Remote Ischemic Post-Conditioning of the Lower Limb During Primary Percutaneous Coronary Intervention Safely Reduces Enzymatic Infarct Size in Anterior Myocardial Infarction

A Randomized Controlled Trial

Gabriele Crimi, MD,* Silvia Pica, MD,* Claudia Raineri, MD,* Ezio Bramucci, MD,* Gaetano M. De Ferrari, MD,* Catherine Klersy, MD, MSc,† Marco Ferlini, MD,* Barbara Marinoni, MD,*, Alessandra Repetto, MD,*, Maurizio Romeo, MD,† Vittorio Rosti, MD,§ Margherita Massa, PtD,§ Arturo Raisaro, MD,* Sergio Leonardi, MD, MHS,* Paolo Rubartelli, MD,† Luigi Oltrona Visconti, MD,* Maurizio Ferrario, MD*

Pavia, and Genova, Italy

Objectives This study sought to evaluate whether remote ischemic post-conditioning (RIPC) could reduce enzymatic infarct size in patients with anterior ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention (pPCI).

Background Myocardial reperfusion injury may attenuate the benefit of pPCI. In animal models, RIPC mitigates myocardial reperfusion injury.

Methods One hundred patients with anterior ST-segment elevation myocardial infarction and occluded left anterior descending artery were randomized to pPCI + RIPC (n = 50) or conventional pPCI (n = 50). RIPC consisted of 3 cycles of 5 min/5 min ischemia/reperfusion by cuff inflation/deflation of the lower limb. The primary endpoint was infarct size assessed by the area under the curve of creatinine kinase-myocardial band release (CK-MB). Secondary endpoints included the following: infarct size assessed by cardiac magnetic resonance delayed enhancement volume; T2-weighted edema volume; ST-segment resolution >50%; TIMI (Thrombolysis In Myocardial Infarction) frame count; and myocardial blush grading.

Results Four patients (2 RIPC, 2 controls) were excluded due to missing samples of CK-MB. A total of 96 patients were analyzed; median area under the curve CK-MB was 8,814 (interquartile range [IQR]: 5,567 to 11,325) arbitrary units in the RIPC group and 10,065 (IQR: 7,465 to 14,004) arbitrary units in control subjects (relative reduction: 20%, 95% confidence interval: 0.2% to 28.7%; p = 0.043). Seventy-seven patients underwent a cardiac magnetic resonance scan 3 to 5 days after randomization, and 66 patients repeated a second scan after 4 months. T2-weighted edema volume was 37 ± 16 cc in RIPC patients and 47 ± 22 cc in control subjects (p = 0.049). ST-segment resolution >50% was 66% in RIPC and 37% in control subjects (p = 0.015). We observed no significant differences in TIMI frame count, myocardial blush grading, and delayed enhancement volume.

Conclusions In patients with anterior ST-segment elevation myocardial infarction, RIPC at the time of pPCI reduced enzymatic infarct size and was also associated with an improvement of T2-weighted edema volume and ST-segment resolution >50%. (Remote Postconditioning in Patients With Acute Myocardial Infarction Treated by Primary Percutaneous Coronary Intervention [PCI] [RemPostCon]; NCT00865722) (J Am Coll Cardiol Intv 2013;6:1055–63) © 2013 by the American College of Cardiology Foundation
ST-segment elevation myocardial infarction (STEMI) is a leading cause of mortality and morbidity worldwide. Infarct size is a key determinant of prognosis (1). Timely and successful reperfusion, best achieved with primary percutaneous coronary intervention (pPCI), is effective at reducing infarct size, preserving ventricular function, and improving outcome (2). Nevertheless, abrupt restoration of blood flow causes a lethal injury of myocardial cells that may limit the benefit of such intervention. In pre-clinical studies, the impact of myocardial reperfusion injury accounts for up to 50% of the final infarct size (3). Among strategies aimed at limiting reperfusion injury, myocardial ischemic post-conditioning, obtained by exposing the ischemic myocardium to brief periods of ischemia/reperfusion immediately after reperfusion, showed promising results in both animal (4) and small clinical studies (5–9). However, the relevance of this intervention in the clinical setting remains unclear (10), and more importantly, the safety of repeated balloon inflations to the infarct-related artery have been recently questioned (11,12).

