Efficacy of electroacupuncture pretreatment for myocardial injury in patients undergoing percutaneous coronary intervention: A randomized clinical trial with a 2-year follow-up

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A B S T R A C T

Electroacupuncture pretreatment (EAP) safely protects the heart from ischemic injury, however, the efficacy of EAP for peri-procedural myocardial injury after percutaneous coronary intervention (PCI) remains unclear. Our aim was to investigate whether EAP prior to PCI reduces post-PCI myocardial injury in patients with coronary artery disease (CAD). 388 patients (≥18 years old) with CAD, undergoing elective PCI were enrolled and randomized, out of those 204 went through the whole trial. EAP was conducted by 30-minute electrical stimulation through 4 electrodes attached to the Antiguan (PC6) and Ximen (PC4) acupoints in the forearm bilaterally 1–2 h prior to PCI. The control group had sham electrodes but no electrical stimulation. The primary end point was the incidence of myocardial infarction type 4a (MI4a) based on serum cTnI values at 24 h after PCI. The secondary end points included post-procedural cardiac function and the major adverse cardiac/cerebrovascular event (MACCE) rate. EAP prior to PCI significantly reduced the incidence of MI4a (serum cTnI ≥ 0.20 ng/mL) 24 h post-PCI compared to the control group (P = 0.0157). Moreover, multivariate logistic regression analysis showed that EAP was associated with decreased likelihood of MACCE (odds ratio 0.327, 95% CI 0.140–0.767, P = 0.010). EAP prior to PCI significantly reduced cTnI release and protected patients with CAD from subsequent myocardial injury after PCI procedure.

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1. Introduction

The current therapy for coronary artery disease (CAD) relies increasingly upon percutaneous coronary intervention (PCI). Unfortunately, some cardiac complications during PCI, such as artery dissection, acute thrombosis formation, slow reflow or branch vessel occlusion, may independently trigger subsequent myocardial injury and heart dysfunction [1]. Approximately one-third of all elective PCI procedures are complicated by myocardial injury, with subsequent cardiovascular events (including arrhythmias, cardiac dysfunction) and mortality [2]. Increased serum cardiac enzymes, including cardiac troponin I (cTnI), occur in more than 25% of post-PCI patients [3,4]. A wealth of evidence supports the correlation of extensive cardiac enzyme release after PCI with cardiac injury [5,6] and delayed mortality [7,8]. Statins [9], beta-blockers [10], cyclosporine [11] and trimetazidine [12] have been reported to limit the rate and extent of PCI-associated myocardial infarction (MI type 4a) [13]. Moreover, non-pharmacological interventions, such as remote ischemic preconditioning, also provide effective protection against PCI-related myocardial injury [14,15]. However, peri-procedural myocardial injury after PCI remains unresolved.

Acupuncture is practiced and accepted worldwide as a promising alternative therapeutic approach in treating diseases such as migraine [16], chronic low back pain [17], and knee osteoarthritis [18]. It also improves exercise tolerance in heart failure patients [19]. A recent clinical trial demonstrated that an acupuncture-assisted anesthesia reduced postoperative morbidity and medical costs in an open-heart surgery cardiopulmonary bypass procedure [20]. Our previous studies
also proved that electroacupuncture pretreatment [EAP, 30-minute electric stimulation through 4 electrodes attached to the bilateral forearm Neiguan (PC6) and Ximen (PC4) acupoints] before surgery significantly attenuated serum cTnI levels during and shortly after surgery in adults undergoing heart valve replacement [21] and in children undergoing cardiac surgery for correcting congenital heart malformation [22]. However, whether EAP attenuates periprocedural myocardial injury after PCI, especially in those patients exhibiting complex coronary lesions, has not been previously investigated. Therefore, the current multi-center clinical trial was designed to evaluate whether EAP reduces PCI-related myocardial injury.

