BRIEF OBSERVATION

THE AMERICAN JOURNAL of MEDICINE®

Remote Ischemic Preconditioning and Endothelial Function in Patients with Acute Myocardial Infarction and Primary PCI

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ABSTRACT

BACKGROUND: Remote ischemic preconditioning by transient limb ischemia reduces myocardial ischemia-reperfusion injury in patients undergoing percutaneous coronary intervention. The aim of the study we report here was to assess the effect of remote ischemic preconditioning on endothelial function in patients with acute myocardial infarction who underwent primary percutaneous coronary intervention.

METHODS: Forty-eight patients with acute myocardial infarction were enrolled. All participants were randomly divided into 2 groups. In Group I (n = 23), remote ischemic preconditioning was performed before primary percutaneous coronary intervention (intermittent arm ischemia-reperfusion through 4 cycles of 5-minute inflation and 5-minute deflation of a blood-pressure cuff to 200 mm Hg). In Group II (n = 25), standard percutaneous coronary intervention without preconditioning was performed. We assessed endothelial function using the flow-mediated dilation test on baseline, then within 1-3 hours after percutaneous coronary intervention, and again on days 2 and 7 after percutaneous coronary intervention.

RESULTS: The brachial artery flow-mediated dilation results were significantly higher on the first day after primary percutaneous coronary intervention in the preconditioning group (Group I) than in the control group (Group II) (12.1% vs 0.0%, $P = .03$, and 11.1% vs 6.3%, $P = .016$, respectively), and this difference remained on the seventh day (12.3% vs 7.4%, $P = .0005$, respectively).

CONCLUSION: We demonstrated for the first time that remote ischemic preconditioning before primary percutaneous coronary intervention significantly improves endothelial function in patients with acute myocardial infarction, and this effect remains constant for at least a week. We suppose that the improvement of endothelial function may be one of the possible explanations of the effect of remote ischemic preconditioning.

 • *The American Journal of Medicine (2014) 127, 670-673*

KEYWORDS: Acute myocardial infarction; Endothelial function; Flow-mediated dilation test; Remote ischemic preconditioning

As has been shown in several studies, remote ischemic preconditioning by transient limb ischemia reduces myocardial ischemia-reperfusion injury in patients undergoing percutaneous coronary intervention.[1-5] Furthermore, according to 2 randomized trials, remote ischemic preconditioning improves long-term clinical prognosis after both primary and elective percutaneous coronary intervention.[4,6] Despite many studies on remote ischemic preconditioning, there are no data on the effect of remote ischemic preconditioning on the endothelium in patients with acute myocardial infarction.

The aim of the study we report here was to assess the effect of remote ischemic preconditioning on endothelial function in patients with acute myocardial infarction who underwent percutaneous coronary intervention.

Funding: This work was supported, in part, by the Russian Federation Government grant "Immunovirology of atherosclerosis" #14.B25.31.0016, and by RFBR grant #11-04-01339-a.

Conflict of interest: None.

Authorship: All authors had access to the data and a role in writing the manuscript.

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0002-9343/$ -see front matter
http://dx.doi.org/10.1016/j.amjmed.2014.02.012

