Remote ischemic preconditioning reduces contrast-induced acute kidney injury in patients with ST-elevation myocardial infarction: a randomized controlled trial

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ABSTRACT

Background: Contrast medium-induced acute kidney injury (CI-AKI) is a cardiovascular complication after myocardial infarction treated with emergency percutaneous coronary intervention. The aim of this randomized, sham-controlled trial was to evaluate the impact of remote ischemic preconditioning (RIPC) on CI-AKI in patients with ST-elevation myocardial infarction who received emergency primary percutaneous coronary intervention.

Methods and Results: Patients with a suspected ST-elevation myocardial infarction were randomly assigned at a 1:1 ratio to receive percutaneous coronary intervention either with (n = 63) or without (n = 62) RIPC (intermittent arm ischemia through three cycles of 5 min of inflation and 5 min of deflation of a blood pressure cuff). A total of 47 RIPC patients and 47 control patients met all study criteria. The primary endpoint was the incidence of CI-AKI, which was defined as an increase in serum creatinine > 0.5 mg/dL or > 25% over the baseline value 48–72 hours after administration of contrast medium. The incidence of CI-AKI was 10% (n = 5) in the RIPC group and 36% (n = 17) in the control group ($p = 0.003$). The odds ratio of CI-AKI in patients who received RIPC was 0.18 (95% confidence interval: 0.05–0.64; $p = 0.008$).

Conclusions: In patients with ST-elevation myocardial infarction, RIPC before percutaneous coronary intervention reduced the incidence of CI-AKI.

Keywords:

Myocardial infarction

Contrast media

Renal failure

Percutaneous coronary intervention

1. Introduction

ST-elevation myocardial infarction (STEMI) is a leading cause of mortality and morbidity. The reduction of myocardial injury is the mainstay of therapy for STEMI and is best achieved by early reperfusion through emergency percutaneous coronary intervention (PCI) [1]. Patients receiving such treatment achieve infarct-related vessel patency and reperfusion, but risk sustaining clinically significant myocardial infarction, even when the procedure is done soon after symptom onset [2]. Cardiac complications after emergency PCI with STEMI, such as heart failure and cardiac rupture, are potentially lethal and lead to an impaired prognosis [3]. Additionally, contrast medium-induced acute kidney injury (CI-AKI), a cardiovascular complication after myocardial infarction, is a frequent complication of emergency PCI and is associated with an increased mortality rate and persistent renal dysfunction [4, 5].

Remote ischemic preconditioning (RIPC) is the phenomenon in which transient nonlethal ischemia and reperfusion applied to one organ or tissue protects another organ or tissue from a subsequent episode of lethal ischemia and reperfusion [6]. A previous study showed that RIPC applied before PCI in patients with evolving STEMI was able to increase myocardial salvage [7]. Additionally, a recent study demonstrated that RIPC performed before administration of contrast medium prevented CI-AKI in moderate- to high-risk patients [8-10]. The role of RIPC in reducing CI-AKI in STEMI patients undergoing emergency PCI is not clear. In this prospective, randomized, sham-controlled pilot study, we evaluated the impact of RIPC on CI-AKI in patients with STEMI who received emergency primary PCI, and hypothesized that RIPC applied before PCI would reduce the incidence of CI-AKI in patients with STEMI.

2. Methods

This study was a prospective, single-blind, multicenter, randomized, sham-controlled parallel-group study conducted from 2012 to 2013 at Saiseikai Imabari Hospital, Ehime Prefectural Central Hospital, and Okayama University Hospital, in Japan. The study was approved by the ethics committees of all three hospitals, and written informed consent was obtained from all participants before beginning the protocol. This study was conducted according to the principles expressed in the Declaration of Helsinki. The study is registered at UMIN Clinical Trials Registry (UMIN000012578).

