registration:

NCT02888652

Data Availability

The following information was supplied regarding data availability:

The raw measurements are available in the [Supplementary File](#).

Supplemental Information

Supplemental information for this article can be found online at <http://dx.doi.org/10.7717/peerj.17493#supplemental-information>.

REFERENCES

- Akçay A, Nguyen Q, Edelstein CL. 2009. Mediators of inflammation in acute kidney injury. *Mediators of Inflammation* 2009:137072 DOI 10.1155/2009/137072.
- Akin F, Celik O, Altun I, Ayca B, Ozturk D, Satilmis S, Ayaz A, Tasbulak O. 2015. Relation of red cell distribution width to contrast-induced acute kidney injury in patients undergoing a primary percutaneous coronary intervention. *Coronary Artery Disease* 26:289–295 DOI 10.1097/MCA.0000000000000223.
- Antoniades C, Bakogiannis C, Leeson P, Guzik TJ, Zhang MH, Tousoulis D, Antonopoulos AS, Demosthenous M, Marinou K, Hale A, Paschalis A, Psarros C, Triantafyllou C, Bendall J, Casadei B, Stefanadis C, Channon KM. 2011. Rapid, direct effects of statin treatment on arterial redox state and nitric oxide bioavailability in human atherosclerosis via tetrahydrobiopterin-mediated endothelial nitric oxide synthase coupling. *Circulation* 124:335–345 DOI 10.1161/CIRCULATIONAHA.110.985150.
- Antoniades C, Bakogiannis C, Tousoulis D, Reilly S, Zhang MH, Paschalis A, Antonopoulos AS, Demosthenous M, Miliou A, Psarros C, Marinou K, Sfyras N, Economopoulos G, Casadei B, Channon KM, Stefanadis C. 2010. Preoperative atorvastatin treatment in CABG patients rapidly improves vein graft redox state by inhibition of Rac1 and NADPH-oxidase activity. *Circulation* 122:S66–S73 DOI 10.1161/CIRCULATIONAHA.109.927376.
- Ascer E, Bertolami MC, Venturinelli ML, Buccheri V, Souza J, Nicolau JC, Ramires JA, Serrano Jr CV. 2004. Atorvastatin reduces proinflammatory markers in hypercholesterolemic patients. *Atherosclerosis* 177:161–166 DOI 10.1016/j.atherosclerosis.2004.07.003.
- Bartholomew BA, Harjai KJ, Dukkipati S, Boura JA, Yerkey MW, Glazier S, Grines CL, O'Neill WW. 2004. Impact of nephropathy after percutaneous coronary intervention and a method for risk stratification. *The American Journal of Cardiology* 93:1515–1519 DOI 10.1016/j.amjcard.2004.03.008.
- Bulcao C, Ribeiro-Filho FF, Sanudo A, Roberta Ferreira SG. 2007. Effects of simvastatin and metformin on inflammation and insulin resistance in individuals with