2. Methods

2.1. Study design

This clinical study was a prospective, randomized, multi-center trial, conducted in 5 central hospitals in China (ClinicalTrials.gov # NCT01020942). The study was approved by the Institutional Ethics Review Committees at all participating hospitals, and the study protocol conformed to the principles outlined in the Declaration of Helsinki. An independent data and safety monitoring board met at least twice annually to oversee the trial. No formal termination rules were specified. The academic members of this trial had full access to all study data, to vouch for its accuracy, complete data analyses, verify protocol fidelity in the study’s conduct, write up the manuscript, and were ultimately responsible for its integrity. The research protocol summary is currently available at ClinicalTrials.gov (NCT01020942).

2.2. Patients

388 patients, who were at least 18 years old with a diagnosis of stable or unstable angina, or silent ischemia, undergoing non-urgent coronary angiography with the intention to undergo elective percutaneous coronary intervention (PCI), and able to give informed consent, were enrolled and randomized. Out of those 204 patients went through the whole trial and were analyzed. Patients underwent angiography, and were diagnosed with one, two, or three-vessel diseases with diameter stenosis ≥ 70%. Inclusion and exclusion criteria are provided in the Supplementary Appendix. All patients provided written consent.

2.3. Treatment and blinding

All the study patients received medication prior to PCI in accordance with current ACCF/AHA/SCAI guidelines for the clinical management of patients with coronary artery disease [23]. Participants were randomly assigned to groups, in a 1:1 ratio, to receive EAP or control (sham pre-treatment). The randomization sequence was computer-generated, and randomization was performed in blocks of randomly varying sizes and was stratified according to participating hospital. Interventionists conducting PCI, measurements of cTnI and inflammatory markers, positron emission tomography/computed tomography (PET/CT) imaging, echocardiography, and telephone follow-up were blinded. The acupuncturists performing EAP who were unmasked to treatment assignments, did not participate in data acquisition and analysis. EAP protocol utilized was 30-minute electrical stimulation through 4 electrodes attached to the Neiguan (PC6) and Ximen (PC4) acupoints in the forearm bilaterally 1–2 h prior to PCI. The control group patients had the same electrodes applied and received sham treatment based on previously described design for patient blinding [24,18]. Details regarding the EAP and PCI procedures are provided in the Supplementary Appendix.

2.4. End points and follow-up

Baseline serum cTnI levels were measured in all patients prior to PCI. The primary end point was the incidence of MI4a based on serum cTnI values at 24 h after PCI. MI4a is arbitrarily defined by the elevation of cardiac troponin values (> 5 × 99th percentile URL) in patients with normal baseline values (≤ 99th percentile URL) according to the Joint ESC/ACC/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction [25]. The secondary end points included post-procedural cardiac function and the major adverse cardiac/cerebrovascular event (MACCE) rate. To evaluate cardiac function in all patients, echocardiography was performed at pre-, 3 and 6 months post-PCI intervals. The MACCE rate was followed up either by clinic visits or by telephone interviews as deemed necessary for 24 months in all 204 patients.

To elucidate potential beneficial effects of EAP, serum levels of high-sensitivity C-reactive protein (hs-CRP), tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), interleukin-10 (IL-10), and high mobility group box 1 (HMBG1) were measured at pre-PCI and 24 h post-PCI. Additionally, patients with left anterior descendant coronary stenosis underwent PET/CT imaging at pre- and at 3 days post-PCI intervals to assess myocardial metabolic activity. Details regarding end point measurements are provided in the Supplementary Appendix. All clinical end points were assessed in a blinded fashion. All serological samples were analyzed in the clinical laboratory of Xijing Hospital.

2.5. Sample size and statistical analysis

The trial was conducted to determine whether EAP was beneficial for reduction in the incidence of MI4a with respect to the primary end point. According to our preliminary pilot data, about 50% of patients have myocardial injury complications after elective PCI procedures. The incidence of the primary end point was estimated to be 40% reduction in patients randomized to the EAP group. Therefore, the minimum number of patients necessary for this trial to enable detection of such reduction at a two-sided type I error rate of 0.05 (α = 0.05) and power of 0.80 (β = 0.20) was 182 total (91 per group).

