Effects of Duration of Using Intraaortic Balloon Pump on Renal Function and Clinical Outcome

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Abstract

Objective:To integrate the effects of duration of using intraaortic balloon pump (IABP) on renal function, major adverse cardiac events (MACEs) and all-cause mortality in patients with acute myocardial infarction (AMI) complicating pump failure. Methods:Between March 2017 and June 2018, a retrospective study enrolled 306 patients with AMI complicating pump failure who underwent coronary artery angiography (CAG) or percutaneous coronary intervention (PCI) was conducted. Patients were divided into the duration [?]4 days and the duration¿4 days in basis of median the IABP duration. We compared the renal function parameters at the three time section of IABP implantation between two groups. Analysis of factors of contrast-induced nephropathy (CIN), 12-month MACEs and all-cause mortality were also performed. Results:There were 146 patients in IABP duration [?]4 days and 92 patients in IABP duration $>$ 4 days. Renal function was only correlated with IABP duration instead of timing of IABP implantation. On multivariate analysis, CIN risk increased by 81.2% (RR= 1.812, 95%CI, 1.167–3.763) for every 100mL increment of contrast agent. Hematocrit, blood platelet, IABP use $>$4 days were significantly inversely associated with CIN. Cox-regression analysis suggested that IABP duration was not significantly correlated with the incidence of 12-month MACEs and all-cause mortality. Conclusion:Longer duration of IABP implantation was beneficial to renal function, but was not significantly correlated with the incidence of 12-month MACEs and all-cause mortality in patients with AMI complicating pump failure. Patients undergoing PCI or CABG should notice that the potential damage of high dose of contrast agents on the renal function.

Introduction

Pump failure was a fatal comorbidity of acute myocardial infarction (AMI), which consists of cardiac failure and cardiogenic shock (CS). It was reported that the incidence of pump failure was from 6.5% to 8.3%[1]. Over the past few decades, the percutaneous coronary intervention (PCI) as a invasive treatment has been increasingly prominent. Howerver, mortality of AMI complicating pump failure was not obviously declining with emergency revascularization.

Intraaortic balloon pump (IABP) was an important ventricular support device for the treatment of heart diseases. The use of IABP contributed to improve peripheral blood circulation, as well as, to stabilize circulatory hemodynamics and increase coronary artery blood perfusion[2]. Especially when severe hypotension and acute cardiac insufficiency occurred in emergency during PCI, IABP adjuvant therapy significantly improved the hemodynamic disturbance[3].

The sharp decrease of cardiac output and blood pressure plummets resulted in renal perfusion insufficiency, and continuous ischemia and hypoxia in the kidney. Energy metabolism disorder in renal tubular epithelial cells made the acute tubular necrosis happened. The necrotic renal tubule epithelium fell off that blocked the tubule, which affectd the glomerular filtration rate [4]. In patients with AMI complicating with pump failure, the incidence of acute kidney injury (AKI) was as high as 50%, and the mortality rates of patients

with AMI once combined with AKI were significantly increased[5,6]. However, the effects of duration of using IABP on renal function have been rarely reported, and need to be confirmed by further studies.

The purpose of this study was to observe the effect of IABP treatment on renal function and prognosis in patients with AMI complicating pump failure at different times, and to explore the optimal therapeutic duration of IABP treatment in patients with AMI combined with pump failure, so as to provide scientific basis for clinical treatment of patients with AMI complicated with pump failure.

Materials and methods

Study objectives

Between March 2017 and June 2018, a retrospective study enrolled 306 patients with AMI complicating pump failure who undergo coronary artery angiography (CAG) or PCI was conducted. Patients were divided into the duration [?]4 days and the duration¿4 days in the basis of median of the IABP duration. This study was approved by the hospital research ethics committee.

Patients of [?]18 years diagnosed as with AMI (STEMI or NSTEMI) complicating pump failure were eligible for the study. Diagnostic criteria for AMI, referring to the 2015 European Society of Cardiology guidelines for the management of non-ST-segment elevation acute coronary syndromes (ACS)[7] ,were established as follows: An increase in cardiac biomarkers (e.g. serum troponin) above 99% of the upper limit of reference values plus two or more of the following evidence of myocardial ischemia including (1) clinical symptoms of myocardial ischemia; (2) new electrocardiographic changes of myocardial ischemia (i.e. new ST-segment changes or new left bundle-branch block); (3)new pathological Q waves appearing in electrocardiogram; (4) radiographic evidence of new cardiac function loss or segmental ventricular motion abnormalities.

The diagnostic criteria were required for pump failure as follows: (1) AMI associated with acute pulmonary edema performance, or both audible lung sounds (dry or wet) with a range of $>$ 50% of the lung field; (2) Systolic blood pressure (SBP)$<$ 90mmHg and/or diastolic blood pressure (DBP) $<$ 60mmHg, or mean arterial pressure (MBP) $<$70mmHg; (3) peripheral circulatory failure such as oliguria, anorexia limbs, etc.