- mild metabolic syndrome. *American Journal of Cardiovascular Drugs* 7:219–224 DOI 10.2165/00129784-200707030-00007.
- Caixeta A, Mehran R. 2010.** Evidence-based management of patients undergoing PCI: contrast-induced acute kidney injury. *Catheterization and Cardiovascular Interventions* 75(Supp 1):S15–S20 DOI 10.1002/ccd.22376.
- Collaboration NCDRF. 2015.** Effects of diabetes definition on global surveillance of diabetes prevalence and diagnosis: a pooled analysis of 96 population-based studies with 331 288 participants. *The Lancet. Diabetes & Endocrinology* 3:624–637 DOI 10.1016/S2213-8587(15)00129-1.
- Davenport MS, Perazella MA, Nallamothu BK. 2023.** Contrast-induced acute kidney injury and cardiovascular imaging: danger or distraction? *Circulation* 147:847–849 DOI 10.1161/CIRCULATIONAHA.122.062783.
- Davenport MS, Perazella MA, Yee J, Dillman JR, Fine D, McDonald RJ, Rodby RA, Wang CL, Weinreb JC. 2020.** Use of intravenous iodinated contrast media in patients with kidney disease: consensus statements from the American College of Radiology and the National Kidney Foundation. *Radiology* 294:660–668 DOI 10.1148/radiol.2019192094.
- Demircelik MB, Kurtul A, Ocek H, Cakmak M, Ureyen C, Eryonucu B. 2015.** Association between platelet-to-lymphocyte ratio and contrast-induced nephropathy in patients undergoing percutaneous coronary intervention for acute coronary syndrome. *CardioRenal Medicine* 5:96–104 DOI 10.1159/000371496.
- Finn WF. 2006.** The clinical and renal consequences of contrast-induced nephropathy. *Nephrology Dialysis Transplantation* 21:i2–i10 DOI 10.1093/ndt/gfl213.
- Gao F, Zhou YJ, Zhu X, Wang ZJ, Yang SW, Shen H. 2011.** C-reactive protein and the risk of contrast-induced acute kidney injury in patients undergoing percutaneous coronary intervention. *American Journal of Nephrology* 34:203–210 DOI 10.1159/000329534.
- Goldfarb S, McCullough PA, McDermott J, Gay SB. 2009.** Contrast-induced acute kidney injury: specialty-specific protocols for interventional radiology, diagnostic computed tomography radiology, and interventional cardiology. *Mayo Clinic Proceedings* 84:170–179.
- Gupta R, Gurm HS, Bhatt DL, Chew DP, Ellis SG. 2005.** Renal failure after percutaneous coronary intervention is associated with high mortality. *Catheterization and Cardiovascular Interventions* 64:442–448 DOI 10.1002/ccd.20316.
- Han YL, Zhu GY, Han LX, Hou FX, Huang WJ, Liu HL, Gan JH, Jiang TM, Li XY, Wang W, Ding SF, Jia SB, Shen WF, Wang DM, Sun L, Qiu J, Wang XZ, Li Y, Deng J, Li J, Xu K, Xu B, Mehran R, Huo Y. 2014.** Short-term rosuvastatin therapy for prevention of contrast-induced acute kidney injury in patients with diabetes and chronic kidney disease. *Journal of the American College of Cardiology* 63:62–70 DOI 10.1016/j.jacc.2013.09.017.
- James MT, Ghali WA, Knudtson ML, Ravani P, Tonelli M, Faris P, Pannu N, Manns BJ, Klarenbach SW, Hemmelgam BR, Outcome APP. 2011.** Associations between acute

- kidney injury and cardiovascular and renal outcomes after coronary angiography. *Circulation* **123**:409–416 DOI [10.1161/Circulationaha.110.970160](https://doi.org/10.1161/Circulationaha.110.970160).
- Jarai R, Dangas G, Huber K, Xu K, Brodie BR, Witzenbichler B, Metzger DC, Radke PW, Yu J, Claessen BE, Genereux P, Mehran R, Stone GW. 2012.** B-type natriuretic peptide and risk of contrast-induced acute kidney injury in acute ST-segment-elevation myocardial infarction: a substudy from the HORIZONS-AMI trial. *Circulation: Cardiovascular Interventions* **5**:813–820 DOI [10.1161/CIRCINTERVENTIONS.112.972356](https://doi.org/10.1161/CIRCINTERVENTIONS.112.972356).
- Jia XW, Fu XH, Zhang J, Gu XS, Xue L, Fan WZ, Hao GZ, Jiang YF, Wu WL, Li SQ. 2009.** Comparison of usefulness of simvastatin 20 mg versus 80 mg in preventing contrast-induced nephropathy in patients with acute coronary syndrome undergoing percutaneous coronary intervention. *American Journal of Cardiology* **104**:519–524 DOI [10.1016/j.amjcard.2009.04.014](https://doi.org/10.1016/j.amjcard.2009.04.014).
- Kocas C, Yildiz A, Abaci O, Karaca OS, Firdin N, Dalgic Y, Bostan C, Ersanli M. 2015.** Platelet-to-lymphocyte ratio predicts contrast-induced nephropathy in patients with non-st-segment elevation acute coronary syndrome. *Angiology* **66**:964–968 DOI [10.1177/0003319715578057](https://doi.org/10.1177/0003319715578057).
- Kumar A, Cannon CP. 2009.** Acute coronary syndromes: diagnosis and management, part I. *Mayo Clinic Proceedings* **84**:917–938.
- Kurtul A, Yarlioglu M, Duran M, Murat SN. 2016.** Association of neutrophil-to-lymphocyte ratio with contrast-induced nephropathy in patients with non-ST-elevation acute coronary syndrome treated with percutaneous coronary intervention. *Heart, Lung and Circulation* **25**:683–690 DOI [10.1016/j.hlc.2016.01.007](https://doi.org/10.1016/j.hlc.2016.01.007).
- Kwasa EA, Vinayak S, Armstrong R. 2014.** The role of inflammation in contrast-induced nephropathy. *The British Journal of Radiology* **87**:20130738 DOI [10.1259/bjr.20130738](https://doi.org/10.1259/bjr.20130738).
- Leoncini M, Toso A, Maioli M, Tropeano F, Villani S, Bellandi F. 2014.** Early high-dose rosuvastatin for contrast-induced nephropathy prevention in acute coronary syndrome: results from the PRATO-ACS Study (Protective Effect of Rosuvastatin and Antiplatelet Therapy On contrast-induced acute kidney injury and myocardial damage in patients with Acute Coronary Syndrome). *Journal of the American College of Cardiology* **63**:71–79 DOI [10.1016/j.jacc.2013.04.105](https://doi.org/10.1016/j.jacc.2013.04.105).
- Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D, Grp MDRDS. 1999.** A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. *Annals of Internal Medicine* **130**(6):461–470 DOI [10.7326/0003-4819-130-6-199903160-00002](https://doi.org/10.7326/0003-4819-130-6-199903160-00002).
- Levine GN, Bates ER, Blankenship JC, Bailey SR, Bittl JA, Cercek B, Chambers CE, Ellis SG, Guyton RA, Hollenberg SM, Khot UN, Lange RA, Mauri L, Mehran R, Moussa ID, Mukherjee D, Nallamothu BK, Ting HH. 2011.** 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines and the Society for Cardiovascular Angiography and Interventions. *Circulation* **124**:e574–e651 DOI [10.1161/CIR.0b013e31823ba622](https://doi.org/10.1161/CIR.0b013e31823ba622).