In 1993, Przyklenk et al. (13) experimentally proved that the cardioprotective effect of myocardial conditioning could also be elicited by brief ischemia/reperfusion cycles applied remotely. This form of myocardial conditioning, termed “remote conditioning,” has shown protective effects (14), even more relevant than “local” conditioning in animals (15). Bøtker et al. (16) tested remote ischemic conditioning in patients with STEMI. They observed an improvement in myocardial salvage, although a reduction of infarct size was only evident in the explorative subgroup analysis of patients with STEMI due to occluded left anterior descending (LAD) artery.

The objective of our study was to evaluate whether remote ischemic post-conditioning (RIPC) could safely reduce enzymatic infarct size in patients with anterior STEMI treated with pPCI within 6 h of symptoms onset. To test this hypothesis, we randomized patients with occluded LAD to pPCI + RIPC or pPCI alone. We also evaluated markers of reperfusion injury such as contrast-enhanced cardiac magnetic resonance (ce-CMR) T2-weighted (T2W) edema and microvascular perfusion (angiographic and electrocardiographic parameters).

Methods

Study population. Patients ages 18 to 80 years, presenting within 6 h of symptoms onset, with anterior STEMI, de novo occlusion of LAD (TIMI [Thrombolysis In Myocardial Infarction] flow grade 0 to 1), and planned pPCI were eligible. Anterior STEMI was defined as the occurrence of >20 min of chest pain and ST-segment elevation (>2 mm) in at least 2 contiguous precordial leads. Exclusion criteria were: previous anterior STEMI or ≤6 months nonanterior STEMI; Killip class IV; evidence of retrograde filling by collaterals at coronary angiography; severe multi-vessel coronary artery disease likely to require further interventions before follow-up ce-CMR (4 months); known severe abdominal aortic aneurysm (>50 mm); or severe peripheral artery disease (class III to IV).

All patients were followed for 1 year with an office visit at 4 months and a telephone call at 12 months. During follow-up, we assessed vital status, recurrent myocardial infarction, repeated myocardial revascularizations, and stroke.

Study design. This was a randomized, controlled, parallel group, open-label trial, with blinded evaluation of the endpoints. The study was conducted in 2 centers in Italy. Randomization was generated via computer-assisted sequence of treatments with permuted blocks of varying size, using sealed opaque envelopes. After diagnostic angiography, eligible patients were randomized 1:1 to pPCI + RIPC or conventional pPCI (Fig. 1). All patients were pre-treated with 250 mg aspirin intravenously, 300 or 600 mg clopidogrel loading dose, and 70 IU/Kg unfractionated heparin. Coronary angiography was performed by either femoral or radial approach. Both groups received pPCI according to standard techniques; the use of thrombectomy and of inhibitors of glycoprotein IIb/IIIa (anti-GP IIb/IIIa) was strongly encouraged. Infusion of anti-GP IIb/IIIa was prolonged for 12 h or 18 h as appropriate. Lifelong 100 mg aspirin, angiotensin-converting enzyme inhibitors, and beta-blockers atinns were prescribed to be taken daily; 75 mg clopidogrel daily was prolonged for 12 months.
ST-segment resolution. ST-segment elevation was evaluated by a single investigator with lens-intensified caliper to the nearest of 0.5 mV, 20 ms after the end of the QRS interval. PR segment was the reference baseline. Electrocardiographs were collected at admission and ≈60 min after reperfusion (time window ±10 min). The lead with maximal ST-segment elevation at baseline was analyzed. ST-segment resolution (STR) was expressed as percentage of change from baseline; cutoffs were set at 50% (STR$_{50}$) and 70% (STR$_{70}$) as previously described (21).