2.1. Patient selection and randomization

Eligible patients were aged 20 years or older; presented with chest pain within 24 hours of onset; had ST-segment elevation of > 0.1 mV in two contiguous leads in the first electrocardiogram recorded on the scene; and were clinically assigned to receive primary PCI. Exclusion criteria were: left bundle branch block; previous coronary bypass surgery; severe heart failure requiring percutaneous cardiopulmonary support; and severe chronic kidney disease requiring dialysis or continuous hemodiafiltration. Patients who did not meet inclusion criteria were excluded either immediately on arrival at the hospital or when biochemical ischemic markers failed to confirm a diagnosis of myocardial infarction. Patients were excluded either when they fulfilled the definition of exclusion or when biochemical markers failed to confirm the diagnosis of myocardial infarction.

Patients were randomly assigned to receive standard primary PCI (control group) or standard primary PCI plus RIPC through intermittent upper-arm ischemia (RIPC group). Patients

were identified and randomized on arrival at any of the three participating hospitals soon after they were screened for eligibility. Randomization was stratified by sex and age (< 70 versus ≥ 70 years). Patients were randomized 1:1 with computer-generated block randomization.

2.2 Procedures

In the RIPC group, RIPC was initiated by medical staff at the hospital immediately after randomization and consisted of three cycles of ischemia/reperfusion of the upper arm achieved by 5 min cuff inflation at 200 mmHg followed by 5 min of complete cuff deflation. The device used to perform RIPC was an automated continuous blood-pressure device (FB-270; Fukuda Denshi, Tokyo, Japan) that had been modified to perform the three cycles of inflation and deflation automatically. If there was insufficient time to complete three cycles of inflation and deflation before entering the catheter laboratory, the RIPC procedure continued before reperfusion was achieved. Control patients had an uninflated cuff placed on the right upper arm for 30 minutes. All patients received standard care according to established clinical practice guidelines. Before PCI, all patients were treated with 200 mg aspirin orally, 300 mg clopidogrel orally, and 0.1 mg/kg/h continuous injection of nicorandil intravenously. After PCI, patients received a lifelong prescription for 100 mg aspirin and 75 mg clopidogrel daily. The hydration protocol involved continuous intravenous infusion of normal saline solution at a dose of 1 mL/kg of body weight per hour (reduced to 0.5 mL/kg of body weight per hour in patients with heart failure or fluid overload) beginning before PCI and continuing for 24 h after PCI. All patients received 0.1 mg/kg/h continuous injection of nicorandil for at least 8 hours after primary PCI [11]. Coronary angiographic measurements were made immediately before revascularization using

standard techniques. At each hospital, all measurements were made by experienced individuals blinded to treatment assignment and clinical data. The choice of materials was left to the operators, with the exception of the radiographic contrast medium, which was a nonionic, low-osmolar solution in all cases.

2.3. Primary and secondary endpoints

The prespecified primary endpoint was incidence of CI-AKI. CI-AKI was defined as an increase in serum creatinine > 0.5 mg/dL from the baseline value or a relative increase of > 25% of the baseline value 48–72 hours after injection of contrast medium (the maximum measured concentration of creatinine during this 24-hour period was used). Prespecified secondary endpoints were 1) maximum reduction in estimated glomerular filtration rate (eGFR), calculated, using the equation for modification of the diet in a renal study of Japanese individuals recommended by the Japanese Society of Nephrology, as: eGFR ($mL \cdot min^{-1} \cdot 1.73\ m^{-2}$) = $194 \times [\text{serum creatine}]^{-1.094} \times [\text{age}]^{-0.287} \times [0.739 \text{ if female}]$ in the 48 hours after PCI; maximum change in serum creatinine from baseline in the 48 hours after PCI; infarct size estimated by peak creatine kinase (CK); left ventricular ejection fraction 2 weeks after PCI; the incidence of sustained ventricular tachycardia or ventricular fibrillation within 24 hours after PCI; and the incidence of major adverse cardiac and cerebral events (MACCE) in the 30 days after PCI. These included hospital admissions with unstable angina or acute coronary syndrome, heart failure, cardiac rupture, cardiac death, stroke, and transient ischemic attack. Patients were followed by telephone on day 30 after PCI. Echocardiography was performed with the Vivid 7 cardiovascular ultrasound system (GE Healthcare, Milwaukee, WI, USA). LV ejection fraction was measured

according to the recommendations of the American Society of Echocardiography [12]. The personnel involved in data collection and handling were blinded to group assignments. Clinical endpoints were blindly adjudicated by two investigators.