All patients were included in the analysis according to groups of original assignment (intention-to-treat analysis). Continuous variables were presented as means and standard deviations (SD) or standard error of the mean (SEM), and categorical data as numbers and percentages. Because cTnI data were skewed, these values were expressed as median with interquartile range (IQR). Baseline clinical and angiographic characteristics and procedural data were compared between the two groups by the Student’s t-test or t-test for continuous variables, and the chi-square test or Fisher’s exact test for categorical variables whenever appropriate. The differences in time course of echocardiographic parameters between study groups and among time points within each group were analyzed by repeated measures analysis of variance. Multivariate logistic regression was constructed to test the association of EAP and MACCE. Covariates included EAP, men sex, age, diabetes mellitus, hypertension and previous MI. Patients with missing values in one of the co-variables were excluded from analysis. Data were presented as odds ratios (ORs) with 95% confidence intervals (CIs). The incidences of MACCE rate was estimated by the Kaplan–Meier method. For each individual, missing values were replaced by the last observed variable value (last observation carried forward). SPSS software package version 19.0 (SPSS, Chicago, IL) was used for data analysis. A P value of less than 0.05 was considered significant.

3. Results

3.1. Baseline clinical characteristics and study termination

At the recommendation of the independent data and safety monitoring board, patient recruitment was terminated on September 18, 2011. 420 patients with CAD were enrolled. 32 patients registered were not
randomized due to elevated cTnI values prior to PCI and 184 patients were excluded from further analysis because of normal coronary angiography or coronary artery stenosis <70%. Therefore, 204 patients were randomly assigned equally into the EAP and control groups (Fig. 1).

Baseline clinical characteristics were similar between the EAP and control groups (Table 1). The average age of the trial participants was 59.6 years; 82.1% of participants were male. Incidences of diabetes, hypertension, and myocardial injury were 24.5%, 47.1%, and 18.1% respectively. Baseline angiographic and peri-procedure data were similar in both the EAP and control groups (Table 1).

3.2. Angiographic and procedural characteristics

There were no major procedure-related complications in either group (death or urgent revascularization within the first 24 h). Angiographic parameters were similar in both groups, and any difference in cTnI release after EAP was not due to lower risk (Table 1). Single-vessel and multi-vessel PCIs were 61.8% and 38.2%, respectively, with approximately half of the patients scoring modified Duke jeopardy values ≥ 6 [26]. Angiographic parameters and complication rates were similar in both groups. Drug-eluting stents were used in all interventions.

3.3. Incidence of MI4a and level of cTnI

Study participants were eligible for the study if the baseline cTnI was below the lower limit of detection for the assay (0.04 ng/mL). As for serum cTnI concentrations 24 h post-PCI, there was significantly less patients [31] with cTnI values exceeding 0.20 ng/mL in the EAP group compared to 51 patients in the control group (30.4% vs 50.0%, P = 0.004), which indicated less incidence of PCI-related MI (MI4a) in patients who received EAP (Table 2).

However, there were no significant differences in the number of patients with cTnI values of ≤0.04 ng/mL and 0.04–0.20 ng/mL between...
the EAP and control groups. Most importantly, when the patients were sub-grouped into complex coronary lesion group (i.e., patients with the EAP and control groups. Most importantly, when the patients were sub-grouped into complex coronary lesion group (i.e., patients with the complex coronary lesions (58.38 ± 0.46% vs 55.29 ± 1.17%, P = 0.023), but not in patients with relatively simple coronary lesions (54.43 ± 1.56% vs 55.80 ± 1.53%, P = 0.557).