Contrast-enhanced cardiac magnetic resonance. Acquisition protocol. We performed ce-CMR 3 to 5 days after randomization and after 4 months. We used a 1.5-T MAGNETOM Symphony (Siemens Healthcare, Erlangen, Germany) with a phased array receiver coil on the patient chest. All subjects were placed in supine position, and left ventricular (LV) function was assessed using breath-hold, steady state, free precession cine-CMR. Contiguous slices were acquired from the atriовentricular plane to the apex in short-axis direction. Imaging parameters were: time to repeat = 46.41 ms; time of echo = 1.79 ms; flip angle = 65$^\circ$; slice thickness = 8 mm; matrix = 166 × 256; field of view = 280 to 350 mm. T2W images were acquired in long-axis and short-axis directions from base to apex using dark-blood T2W short tau inversion-recovery fast spin-echo sequences. Imaging parameters were: time to repeat = 750 to 2,000 ms; time of echo = 69 ms; flip angle = 180$^\circ$; slice thickness = 8 mm; matrix = 128 × 256; field of view = 300 to 380 mm. Intravenous bolus of gadolinium with diethylene-triaminepentaacetae (Magnevist, Schering, Berlin, Germany) 0.2 mmol/kg was administered. Early (≈5 min) contrast images were used to evaluate microvascular obstruction; late images (≈15 min) were used to evaluate infarct size. Images were acquired in short- and long-axis with T$_1$-weighted inversion-recovery sequences (inversion time: 240 to 300 ms).

Image analysis. Two senior investigators computed parameters offline (Argus, Siemens Medical solutions, Malvern, Pennsylvania); disagreement was solved by consensus. LV endocardial and epicardial borders were manually traced. Each short-axis slice at both end diastole and end systole was evaluated. Myocardial mass was calculated by multiplying myocardial volume by tissue density (i.e., 1.05 g/ml). The hyperintense signal in T2W short tau inversion-recovery fast spin-echo images was considered for myocardial edema. Edema volume was computed including signal at least 2 SD above the mean of noninfarcted myocardium. Hyperintense signal from the blood pool was excluded. Myocardial hemorrhage was defined as a hypo-intense signal within the area of edema. Hemorrhage was included in the computation of T2W edema volume. Infarct size was assessed on late-contrast images (≈15 min after gadolinium administration) by manually tracing the hyperintense area in each short-axis slice. Microvascular...
obstruction was defined as a hypointense signal in the infarct-related myocardium and was assessed by manually tracing the suspected area in each short-axis slice.

**Sample size.** At the time of the study design, limited clinical data were available for sample size estimation (5). We conservatively planned to enroll a total of 100 patients (50 per group) to obtain 92 valid patients (power: 90%, alpha 2-sided: 5%, effect size: 0.678, corresponding to a mean area under the curve of 326,095 in the control group and of 241,400 in the treatment group, with a common SD of 125,000). Two interim analyses were performed for efficacy and adaptation of sample size after the enrollment of 40 and 60 patients, respectively (Lan-DeMets group sequential method, O’Brien-Fleming type alpha spending function). To preserve an overall alpha of 0.050, the p values to reject the null hypothesis of no difference between treatments at the interim analyses was computed to 0.0005 and 0.014, respectively, and 0.045 at the final analysis (22).

Calculations were performed with WinLD (Programs for Computing Group Sequential Boundaries Using the Lan-DeMets Method, version 2, D. M. Reboussin, D. L DeMets, and K. K. G. Lan, Madison, Wisconsin) and Stata (version 12, StataCorp, College Station, Texas).

**Statistical analysis.** Data were described as mean ± SD or median (interquartile range [IQR]) if continuous and counts and percentages if categorical. The log-transformed primary outcome measure was compared between groups with the Student t test. The difference between groups was then back-transformed and presented as ratios of control versus treatment, with 95% confidence interval (CI). Secondary outcome measures were compared with the Fisher exact test if categorical and either the Student t test or the Mann Whitney U test (depending on their distribution) if continuous. Association between continuous variables was measured with the Spearman R. Finally, an exploratory analysis of the primary endpoint to verify whether differential effects of treatment were present in pre-defined
subgroups of patients (age, sex, diabetes mellitus, pre-
infarction angina, morphine administration, pain to balloon
time, or presence of a multivessel disease) by fitting a
multiple general linear model with inclusion of an inter-
action term between treatment and subgroup. Model
assumption was verified by inspection of residuals.
Stata was used for computation. A 2-sided p value of
<0.05 was considered statistically significant.