- Liu L, Zhou L, Li W, Chen H, Li H. 2023.** Role of modified hydration for preventing contrast-associated acute kidney injury in patients with ST-segment elevation myocardial infarction after primary percutaneous coronary intervention. *Internal and Emergency Medicine* **18**:67–76 DOI [10.1007/s11739-022-03109-3](https://doi.org/10.1007/s11739-022-03109-3).
- Liu Y, Tan N, Zhou YL, Chen YY, Chen JY, Chen J, Luo JF. 2012.** High-sensitivity C-reactive protein predicts contrast-induced nephropathy after primary percutaneous coronary intervention. *Journal of Nephrology* **25**:332–340.
- Maioli M, Toso A, Leoncini M, Gallopin M, Musilli N, Bellandi F. 2012.** Persistent renal damage after contrast-induced acute kidney injury: incidence, evolution, risk factors, and prognosis. *Circulation* **125**:3099–3107 DOI [10.1161/CIRCULATIONAHA.111.085290](https://doi.org/10.1161/CIRCULATIONAHA.111.085290).
- McCullough PA, Adam A, Becker CR, Davidson C, Lameire N, Stacul F, Tumlin J, Panel CCW. 2006.** Epidemiology and prognostic implications of contrast-induced nephropathy. *American Journal of Cardiology* **98**:5–13 DOI [10.1016/j.amjcard.2006.01.019](https://doi.org/10.1016/j.amjcard.2006.01.019).
- McCullough PA, Choi JP, Feghali GA, Schussler JM, Stoler RM, Vallabahn RC, Mehta A. 2016.** Contrast-induced acute kidney injury. *Journal of the American College of Cardiology* **68**:1465–1473 DOI [10.1016/j.jacc.2016.05.099](https://doi.org/10.1016/j.jacc.2016.05.099).
- McCullough PA, Wolyn R, Rocher LL, Levin RN, O'Neill WW. 1997.** Acute renal failure after coronary intervention: incidence, risk factors, and relationship to mortality. *The American Journal of Medicine* **103**:368–375 DOI [10.1016/S0002-9343\(97\)00150-2](https://doi.org/10.1016/S0002-9343(97)00150-2).
- Mehran R, Aymong ED, Nikolsky E, Lasic Z, Iakovou I, Fahy M, Mintz GS, Lansky AJ, Moses JW, Stone GW, Leon MB, Dangas G. 2004.** A simple risk score for prediction of contrast-induced nephropathy after percutaneous coronary intervention: development and initial validation. *Journal of the American College of Cardiology* **44**:1393–1399 DOI [10.1016/j.jacc.2004.06.068](https://doi.org/10.1016/j.jacc.2004.06.068).
- Murat SN, Kurtul A, Yarlioglu M. 2015.** Impact of serum albumin levels on contrast-induced acute kidney injury in patients with acute coronary syndromes treated with percutaneous coronary intervention. *Angiology* **66**:732–737 DOI [10.1177/0003319714551979](https://doi.org/10.1177/0003319714551979).
- Van de Ree MA, Huisman MV, Princen HMG, Meinders AE, Kluft C, Grp D-S. 2003.** Strong decrease of high sensitivity C-reactive protein with high-dose atorvastatin in patients with type 2 diabetes mellitus. *Atherosclerosis* **166**:129–135 DOI [10.1016/S0021-9150\(02\)00316-7](https://doi.org/10.1016/S0021-9150(02)00316-7).
- Rihal CS, Textor SC, Grill DE, Berger PB, Ting HH, Best PJ, Singh M, Bell MR, Barsness GW, Mathew V, Garratt KN, Holmes Jr DR. 2002.** Incidence and prognostic importance of acute renal failure after percutaneous coronary intervention. *Circulation* **105**:2259–2264 DOI [10.1161/01.CIR.0000016043.87291.33](https://doi.org/10.1161/01.CIR.0000016043.87291.33).
- Seeliger E, Sendeski M, Rihal CS, Persson PB. 2012.** Contrast-induced kidney injury: mechanisms, risk factors, and prevention. *European Heart Journal* **33**:2007–2015 DOI [10.1093/eurheartj/ehr494](https://doi.org/10.1093/eurheartj/ehr494).