3.5. MACCE rate

In the period of 24-month follow-up, 11 (10.8%) of the 102 patients in the EAP group and 25 (24.5%) of the 102 controls had at least 1 MACCE, resulting in a statistically significant reduction in the MACCE rate in the EAP group compared with control (Log-rank Chi-square = 5.83, P = 0.0157). EAP was associated with decreased likelihood of MACCE (odds ratio 0.327, 95% CI 0.140–0.767) (Table 4). For the MACCE rate, the Kaplan–Meier curves for the EAP and control groups began to separate at approximately 18 months after PCI and continue to diverge up to study termination (Fig. 2).

3.6. Systemic inflammatory markers

As shown in Fig. 3, the baseline of systemic inflammatory mediators (hs-CRP, HMGB1, TNF-α, IL-6 and IL-10) was similar in both groups. At 24 h after PCI, the mean levels of inflammatory cytokines were elevated. The post-procedural serum TNF-α and IL-6 concentrations were significantly lower in the EAP group (P = 0.021 and 0.010, respectively), whereas the IL-10 level was significantly higher (P = 0.004). However, the concentrations of hs-CRP and HMGB1 were not significantly different (P = 0.120 and 0.053, respectively) between the two groups.

Table 3 Cardiac function of patients by echocardiographic analyses.

<table>
<thead>
<tr>
<th>Echocardiographic parameter</th>
<th>CON (n = 102)</th>
<th>EAP (n = 102)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF</td>
<td>0 month</td>
<td>52.81 ± 0.97</td>
<td>54.56 ± 0.77</td>
</tr>
<tr>
<td></td>
<td>3th month</td>
<td>52.43 ± 1.41</td>
<td>55.96 ± 0.81</td>
</tr>
<tr>
<td></td>
<td>6th month</td>
<td>54.90 ± 0.67</td>
<td>57.15 ± 0.50</td>
</tr>
<tr>
<td>LVEDD</td>
<td>0 month</td>
<td>49.38 ± 0.67</td>
<td>49.74 ± 0.77</td>
</tr>
<tr>
<td></td>
<td>3th month</td>
<td>48.70 ± 0.79</td>
<td>50.68 ± 1.12</td>
</tr>
<tr>
<td></td>
<td>6th month</td>
<td>47.28 ± 0.93</td>
<td>45.10 ± 1.16</td>
</tr>
<tr>
<td>EDV</td>
<td>0 month</td>
<td>96.48 ± 3.24</td>
<td>99.51 ± 3.82</td>
</tr>
<tr>
<td></td>
<td>3th month</td>
<td>92.96 ± 5.88</td>
<td>92.64 ± 6.19</td>
</tr>
<tr>
<td></td>
<td>6th month</td>
<td>96.24 ± 5.41</td>
<td>83.47 ± 3.23</td>
</tr>
<tr>
<td>SV</td>
<td>0 month</td>
<td>53.85 ± 1.56</td>
<td>55.63 ± 1.97</td>
</tr>
<tr>
<td></td>
<td>3th month</td>
<td>53.85 ± 2.78</td>
<td>54.50 ± 3.08</td>
</tr>
<tr>
<td></td>
<td>6th month</td>
<td>58.68 ± 1.72</td>
<td>65.68 ± 2.17</td>
</tr>
<tr>
<td>E/A</td>
<td>0 month</td>
<td>0.78 ± 0.05</td>
<td>0.76 ± 0.02</td>
</tr>
<tr>
<td></td>
<td>3th month</td>
<td>0.64 ± 0.07</td>
<td>0.70 ± 0.03</td>
</tr>
<tr>
<td></td>
<td>6th month</td>
<td>0.74 ± 0.04</td>
<td>0.73 ± 0.03</td>
</tr>
<tr>
<td>FS</td>
<td>0 month</td>
<td>29.05 ± 0.69</td>
<td>29.42 ± 0.54</td>
</tr>
<tr>
<td></td>
<td>3th month</td>
<td>32.40 ± 1.37</td>
<td>29.71 ± 0.90</td>
</tr>
<tr>
<td></td>
<td>6th month</td>
<td>31.53 ± 1.44</td>
<td>30.84 ± 1.66</td>
</tr>
</tbody>
</table>

Values are mean ± SD. CON = control; E/A = Doppler mitral flow E/A ratio; EAP = electroacupuncture pretreatment; EDV = left ventricular end-diastolic volume; FS = fractional shortening; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; SV = stroke volume.