Exclusion criteria included: (1) statin intake within 1 month; (2) contrast agent using within 2 weeks; (3) severe renal dysfunction (estimated glomerular filtration rate [eGFR] $<$30 mL/min/1.73 m^2) (4) any mechanical complications of AMI such as left ventricular free wall rupture, interventricular septum perforation, papillary muscle rupture; (5) severe aortic valve insufficiency, abdominal aorta or aortic aneurysm, aortic dissection.

Study Methods

All patients were treated with PCI or CAG. IABP implantation was performed before CAG or PCI, or when SBP was less than 90mmHg after the emergency PCI.

CAG and PCI Method

Using Siemens AXIom-Artis DTA from Germany and GE Innova 2000 angiography system from the United States, selective CAG was performed by Judkins method from the femoral artery or radial artery pathways respectively. Diseased vessels were clarified by multi-angle imaging. GE Conduct CAG image analysis was conducted by Centricity AI 1000-GE Mnet (Version 4.2.7.05) and relevant data of interventional therapy were recorded.

IABP implantation

The patients were punctured in the right or left femoral artery, which were placed a 40mL IABP catheter through the 8F sheath with air drained in the 2cm below the opening of the left subclavian artery. At the same time, the catheter was connected to the IABP (IABP System 98; Datascope; Fairfield, NJ) machine. The ratio of counter pulsation frequency and heart rate ranged from 1:1 to 1:2. The IABP might be removed for those with urine volume$>$ 30 mL/h, heart rate $<$ 100 times /min, ventricular prephase contraction $<$ 6 times /min.

Data Collection and Definition of Variables

Baseline variables were collected including age, gender, weight, smoking history, blood pressure, heart rate, several cardiovascular risk factors such as hypertension, diabetes mellitus, dyslipidemia, history of CABG or PCI, cerebral infarction and old myocardial infarction (OMI). In addition, left ventricular ejection fraction (LVEF), serum creatinine (SCr), chronic renal insufficiency, cardiac shock (CS), lipid metabolism index (triglycerides (TG), total cholesterol (T-CHO), low density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C)), blood routine examination (hemoglobin (Hgb), red blood cells (RBC), white blood cells (WBC), blood platelet (PLT), hematocrit (HCT)), uric acid (UA) were immediately measured when patients admitted to hospital, and the results were recorded.

In this study, the definitions of CIN were shown as follows: the absolute value of SCr increased by 44.2 mol /L, or by more than 25%, within 24 ˜ 72 h after using the contrast agent (0.5 mg /dL). Hypertension was defined as SBP [?]140 mmHg and/or DBP [?]90 mmHg. Diabetes mellitus was defined as fasting blood glucose [?]7.0 mmol /L. eGFR was estimated as follows: eGFR =186×SCr-1.154×age-0.203(Female:x0.742)。

Statistical analysis

The above-mentioned variables were expressed as mean ± standard deviation (SDs), median (range) or number (percentage) of each group according to the distribution and type of data, which were compared by Student's t-test, Mann-Whitney test, chi-square test or Fisher exact test, respectively. Hazard ratios (HRs) were presented with their 95% confidence intervals (CIs). Kaplan–Meier curves were used to estimate the clinic outcomes and the significant differences between two groups, which were compared with the log-rank test. The effects of risks on CIN were identifed by log-binomial regression models with forward stepwise selection. Statistical analyses were carried out using software programs (SPSS for Windows, version 22.0; IBM Corporation, Armonk, NY, USA). All tests were two-tailed and P -value of <0.05 was supposed to be statistically signifcant.

Results

Comparisons of characteristics between two groups

There were 146 patients in IABP duration [?]4 days and 92 patients in IABP duration > 4 days. Comparisons of characteristics between the two groups were conducted and the results were presented in**Table 1** . The values of age, LVEF, LDL-C, SPB, DPB were significantly more of patients in IABP duration[?]4 days than IABP duration > 4 days. The values of SCr, WBC, RBC, UA, and rates of cardiac shock, Killip class (more than II),STEMI, heart rate of patients in IABP duration [?] 4 days were significantly lower than the IABP duration > 4 days. Patients belonging to IABP duration [?]4 days showed a lower prevalence of male and cerebral infarction as compared to the IABP duration > 4 days.

Renal function parameters at different times between two groups

As shown in **Table 2** , both for SCr or eGFR, there was no statistically significant difference among the before IABP implantation, three days after implantation, and after IABP removing. However, as for before IABP implantation group and three days after implantation group, the values of SCr and eGFR were significantly lower in the IABP duration [?]4 days group compared to the IABP duration > 4 days. Significant differences of eGFR between the two groups were also found after IABP removing. It demonstrated that renal function was only correlated with IABP duration instead of timing of IABP implantation.

Analysis of risk factors of contrast-induced nephropathy

There were ten variables significantly correlated with CIN in univariate analyses. Subsequently, forward stepwise selection in multivariate log-binomial regression modeling showed that the following four variables were independent risk factors for CIN: HCT, PLT, IABP durations, dosage of contrast agent. (**Table 3**). On multivariate analysis, HCT (HR, 0.913; 95% CI, 0.848-0.984; P = 0.017), PLT (HR, 0.988; 95% CI, 0.980-0.995; P = 0.002), IABP use >4 days (HR, 0.535; 95% CI, 0.356-0.712; P = 0.012), dosage of contrast agent (HR, 1.812; 95% CI, 1.167-3.763; P <0.001) were each independently associated with CIN.