Results

Patients. Between March 2009 and December 2011, 753
pPCI were performed, including 224 anterior STEMI. The
main reason for study ineligibility was severe multivessel
disease that was likely to require staged PCI (Fig. 2) (23).
We enrolled 100 patients. Four patients (2 RIPC and 2
control) had missing blood samples for primary endpoint
assessment and were excluded. The primary analysis
included 96 patients. Baseline characteristics were balanced
between the study groups (Table 1, Online Table 1). Mean
age was 58.4 ± 10.9 years, 88% of patients were males, 12%
were diabetics, and 63% had single-vessel disease. Median
ischemia time (pain to balloon) was 182 min (IQR: 145 to
239) with no differences between the study groups. Overall,
96% of patients were treated with anti-GP IIb/IIIa and 81%
with thrombectomy. Morphine (5- to 10-mg IV boluses)
was administered before or during the procedure in 57% of
patients.

Enzymatic infarct size. The median area under the curve of
CK-MB release (data not shown).

Angiographic endpoints. TIMI frame count was similar
between the RIPC and control groups. The proportion of
patients with MBG 2 or 3 was numerically higher in
RIPC patients than in control subjects (p = 0.049) (Fig. 4).
Myocardial edema correlated well with enzymatic
infarct size (R² = 0.70, p < 0.001), T2W edema
volume (R² = 0.70, p < 0.001), and follow-up ce-CMR
DE volume at follow-up (R² = 0.001) (Fig. 2). We observed a numerical difference in
favor of RIPC in acute DE volume (relative reduction: 20.7%,
95% CI: –2.3% to 39.1%) and LV ejection fraction. After 4
months of follow-up, the relative reduction of DE volume in
the RIPC group was 10% (95% CI: –16.1% to 37.5%). Acute
ce-CMR DE volume (R = 0.70, p < 0.001), T2W edema
volume (R = 0.65, p < 0.001), and follow-up ce-CMR DE
volume (R = 0.66, p < 0.001) correlated well with enzymatic

<table>
<thead>
<tr>
<th>Table 1. Baseline Characteristics and Procedural Data</th>
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<tr>
<td>pPCI + RIPC (n = 48)</td>
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<tr>
<td>Age, yrs</td>
</tr>
<tr>
<td>Male</td>
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<tr>
<td>Body mass index, kg/m²</td>
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<tr>
<td>Family history of coronary artery disease</td>
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<tr>
<td>Hypertension</td>
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<td>Active smokers</td>
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<td>Dyslipidemia</td>
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<td>Diabetes mellitus</td>
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<td>Previous myocardial infarction</td>
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<td>Previous percutaneous coronary interventions</td>
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<tr>
<td>Pre-infarct angina</td>
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<tr>
<td>Baseline heart rate, beats/min</td>
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<tr>
<td>Baseline serum creatinine, mg/dl</td>
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<tr>
<td>Out of hospital cardiac arrest</td>
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<tr>
<td>Pain to balloon time, min</td>
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<tr>
<td>Vessels with critical stenosis</td>
</tr>
<tr>
<td>1-vessel disease</td>
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<tr>
<td>2-vessel disease</td>
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<tr>
<td>3-vessel disease</td>
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<tr>
<td>LAD segment of occlusion:</td>
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<tr>
<td>Proximal</td>
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<tr>
<td>Medium</td>
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<tr>
<td>Distal</td>
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<tr>
<td>Initial TIMI flow grade 1</td>
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<tr>
<td>Anti-GP IIb/IIIa</td>
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<tr>
<td>Thrombectomy</td>
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<tr>
<td>Stent</td>
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<tr>
<td>Bare-metal</td>
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<tr>
<td>Drug-eluting</td>
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<tr>
<td>POBA</td>
</tr>
<tr>
<td>Contrast volume, cc</td>
</tr>
<tr>
<td>Morphine</td>
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<tr>
<td>Inotropes</td>
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<td>Intra-aortic balloon pump</td>
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Values are mean ± SD, n (%), or median (interquartile range).
anti-GP IIb/IIIa = inhibitors of glycoprotein IIb/IIIa; LAD = left anterior descending; POBA = plain only balloon angioplasty; pPCI = primary percutaneous coronary intervention; RIPC = remote ischemic post-conditioning; TIMI = Thrombolysis In Myocardial Infarction.
infarct size (Online Figs. 1 and 2). Based on the observed effect size, the post-hoc power analysis to detect a difference in acute and follow-up DE volume were $1 - \beta = 0.46$ and $1 - \beta = 0.10$, respectively.