2.4. Statistical analysis

At the time of study design, limited clinical data were available for estimation of sample size [[10]]. The sample size was determined on the basis of the primary outcome, incidence of CI-AKI. We assumed that incidence of CI-AKI to be 30% and that RIPC would reduce the prevalence of CI-AKI by 10%; therefore, 94 patients were recruited into the study to enable such a reduction to be detected (power 90%, $\alpha = 0.05$).

Intention-to-treat analysis of patients fulfilling inclusion criteria was performed. Continuous data are presented as mean ± SD and categorical data are presented as frequencies. Continuous variables were compared across groups (control, RIPC) using paired and unpaired Student's *t* tests. Categorical variables were compared across groups using chi-square statistics and Fisher's exact test. Pre-procedural estimated risk of CI-AKI was calculated using the Mehran Contrast-Induced Nephropathy (CIN) risk score [13]. A two-step analysis was used to identify the independent predictors of CI-AKI. First, a univariate analysis was used to identify the clinical, angiographic, or procedural risk factors for CI-AKI. Continuous variables were transformed to binary data according to the median value, with 1 indicating the presence of assumed risk factors and 0 otherwise. Second, univariate predictors with $p < 0.05$ were entered into a multivariate logistic regression model. The odds ratios (ORs) and 95% confidence intervals (CIs) from the final multivariate model are presented. Statistical significance was accepted for all *p*

values < 0.05.

3. Results

3.1. Study flow and patient characteristics

A flow diagram is shown in Fig. 1. One hundred twenty-five STEMI patients were randomized to receive RIPC before PCI (n = 63) or primary PCI alone (n = 62). Twenty-nine patients (15 in the RIPC group and 14 in the control group) were excluded because of no enzymatic evidence of infarction (n = 13), greater than 24-hour symptom-to-balloon time (n = 5), severe heart failure requiring percutaneous cardiopulmonary support (n = 8), receiving hemodialysis (n = 3), and withdrawal of informed consent (n = 2). Thus, 47 patients in the RIPC group and 47 patients in the control group met inclusion criteria and formed the study population for the analysis.

Baseline characteristics of all patients and those who met inclusion criteria are shown in Table 1. In patients with patients who met inclusion criteria, mean baseline serum creatinine value, eGFR, and Mehran CIN risk score were also not significantly different in the two groups (for RIPC and control, respectively: serum creatinine, 0.82 ± 0.21 versus 0.87 ± 0.44 mg/dL; eGFR, 73 ± 20 versus 79 ± 33 mL/min/1.73m^2; Mehran CIN risk score, 7.8 ± 6.0 versus 7.4 ± 5.7). The amount of contrast medium in patients with patients who met inclusion criteria was also similar in the two groups (177 ± 53 versus 199 ± 87 mL for RIPC and control, respectively; $p = 0.08$). The time from completion of RIPC to injection of contrast medium was 16.9 ± 15.9 min. RIPC was successfully completed without complications in 47 patients. There

were no major PCI-related complications (death or urgent revascularization within the first 24 hours) in either group. Angiographic parameters were similar between the two groups (Table 2). There were no significant differences in the infarct-related artery, Thrombolysis in Myocardial Infarction (TIMI) flow grade, symptom-to-balloon time, and intra-aortic balloon pump (IABP) support. Concomitant medications between completion of RIPC and the primary endpoint were similar between groups (Table 3).

3.2. Primary endpoint

The incidence of CI-AKI after PCI was lower in the RIPC group (n = 5 patients, 10%) than in the control group (n = 17 patients, 36%; $p = 0.003$; Fig. 2A). Twenty-nine factors potentially associated with CI-AKI were analyzed by univariate analysis. Continuous variables were converted to binary data according to median value (Table 4). Two factors (age > 68 years and left anterior descending artery as the culprit artery) were positive predictors of CI-AKI, and four factors (male, current smoker, 50% or more ST-segment resolution and RIPC) were negative predictors of CI-AKI (Table 4). These six factors were entered into a .multivariate logistic regression model, which revealed that RIPC (OR: 0.40; 95% CI: 0.05 to 0.64; $p = 0.008$) and left anterior descending artery as culprit artery (OR: 3.50; 95% CI: 1.08 to 11.31; $p = 0.03$) were significant predictors of CI-AKI (Table 4).