Clinical outcomes of following up for 12 months

There was no signifcant difference in overall MACEs and all-cause mortality between the IABP duration [?]4 days group as compared with the IABP duration > 4 days group at 12-month follow up. No significant differences were also found in the prevalence of recurrent MI, CABG, repeated PCI, or cardiac death between the two groups (**Table 4**). The corresponding Kaplan–Meier curves for overall, MACE-free, cardiac survival were established (**Fig 2A, 2B and 2C**). The log-rank test identified that MACEs, all-cause mortality and cardiac death were not significantly associated with IABP duration. Cox-regression analysis suggested that IABP duration was not significantly correlated with the incidence of 12-month MACEs (**data not shown**).

Discussions

At present, the pathophysiological mechanism of CIN was not fully clear, which might be involved by multiple factors, including the direct toxicity of contrast agent on the kidney, renal hemodynamic changes and oxidative stress reaction, inflammation, and renal tubular obstruction, etc[8-10]. Contrast agent cloud induce that vacuoles formation, intracellular Ca^{2+} overload and adenosine triphosphate decreased in renal tubular epithelial cells, thus inducing apoptosis. There were two-phase effects of contrast agent on renal hemodynamics. Firstly, the application of contrast agent lead to renal vascular dilatation that mediators were consequently released. For example, endoderin stimulated progressive and continuous contraction of renal vessels, thereby leading to eGFR declining[11]. The generation of reactive oxygen species and oxygen free radicals increased dramatically. After binding with some amino acid residues of tissue proteins, proteins were easy to be hydrolyzed, polymerized and cross-linked, which affected the structure and function of cells and lead to oxidative stress reaction. Secondly, when contrast agents were filtered through the glomerulus into the renal tubules, they were viscous as a result of the absence of water in the tubules, which might lead to tubules obstruction and aggravate renal damage[12]. In this study, results showed that dosage of contrast agent had a positive association with CIN, which was similar to the previous studies[13,14].

Studies had shown that the use of IABP as adjuvant therapy of PCI could effectively improve renal blood perfusion and have protective effects on renal function, which markedly reduced the incidence of postoperative renal insufficiency[15,16]. In this study, we found that the values of eGFR were significantly lower in the IABP duration [?]4 days group as compared to the IABP duration>4 days group in the three time section of IABP implantation. However, there were no significant differences in the values of eGFR, SCr among three time section of IABP implantation in any group. It manifested that IABP contributed to increase the patient's urine output and improve serum creatinine level as soon as possible, which were conducive to reduce the occurrence of renal insufficiency and protect the patient's kidney function.

AMI complicating pump failure was common in patients that areas of myocardial infarction accounted for more than 40% of the left ventricle, which significantly influenced cardiac pumping function. The aggravation of left ventricular filling pressure strengthened the myocardial oxygen consumption. Eventually, interaction of myocardial hypoxia, pump failure and myocardial ischemia necrosis developed into cardiac shock[17]. IABP using could alleviate the burden of the left ventricle and improve cardiac function through reducing left ventricular ejection resistance. Studies have shown that IABP enhanced the pulsation of coronary arteries and provided pulsed blood flow, which were beneficial to reduce the occurrence of acute occlusion and no reflow after PCI treatment[18].

In this study, the duration of using IABP was not obviously related to incidence of 12-month MACEs and all-cause mortality. This reason might be explained that the patients with AMI complicating pump failure was in a state of severe ischemia, hypoxia, or even necrosis. Consequently, the perfusion of important organs suffered serious damage. At this time, IABP therapeutic therapy was often ineffective. Especially, elderly patients with AMI complicating CS were more likely to be complicated by vital organ dysfunction. There were more complications and higher mortality rates when they underwent IABP adjuvant therapy. A study indicated that the clinical implications were significantly increased with IABP using for more than two days[19].

Several limitations should be recognized in this study. First, in consideration of patient safety, the control group without IABP treatment was not set up. Secondly, due to the lack of long-term follow-up data, the follow-up time could be appropriately extended and the long-term prognosis of patients could be further analyzed in detail. Finally, this study was a single-center, retrospective study, and the sample size was small, so the results of this study should be interpreted with caution.

In conclusion, longer duration of IABP implantation was beneficial to renal function, but was not significantly correlated with the incidence of 12-month MACEs and all-cause mortality in patients with AMI complicating pump failure. Patients undergoing PCI or CABG should notice that the potential damage of high dose of contrast agents on the renal function.

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Informed consent All participants provided informed consent, and approval to conduct the survey.

Ethical approval This study was granted by the Research Ethics Committee of University of Science and Technology of China.

Conflict of interest Statement The authors declare that they have no conflict of interest.

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Figure Legend:

Fig 1. Flow diagram of the study.

Fig 2 . The corresponding Kaplan–Meier curves for overall, MACE-free, cardiac survival curves in enrolled patients.

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