Table 2 Serum cTnI values at 24 h after PCI.

<table>
<thead>
<tr>
<th>cTnI value</th>
<th>CON (n = 102)</th>
<th>EAP (n = 102)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>cTnI (ng/mL)</td>
<td>0.01–0.05</td>
<td>0.01–0.02</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>0.10–0.15</td>
<td>0.09–0.10</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td>0.20–0.25</td>
<td>0.19–0.20</td>
<td>0.003</td>
</tr>
<tr>
<td></td>
<td>0.30–0.35</td>
<td>0.29–0.30</td>
<td>0.004</td>
</tr>
<tr>
<td></td>
<td>0.40–0.45</td>
<td>0.39–0.40</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>0.50–0.55</td>
<td>0.49–0.50</td>
<td>0.006</td>
</tr>
<tr>
<td></td>
<td>0.60–0.65</td>
<td>0.59–0.60</td>
<td>0.007</td>
</tr>
<tr>
<td></td>
<td>0.70–0.75</td>
<td>0.69–0.70</td>
<td>0.008</td>
</tr>
<tr>
<td></td>
<td>0.80–0.85</td>
<td>0.79–0.80</td>
<td>0.009</td>
</tr>
<tr>
<td></td>
<td>0.90–0.95</td>
<td>0.89–0.90</td>
<td>0.010</td>
</tr>
<tr>
<td></td>
<td>1.00–1.05</td>
<td>0.99–1.00</td>
<td>0.011</td>
</tr>
</tbody>
</table>

Values are mean ± SD. CON = control; cTnI = cardiac troponin I; EAP = electroacupuncture pretreatment; LVEDD = left ventricular ejection fraction; MI = myocardial infarction; MI4a = myocardial infarction type 4a.
patients compared to the control group (Fig. 4B). But PET/CT imaging demonstrated an obvious increase in arterial 18F-FDG standardized uptake value (SUV) in the anterior (5.68 ± 0.16 vs 6.82 ± 0.24, P = 0.039) but not posterior cardiac wall (5.58 ± 0.17 vs 5.82 ± 0.16, P > 0.05) in EAP patients compared to the control group (Fig. 4B).

### 3.7. PET/CT imaging

Owing to patients’ rejection (15 patients) and unsuitable serum glucose level (8 patients), ultimately 40 patients with left anterior descending coronary stenosis received PET/CT imaging pre- and at 3 days post-PCI. Two representative PET/CT images are shown in Fig. 4A. Except for the differences in man sex and smoker, the clinical characteristics, angiographic and peri-procedure data, and coronary artery stenosis severity of these 40 patients were similar between the EAP and control groups (Table S1). But PET/CT imaging demonstrated an obvious increase in arterial 18F-FDG standardized uptake value (SUV) in the anterior (5.68 ± 0.16 vs 6.82 ± 0.24, P = 0.039) but not posterior cardiac wall (5.58 ± 0.17 vs 5.82 ± 0.16, P > 0.05) in EAP patients compared to the control group (Fig. 4B).

### 4. Discussion

Previous studies have demonstrated that electroacupuncture pretreatment (EAP) not only protects the heart from ischemic injury in animal models [27,28], but also reduces overall serum cTnI levels after cardiac surgery in both adults [21] and children [22]. Our current prospective, randomized study in patients with CAD represents the first multi-center clinical trial evaluating the safety and efficacy of EAP in patients undergoing PCI. We demonstrated that EAP reduced the incidence of MI4a based on serum cTnI values (≥0.20 ng/mL) at 24 h after PCI, improved cardiac function 6 months after PCI, and decreased the MACCE rate at 24-month follow-up after PCI.