- Sendeski MM. 2011.** Pathophysiology of renal tissue damage by iodinated contrast media. *Clinical and Experimental Pharmacology and Physiology* **38**:292–299 DOI [10.1111/j.1440-1681.2011.05503.x](https://doi.org/10.1111/j.1440-1681.2011.05503.x).
- Shacham Y, Leshem-Rubinow E, Steinvil A, Keren G, Roth A, Arbel Y. 2015.** High sensitive C-reactive protein and the risk of acute kidney injury among ST elevation myocardial infarction patients undergoing primary percutaneous intervention. *Clinical and Experimental Nephrology* **19**:838–843 DOI [10.1007/s10157-014-1071-1](https://doi.org/10.1007/s10157-014-1071-1).
- Shah B, Baber U, Pocock SJ, Krucoff MW, Ariti C, Gibson CM, Steg PG, Weisz G, Witzeneichler B, Henry TD, Kini AS, Stuckey T, Cohen DJ, Iakovou I, Dangas G, Aquino MB, Sartori S, Chieffo A, Moliterno DJ, Colombo A, Mehran R. 2017.** White blood cell count and major adverse cardiovascular events after percutaneous coronary intervention in the contemporary era: insights from the PARIS Study (patterns of non-adherence to anti-platelet regimens in stented patients registry). *Circulation: Cardiovascular Interventions* **10**(9):e004981 DOI [10.1161/CIRCINTERVENTIONS.117.004981](https://doi.org/10.1161/CIRCINTERVENTIONS.117.004981).
- Stacul F, Van der Molen AJ, Reimer P, Webb JA, Thomsen HS, Morcos SK, Almen T, Aspelin P, Bellin MF, Clement O, Heinz-Peer G, Contrast Media Safety Committee of European Society of Urogenital R. 2011.** Contrast induced nephropathy: updated ESUR Contrast Media Safety Committee guidelines. *European Radiology* **21**:2527–2541 DOI [10.1007/s00330-011-2225-0](https://doi.org/10.1007/s00330-011-2225-0).
- Sun XP, Li J, Zhu WW, Li DB, Chen H, Li HW, Chen WM, Hua Q. 2018.** Platelet to lymphocyte ratio predicts contrast-induced nephropathy in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. *Angiology* **69**:71–78 DOI [10.1177/0003319717707410](https://doi.org/10.1177/0003319717707410).
- Thomsen HS. 2003.** Guidelines for contrast media from the European Society of Urogenital Radiology. *American Journal of Roentgenology* **181**:1463–1471 DOI [10.2214/ajr.181.6.1811463](https://doi.org/10.2214/ajr.181.6.1811463).
- Toso A, Leoncini M, Maioli M, Tropeano F, Bellandi F. 2014.** Pharmacologic prophylaxis for contrast-induced acute kidney injury. *Interventional Cardiology Clinics* **3**:405–419 DOI [10.1016/j.iccl.2014.03.010](https://doi.org/10.1016/j.iccl.2014.03.010).
- Wi J, Ko YG, Shin DH, Kim JS, Kim BK, Choi D, Ha JW, Hong MK, Jang Y. 2013.** Prediction of Contrast-induced nephropathy with persistent renal dysfunction and adverse long-term outcomes in patients with acute myocardial infarction using the mehran risk score. *Clinical Cardiology* **36**:46–53 DOI [10.1002/clc.22060](https://doi.org/10.1002/clc.22060).
- Yuan Y, Qiu H, Hu X, Luo T, Gao X, Zhao X, Zhang J, Wu Y, Qiao S, Yang Y, Gao R. 2017.** Predictive value of inflammatory factors on contrast-induced acute kidney injury in patients who underwent an emergency percutaneous coronary intervention. *Clinical Cardiology* **40**:719–725 DOI [10.1002/clc.22722](https://doi.org/10.1002/clc.22722).