**Subgroup analysis.** In subgroup analysis, no significant interaction was observed between RIPC and the pre-specified subgroups: age (<60 vs. ≥60 years); sex; diabetes mellitus; pre-infarction angina; morphine administration; pain-to-balloon time (tertiles); and single-vessel versus multivessel disease.

**Secondary clinical endpoints and adverse events.** RIPC was successfully administered to all patients. Major adverse cardiac events are outlined in Table 3. One patient died in the control group (refractory heart failure) and none in the RIPC group. In the control group, we observed 1 reinfarction due to subacute stent thrombosis requiring re-PCI and 1 ischemic stroke. In the RIPC group, we observed 4 repeated coronary revascularization (3 treated with PCI, 1 with coronary artery bypass graft). Vital status was assessed after 1-year follow-up in all but 1 patient who moved to another country (RIPC group).

**Discussion**

Our study shows that RIPC of the lower limb at the time of pPCI can reduce enzymatic infarct size by 20% (95% CI: 0.2% to 28.7%) in patients with anterior STEMI and occluded LAD undergoing pPCI within 6 h of symptoms onset. The benefit observed, though smaller than expected and marginally significant, was directionally consistent with markers of myocardial reperfusion injury and successful reperfusion such as the reduction of T2W edema volume and the improvement of STR. Notably these effects were obtained on top to optimal thrombus management with thrombectomy and anti-GP IIb/IIIa.

Most of the clinical studies that explored the effect of myocardial post-conditioning in humans, applied brief cycles of ischemia/reperfusion to the culprit artery after stenting. The protective effect of local post-conditioning in STEMI patients remain unclear and recently prompted safety concerns related to possible thrombus microembolization occurring during repeated balloon inflations (12) to the infarct-related artery.

To date, there are only 2 studies exploring the effects of remote conditioning in patients undergoing pPCI (16,24). However, this is the first study to assess the effects of remote post-conditioning as ischemia/reperfusion of the remote district (the lower limb) was initiated after coronary reperfusion rather than before. Bøtker et al. (16) studied remote conditioning performed during hospital transportation, before pPCI. The primary endpoint was myocardial salvage assessed by myocardial perfusion imaging. Myocardial salvage was improved in remote conditioned patients, but no
effects on infarct size, STR, and troponin-T release were observed.