3.3. Secondary endpoints

The maximum decrease in eGFR was significantly greater in the control group than in

the RIPC group (10.2 ± 17.1 versus 0.17 ± 16.9 mL/min/1.73m^2, respectively; $p = 0.003$; Fig. 2B). The maximum change in serum creatinine tended to be greater in the control group than in the RIPC group (0.15 ± 0.31 versus 0.03 ± 0.26 mg/dl; $p = 0.06$). Fig. 2C shows the serial change in serum creatinine. Serum creatinine in the control group was significantly higher than that in the RIPC group 48–72 hours after contrast injection (1.03 ± 0.61 versus 0.81 ± 0.21 mg/dL; $p = 0.02$).

Table 5 shows other secondary outcomes. Peak CK was significantly higher in the control group than in the RIPC group (3,653 ± 2,894 versus 2,648 ± 1,926 IU/L; $p = 0.04$). There was no difference in left ventricular ejection fraction 2 weeks after PCI between the control group and the RIPC group. The incidence of ventricular sustained tachycardia or ventricular fibrillation within 24 hours after PCI was significantly lower in the RIPC group (one patient, 2%) than that in the control group (seven patients, 14%; $p = 0.01$). The incidence of MACCE in the RIPC group (two patients, 4%) tended to be lower than that in the control group (seven patients, 14%), but the difference was not statistically significant ($p = 0.07$). The MACCE in the RIPC group were severe heart failure (n = 1) and ischemic stroke (n = 1), and in the control group were severe heart failure (n = 3), left ventricular perforation (n = 1), death due to refractory heart failure (n = 2), and death due to heart rupture (n = 1).

4. Discussion

The main finding of this prospective, multicenter, randomized study was that RIPC induced by intermittent upper-arm ischemia before emergency PCI dramatically reduced the incidence of CI-AKI in patients with STEMI. Multivariate logistic analysis revealed that this

protective effect was independent of other risk factors. Additionally, the reduction in CI-AKI was accompanied by a reduction in infarct size and dysrhythmic events within 24 hours after PCI.

To date, there is no effective prophylactic drug regimen to prevent CI-AKI. Atrial natriuretic peptide, dopamine, fenoldopam, furosemide, mannitol, aminophylline, captopril, and calcium-channel blockers have been reported to be ineffective at reducing the incidence of CI-AKI [14-17]. The effect of *N*-acetylcysteine remains controversial. Initial studies showed that *N*-acetylcysteine was effective at preventing CI-AKI [18**]**; however, subsequent larger trials failed to demonstrate any benefit [19, 20]. RIPC has been reported to decrease the incidence of myocardial injury during cardiac surgery [9, 21] and PCI [22] and to reduce the incidence of both myocardial injury and renal injury during endovascular surgery [23] and surgical repair of abdominal aortic aneurysm [24]. Furthermore, a recent study showed that RIPC before PCI attenuated CIN in patients undergoing elective coronary angiography [10]. Consistent with these results, our study clearly demonstrated a nephroprotective effect of RIPC in STEMI patients who underwent PCI. RIPC can be applied easily and without safety concerns if it is performed appropriately. Given the results of the present study, RIPC before PCI may be considered for the prevention of CI-AKI in patients with STEMI.

CI-AKI is a frequent and serious complication after coronary angiography and is an independent predictor of mortality in patients with coronary artery disease [4, 5]. Mehran et al. [13] developed a system of risk stratification to predict the risk of CIN in patients undergoing elective coronary angiography. This risk-stratification score includes eight clinical and procedural variables and is divided into four risk classes: low risk (score < 5), moderate risk (6–10), high risk (11–15), and very high risk (≥16). In this study, the mean score was 7 in both groups, indicating that our study population was at moderate risk of developing CI-AKI. Indeed, the

CI-AKI incidence of 35% in the control group is within the reported range [25] and corresponds to the incidence predicted by Mehran et al. [13].