METHODS

Forty-eight patients admitted to the Moscow City Hospital #23 with acute myocardial infarction (45 patients with ST-elevation myocardial infarction, 3 with non-ST-elevation myocardial infarction) were enrolled. All patients were randomly divided into 2 groups. In Group I (n = 23), remote ischemic preconditioning was performed before percutaneous coronary intervention (intermittent arm ischemia-reperfusion through 4 cycles of 5 minutes of inflation and 5 minutes of deflation of a blood-pressure cuff to 200 mm Hg). Remote ischemic preconditioning was performed while there were preparations for percutaneous coronary intervention and did not delay the onset of percutaneous coronary intervention. In Group II (n = 25), standard percutaneous coronary intervention without preconditioning was performed. In both groups, standard medical therapy was carried out. We assessed endothelial function using the brachial artery flow-mediated dilation test, performed according to guidelines published by Thijssen et al.[7] In both groups, the flow-mediated dilation test was performed immediately upon admission, then within 1 to 3 hours after percutaneous coronary intervention, and again on days 2 and 7 after percutaneous coronary intervention. Also, at admission and on day 7, the left ventricular ejection fraction, the left ventricular end-diastolic size, and the left ventricle end-diastolic volume were evaluated. We performed coronary angiography and percutaneous coronary intervention using standard methods,[8] and assessed the antegrade coronary flow in the infarct-related artery using thrombolysis in myocardial infarction (TIMI) flow grade, as defined previously.[9] The corrected TIMI frame count (CTFC) was assessed according to the protocol described by Gibson et al.[10] The TIMI flow grade and the CTFC were assessed at the start of coronary angiography (when possible) and on the final (ie, post-percutaneous coronary intervention) coronary angiogram. Informed consent was obtained from all the participants.

Statistical Analysis

Statistical analysis was performed with nonparametric tests. We used the Mann-Whitney *U* test and Fisher's exact test to compare groups. The statistical significance of the differences of flow-mediated dilation -test results in both groups was evaluated with the nonparametric Wilcoxon test. The threshold *P* value was .05. Statistical analysis was done with Statistica 8.0 (StatSoft, Tulsa, Okla).

CLINICAL SIGNIFICANCE

- Remote ischemic preconditioning before percutaneous coronary intervention significantly improves endothelial function in patients with acute myocardial infarction on the first day after percutaneous coronary intervention, and this effect remains constant for at least a week.
- Improvement of endothelial function may be one of the possible explanations of the remote ischemic preconditioning effect.

RESULTS AND DISCUSSION

The demographic characteristics and cardiovascular risk factors didn't differ significantly between the groups (Table).

In the 2 tested groups, the functional conditions of the endothelium as assessed with the flow-mediated dilation test at the baseline were not significantly different. The brachial artery flow-mediated dilation test results were significantly higher on the first day after percutaneous coronary intervention in the preconditioning group than in the control group, and this difference continued to be significant on the seventh day (Figure).

The results of baseline and post-percutaneous coronary intervention angiography between the groups didn't differ significantly. The post-percutaneous coronary intervention TIMI III flow grade was observed in 82.6% (n = 19) in Group 1, versus 80% (n = 20) in Group 2 (*P* = 1.0). The median post-percutaneous coronary intervention CTFC also didn't differ significantly between the 2 groups: 24 frames (interquartile range: 16.5-30.5) in Group I vs 19 frames (interquartile range: 15.3-26.1) in Group II; *P* = .36.

Also, there were no significant differences between the 2 groups in echocardiographic parameters such as left ventricular ejection fraction, left ventricular end-diastolic size, and left ventricle end-diastolic volume. Note that we observed in the preconditioning group a tendency to reduce the rate of left ventricle aneurysms compared with the control group (31.8% vs 60.0 %; *P* = .08); this

Table Demographic Characteristics and Cardiovascular Risk Factors

Patient Characteristics	Group I n = 23	Group II n = 25	*P* Value
Age, median, years	63	61	.8
Male	52.1% (12)	56.0% (14)	1.0
Female	47.8% (11)	44.0% (11)	1.0
Hypertension	91.3% (21)	84.0% (21)	.66
Smoking	60.8% (14)	40.0% (10)	.24
Diabetes mellitus	13.0% (3)	28.0% (7)	.29
Dyslipidemia	39.1% (9)	56.0% (14)	.26
Previous MI	4.3% (1)	16.0% (4)	.34
Previous angina	47.8% (11)	44.0% (11)	1.0
Previous PCI	4.3% (1)	8.0% (2)	1.0
STEMI	95.7% (22)	92.0% (23)	1.0
NSTEMI	4.3% (1)	8.0% (2)	1.0

MI = myocardial infarction; NSTEMI = non-ST-elevation myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST-elevation myocardial infarction.