Rentoukas et al. (24) tested the effects of remote conditioning initiated prior to pPCI combined with morphine administration in patients with STEMI. They enrolled 96 STEMI patients who presented within 6 h of symptom onset who were randomly assigned to 1 of 3 reperfusion strategies (RIPC + pPCI, RIPC + pPCI + morphine, pPCI alone). The primary endpoint of full STR was reduced by Zhao et al. (4) because it was initiated after the onset of ischemia/reperfusion before pPCI. This protocol differs from the original concept of post-conditioning described by Zhao et al. (4) because it was initiated after the onset of ischemia, but before reperfusion. This strategy could be defined as a late remote pre-conditioning. Rentoukas et al. (24) started 3 cycles of remote ischemia/reperfusion 10 min before the estimated time of reperfusion and continued 5 min after. In fact, they termed it “remote perconditioning.” We designed the present study to closely translate the pre-clinical model (14) of remote post-conditioning into clinical practice. We randomized patients with occluded LAD without evidence of retrograde filling to avoid potential confounders due to spontaneous reperfusion and/or collateral protection. RIPC consisted of 3 cycles of leg ischemia/reperfusion started at the time of reperfusion. We believe that timing could have potentially relevant implications beyond classification. In particular, we hypothesize that any circulating factor potentially mediating the cardioprotective effects (e.g., pH shifts, endogenous adenosine, opioids, cytokines) has to reach the target area (i.e., the ischemic myocardium) to mediate its effect, that require a patent culprit artery.

### Site
Both the previous studies applied ischemia/reperfusion cycles to 1 arm. A dose-response effect, with regard to both site and number of cycles of remote ischemia/reperfusion was elegantly demonstrated by Loukogeorgakis et al. (25). They explored the protective effect of remote conditioning to mitigate endothelial ischemia/reperfusion injury of the arm. They assessed flow-mediated dilation before and after 20 min of ischemia of the arm obtained with extrinsic compression. A dose-response protective effect was reported with a maximum degree of protection obtained with 3 cycles of ischemia/reperfusion of the leg and a threshold effect of at least 2 cycles of the arm. According to these data, we hypothesized a dose-response effect proportional to the mass and potential distal embolization might be important confounders. For this reason, the use of both anti-GP IIb/IIIa and thrombectomy (95% and 84%, respectively) were strongly encouraged in our study. In the study by Bøtker et al. (16), anti-GP IIb/IIIa were administered in ≈84% of patients, whereas data regarding the use of thrombectomy were not reported. In the study by Rentoukas neither anti-GP IIb/IIIa nor thrombectomy data were reported (24).

### Table 4. Contrast-Enhanced Magnetic Resonance Results, Acute Phase, and 4-Month Follow-Up

<table>
<thead>
<tr>
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<th>Acute Phase (3 to 5 Days)</th>
<th>Follow-Up (4 Months)</th>
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<tr>
<td></td>
<td>pPCI + RIPC (n = 35)</td>
<td>pPCI (n = 42)</td>
</tr>
<tr>
<td>Days to ce-CMR</td>
<td>4.7 ± 2.4</td>
<td>5.1 ± 1.8</td>
</tr>
<tr>
<td>LV end-diastolic volume, ml</td>
<td>148 ± 37</td>
<td>169 ± 52</td>
</tr>
<tr>
<td>LV end-systolic volume, ml</td>
<td>84 ± 26</td>
<td>102 ± 46</td>
</tr>
<tr>
<td>LV ejection fraction, %</td>
<td>44 ± 9</td>
<td>41 ± 9</td>
</tr>
<tr>
<td>LV mass, g</td>
<td>111 ± 26</td>
<td>125 ± 38</td>
</tr>
<tr>
<td>Delayed enhancement, ml</td>
<td>27 ± 14</td>
<td>34 ± 19</td>
</tr>
<tr>
<td>Delayed enhancement/LV mass ratio, %</td>
<td>24 ± 10</td>
<td>26 ± 13</td>
</tr>
<tr>
<td>Edema, ml</td>
<td>37 ± 16</td>
<td>47 ± 22</td>
</tr>
<tr>
<td>Edema/LV mass ratio, %</td>
<td>33 ± 11</td>
<td>36 ± 15</td>
</tr>
<tr>
<td>Delayed enhancement/edema ratio, %</td>
<td>72 ± 17</td>
<td>72 ± 19</td>
</tr>
<tr>
<td>Presence of hemorrhage, %</td>
<td>19 (68)</td>
<td>16 (53)</td>
</tr>
<tr>
<td>Presence of microvascular obstruction</td>
<td>24 (77)</td>
<td>27 (75)</td>
</tr>
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</table>

Values are mean ± SD, n (%), or median [interquartile range], or n (%).