In this study, the risk of CI-AKI in patients with STEMI was associated with RIPC and left anterior descending artery as the culprit artery. The number of the Mehran risk-score points assigned for a hemodynamic status such as hypotension, use of the intra-aortic balloon pump, or chronic heart failure was higher than the number of points assigned for level of renal function and volume of contrast medium in patients undergoing elective coronary angiography. Our results indicate that the risk of CI-AKI in STEMI patients undergoing emergency PCI may be associated with hemodynamic status.

Despite its potential clinical significance, the precise pathophysiological mechanisms of the action of RIPC on CI-AKI have not yet been elucidated. The pathogenesis of CI-AKI is multifactorial and involves vascular, hemodynamic, and tubular factors. The most common theory of pathophysiology of CI-AKI is the induction of renal ischemic injury, possibly caused by iodinated contrast medium-induced reduction in renal blood flow and oxygen free-radical-mediated direct tubular toxicity [22]. Beneficial effects of RIPC on CI-AKI could be associated with effects on mitochondria [26], circulating inflammatory cells [27], transcriptional upregulation of protective pathways [28, 29], and neural pathways [7].

There are several limitations to this study. This pilot investigation of the beneficial effects of RIPC on renal function had a limited number of subjects. Although we sought to prevent any bias by blinding the patients and the data-analysis team, the study design cannot prevent all potential bias. The calculation of sample size was based on inaccurate assumptions because of the pilot nature of the study. Additionally, although CI-AKI is a valid surrogate maker of renal damage and has been described extensively in the literature, it is not a clinical endpoint.

The trends toward a lower incidence of ventricular arrhythmia within 24 hours after PCI and fewer MACCE in the 30 days after PCI observed in the RIPC group are important, but do not equate to a primary outcome measure, for which a study with greater statistical power is needed.

In conclusion, we have demonstrated that RIPC before PCI in patients with STEMI reduced the incidence of CI-AKI. Moreover, the reduction of CI-AKI translated to a trend toward better clinical outcomes in the 30-day follow-up period. The described RIPC protocol is simple and well tolerated and thus may be a feasible and attractive therapeutic option. Nonetheless, a large-scale clinical trial is needed to confirm the efficacy of this approach.

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Figure legends

Fig. 1. Study flow diagram.

Fig. 2. Incidence of (A) CI-AKI and (B) maximum decrease in eGFR 48–72 hours after injection of contrast medium in the RIPC and control groups. (C) Serial changes in serum creatinine in the RIPC and control groups. CI-AKI, contrast-induced acute kidney injury; eGFR, estimated glomerular filtration rate; RIPC, remote ischemic preconditioning. Data expressed as mean ± standard deviation.

Table 1

Baseline clinical characteristics.

	All patients (n=125)			Patients who met criteria (n=94)		
	Control group (n = 62)	RIPC group (n = 63)	*p* value	Control group (n = 47)	RIPC group (n = 47)	*p* value
Age, years	68 ± 14	67 ± 12	0.70	67 ± 15	67 ± 12	0.90
Male, n (%)	43 (69)	46 (73)	0.75	36 (76)	34 (76)	1.00
Hypertension, n (%)	35 (56)	37 (58)	0.97	31 (65)	29 (61)	0.67
Dyslipidemia, n (%)	29 (46)	28 (44)	0.65	25 (53)	24 (51)	0.84
Diabetes, n (%)	22 (35)	18 (28)	0.33	17 (37)	14 (31)	0.56
Hemoglobin index, mg/dl	13.4 ± 2.0	13.5 ± 2.0	0.95	13.7 ± 2.0	13.7 ± 1.8	0.92
Current smoker, n (%)	26 (41)	33 (52)	0.31	24 (51)	28 (59)	0.42
Previous MI, n (%)	3 (4)	7 (11)	0.21	3 (6)	7 (14)	0.15
Pre-MI angina pectoris, n (%)	31 (50)	30 (47)	0.99	28 (59)	24 (51)	0.35
Killip grade	1.4 ± 0.9	1.5 ± 0.8	0.64	1.3 ± 0.6	1.4 ± 0.7	0.44

Systolic blood pressure, mmHg	131 ± 27	129 ± 29	0.68	136 ± 25	133 ± 30	0.59
Serum creatinine at admission, mg/dl	0.91 ± 0.44	1.0 ± 1.15	0.55	0.87 ± 0.44	0.82 ± 0.21	0.42
eGFR at admission, ml/min/1.73m^2	75 ± 32	71 ± 25	0.55	79 ± 33	73 ± 20	0.22
Mehran CIN risk score	7.9 ± 6.0	8.2 ± 6.0	0.80	7.4 ± 5.6	7.8 ± 6.0	0.73
Pre-MI medications						
Antiplatelets, n (%)	8 (12)	6 (9)	0.48	8 (17)	3 (6)	0.13
β-blockers, n (%)	2 (3)	3 (4)	0.70	2 (4)	3 (6)	0.65
Calcium channel blockers, n (%)	10 (16)	18 (27)	0.12	9 (19)	13 (27)	0.32
ACEI/ARB, n (%)	14 (22)	16 (25)	0.83	13 (27)	13 (27)	1.00
Statins, n (%)	9 (14)	10 (15)	0.92	7 (14)	8 (17)	0.78

Values expressed as mean ± SD or n (%).

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin II-receptor blocker; CIN = contrast medium-induced

nephropathy; eGFR = estimated glomerular filtration rate; MI = myocardial infarction; RIPC = remote ischemic preconditioning.

Table 2

Procedural results.

	All patients (n=125)			Patients who met criteria (n=94)		
	Control group (n = 62)	RIPC group (n = 63)	*p* value	Control group (n = 47)	RIPC group (n = 47)	*p* value
Infarct-related coronary artery						
LAD artery	26 (41)	23 (36)	0.48	21 (44)	19 (40)	0.67
Non-LAD artery	36 (59)	40 (64)	0.48	26 (56)	28 (60)	0.67
TIMI flow grade at admission	0.7 ± 1.0	0.8 ± 1.1	0.70	0.5 ± 0.8	0.5 ± 1.0	0.81
Symptom-to-balloon time, min	615 ± 925	638 ± 1072	0.90	360 ± 274	326 ± 278	0.41
Door-to-balloon time, min	106 ± 39	115 ± 72	0.45	104 ± 35	115 ± 74	0.80
Stenting of culprit lesion by PCI	53 (85)	49 (77)	0.14	46 (97)	44 (93)	0.32
IABP support	15 (24)	13 (20)	0.79	10 (21)	9 (19)	0.79
TIMI flow grade after procedure	2.7 ± 0.4	2.7 ± 0.4	0.73	2.6 ± 0.5	2.7 ± 0.4	0.31
Collected TIMI flow counts after procedure, counts	20 ± 11	23 ± 26	0.53	22 ± 12	20 ± 14	0.54

Values expressed as mean ± SD or n (%).

IABP = intra-aortic balloon pump; LAD = left anterior descending; PCI = percutaneous coronary intervention; RIPC = remote ischemic preconditioning; TIMI = thrombolysis in myocardial infarction.

Table 3. Concomitant medications between completion of RIPC and primary end point.

	Control group (n=47)	RIPC group (n=47)	p value
Furosemide (intravenous)	5 (10)	3 (6)	0.48
Furosemide (oral)	3 (6)	5 (10)	0.48
Spironolactone (oral)	3 (6)	1 (2)	0.32
Carperitide (intravenous)	4 (8)	3 (6)	0.70
Isosorbide (oral)	2 (4)	3 (6)	0.65
Nicorandil (oral)	30 (63)	26 (55)	0.41
Dopamine (intravenous)	4 (8)	4 (8)	1.00
Dobutamine (intravenous)	1 (2)	1 (2)	1.00

Values are n (%).