ce-CMR = contrast enhanced cardiac magnetic resonance; LV = left ventricle/ventricular; other abbreviations as in Table 1.
Infarct size reduction observed in RIPC patients with enzymatic CK-MB release was less evident when assessed by ce-CMR imaging. DE volume was non significantly reduced in RIPC patients. The reason for this difference is unclear. There was a good correlation between enzymatic infarct size and DE volume in both the acute phase and the follow-up and the point estimate of the mean infarct size reduction was similar using both enzymatic and DE volume criteria (Fig. 4). However, DE volume was measured in 80% of patients. So it might be possible that the lack of difference was due to insufficient power. Furthermore, the small improvement in DE volume and LV ejection fraction associated with RIPC in the acute phase was no longer evident at 4 months. This finding, similar to that reported by Bøtker et al. (16) as by other studies testing local post-conditioning (11,12) could be the result of infarct size shrinkage and left ventricle remodeling that further reduced power during follow-up.

The results of secondary endpoints support the hypothesis that RIPC might reduce infarct size by limiting myocardial reperfusion injury.

RIPC was associated with a reduction of myocardial T2W edema volume, a potential marker of reperfusion injury (17). Edema usually starts during the ischemic phase and expands in the interstitial space during reperfusion, thus increasing hydrostatic pressure, causing capillary compression and potentially limit tissue perfusion. Myocardial edema could have an indirect negative effect on myocardium and contribute to the pathogenesis of reperfusion injury (26,27).

RIPC significantly improved STR. STR has been proposed as a marker of efficient microvascular reperfusion, and it yields prognostic information beyond that provided by coronary TIMI flow grade. Several studies have shown a consistent relationship between STR and subsequent mortality (28).

RIPC was also associated with a trend of improvement in MBG, whereas no difference was found in TIMI frame count. MBG has been proposed as a more efficient marker of successful microvascular reperfusion than TIMI flow grade and TIMI frame count and has been positively associated with long-term mortality (20) in STEMI patients.

RIPC was easy to perform, inexpensive, and well tolerated. We observed no adverse effect related to RIPC during hospitalization. No patient died in the RIPC group at 12 months. During follow-up, we observed 4 repeated revascularizations in RIPC patients. These clinical events were due to in-stent restenosis following bare-metal stent implantation, so the relationship with the study treatment is unlikely.

**Study limitations.** The study was not double-blinded. However, to limit potential source of bias, all patients were prepared with tight-sized cuffs, and the endpoints were evaluated by investigators blinded to treatment allocation.

The results reflect a selected population of patients with STEMI. Moreover, the ratio between patients screened and randomized was higher and the period of enrollment was longer than originally planned. However, no major changes were observed in the managements of patients with STEMI during this time, so it is likely that the impact of this aspect is limited.

We did not assess the area at risk, nevertheless we enrolled only patients with occluded LAD and the segment of occlusion, a surrogate of area at risk, was not different between the groups.
The study was not adequately powered to detect a difference in DE volume both in the acute phase and at follow-up.

Conclusions

RIPC of the lower limb at the time of primary PCI in patients with anterior STEMI due to occluded LAD within 6 h of symptoms onset, reduces enzymatic infarct size and is associated with the improvement of markers of myocardial reperfusion injury (T2W edema volume) and microvascular reperfusion (STR). Given its excellent feasibility, safety associated with the improvement of markers of myocardial reperfusion injury (T2W edema volume) and microvascular reperfusion (STR). Given its excellent feasibility, safety profile, and minimal costs, these encouraging results warrant further investigations.

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Reprint requests and correspondence: Dr. Gabriele Crimi, SC Cardiologia, ASL3 Ospedale Villa Scassi, Corso Scassi 1, 16149 Genoa, Italy. E-mail: gabrielecrimi@gmail.com.

REFERENCES


Key Words: cardiac magnetic resonance imaging — myocardial conditioning — myocardial infarction — myocardial reperfusion injury — primary angioplasty.

APPENDIX

For supplemental figures and tables, please see the online version of this paper.