RIPC = remote ischemic preconditioning.

Table 4

Results of logistic regression analyses for CI-AKI.

	Univariate analysis			Multivariate analysis		
	Odds ratio	95% CI	*p* value	Odds ratio	95% CI	*p* value
Age >68 years	4.49	1.49–13.5	0.007	3.38	0.88-12.88	0.07
Male	0.31	0.11–0.90	0.03	0.55	0.13-2.30	0.41
Hypertension	1.69	0.59–4.85	0.32			
Dyslipidemia	0.89	0.34–2.32	0.81			
Diabetes	0.93	0.33–2.59	0.89			
Current smoker	0.28	0.10–0.77	0.01	0.73	0.19–2.79	0.64
Previous MI	0.33	0.04–2.78	0.31			
Systolic blood pressure >136 mmHg	2.06	0.77–5.53	0.14			
Hemoglobin <13.8 mg/dl	1.70	0.64–4.49	0.27			
Killip grade >1	0.91	0.31–2.64	0.86			
TIMI flow grade at	0.99	0.35–2.77	0.99			

admission >0						
Pre-MI angina pectoris	2.66	0.93–7.58	0.06			
LAD as ‘culprit artery’	4.02	1.45–11.17	0.007	3.50	1.08–11.31	0.03
Bare metal stent use	0.97	0.33–2.84	0.96			
Symptom-to-balloon time >238 minutes	2.67	0.97–7.35	0.05			
TIMI flow grade after procedure <3	1.23	0.43–3.41	0.71			
Collected TIMI flow counts after procedure >18 counts	1.68	0.64–4.39	0.29			
CK >2760 IU/L	1.70	0.64–4.49	0.27			
CK-MB >222 IU/L	2.18	0.81–5.85	0.11			
LVEF <55%	0.84	0.31–2.27	0.74			
IABP	1.21	0.38–3.86	0.81			
VF or sustained VT within 24 hours after PCI	0.90	0.17-4.86	0.91			

50% or more ST-segment resolution	0.35	0.13-0.96	0.04	0.48	0.15-1.54	0.22
Mehran CIN risk score >6	1.25	0.48–3.25	0.64			
Creatinine >0.77 mg/dl *	0.54	0.20–1.44	0.22			
eGFR <74 ml/min/1.73m^2	1.95	0.73–5.23	0.18			
Contrast medium >175 ml	1.26	0.48–3.30	0.62			
RIPC	0.21	0.07–0.63	0.006	0.18	0.05–0.64	0.008

Continuous variables were transformed to binary data according to median value. CI-AKI = contrast medium-induced acute kidney injury; CIN = contrast medium-induced nephropathy; CK = creatine kinase; IABP = intra-aortic balloon pump; LAD = left anterior descending; LVEF = left ventricular ejection fraction; MB = myocardial band; MI = myocardial infarction; RIPC = remote ischemic preconditioning; TIMI = thrombolysis in myocardial infarction; VF = ventricular fibrillation; VT = ventricular tachycardia.

Table 5

Secondary outcomes.

	Control group (n = 47)	RIPC group (n = 47)	*p* value
Peak CK, IU/L	3653 ± 2894	2648 ± 1929	0.04
Peak CK-MB, IU/L	303 ± 267	238 ± 159	0.15
VF or sustained VT within 24 hours after PCI	7	1	0.02
% ST-segment resolution, %	51 ± 33	62 ± 28	0.09
50% or more ST-segment resolution	29 (61)	35 (74)	0.18
Left ventricular ejection fraction, %	54 ± 13	54 ± 12	0.84
MACCE			
Total	7 (14)	2 (4)	0.07
Cardiac death	3	0	
Heart failure	3	1	
Ventricular perforation	1	0	
Stroke	0	1	

Values expressed as mean ± SD or n (%).

CK = creatine kinase; LVEF = left ventricular ejection fraction; MACCE = major adverse cardiac and cerebral events; MB = myocardial band; RIPC = remote ischemic preconditioning; VF = ventricular fibrillation; VT = ventricular tachycardia.