The preferred biomarker of myocardial injury, cTn (I or T) [25], has both high myocardial tissue specificity and sensitivity. Several studies demonstrated that PCI-related release of myocardial cTnI is associated with poor prognosis, especially in patients with markedly increased serum cTnI levels [14,15]. In 2012, the Joint ESC/ACC/AHA/World Health Federation defined a PCI-related myocardial infarction (MI type 4a) in patients undergoing PCI with normal (>99th percentile URL) baseline cTnI concentrations, as elevations of cTnI >5 × 99th percentile URL occurring within 48 h of the procedure [25]. The cTnI release is a solid predictor of PCI-related cardiovascular events [4], and was therefore chosen as the primary end point in the present trial. There was significantly less patients (30.4%) with cTnI values ≥0.20 ng/mL in the EAP group compared to 50% patients in control group at 24 h after PCI in the present study, which indicated less incidence of PCI-related MI (MI4a) in patients who received EAP. It is well-known that several factors, including stent length and acute lumen gain in vessel diameter, have been shown to be related to PCI-associated cTnI release [34]. However, the factors of stent length, acute vessel lumen gain, and contrast dosage were not significantly different between the EAP and control groups in this trial.

### Table 4

Multivariate logistic regression model of predictors of MACCE.

<table>
<thead>
<tr>
<th></th>
<th>MACCE n (%)</th>
<th>Odds ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>EAP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>11/102 (10.8%)</td>
<td>0.327 (0.140–0.767)</td>
<td>0.010</td>
</tr>
<tr>
<td>No</td>
<td>25/102 (24.5%)</td>
<td>2.912 (1.194–7.099)</td>
<td>0.019</td>
</tr>
<tr>
<td>Previous MI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>14/37 (37.8%)</td>
<td>2.195 (0.939–5.130)</td>
<td>0.069</td>
</tr>
<tr>
<td>No</td>
<td>22/167 (13.2%)</td>
<td>0.941 (0.407–2.176)</td>
<td>0.887</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>12/50 (24.0%)</td>
<td>1.103 (0.408–2.982)</td>
<td>0.847</td>
</tr>
<tr>
<td>No</td>
<td>24/154 (15.6%)</td>
<td>1.001 (0.962–1.042)</td>
<td>0.951</td>
</tr>
<tr>
<td>Men sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>28/148 (18.9%)</td>
<td>59.9 ± 10.1</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>8/56 (14.3%)</td>
<td>60.1 ± 9.5</td>
<td></td>
</tr>
</tbody>
</table>

Values are mean ± SD or n (%). CI = confidence interval; EAP = electroacupuncture pretreatment; MACCE = major adverse cardiac/cerebrovascular events; MI = myocardial infarction.
It is well-known that coronary stent implantation elicits local and systemic inflammatory responses and induces the release of multiple inflammatory mediators whose intensity and magnitude are associated with an adverse clinical outcome and increased rate of stent re-stenosis [35,36]. TNF-α, hs-CRP, IL-6, and HMGB1 are well described as pro-inflammatory mediators, while IL-10 predominantly acts as an anti-inflammatory cytokine [37]. In this trial, the plasma levels of TNF-α and IL-6 in the EAP group were significantly lower whereas the levels of IL-10 were markedly higher than those in the control group, indicating the anti-inflammatory effects of EAP stimulation. Acupuncture was reported to exert anti-inflammatory actions through central inhibition of the innate immune system in animals [38]. Moreover, a systematic review concluded that endogenous cannabinoids impact the immune response system and then affect the function of the cytokine network [39]. Our previous studies verified that the endocannabinoid system and its downstream molecular pathways play an important role in EAP-induced protective effects against ischemia–reperfusion [40–42].

Based on the evidence gathered from animal studies [43,44], it is possible that acupoint stimulation at P6 decreases the myocardial metabolism and subsequently slows the energy consumption, resulting in the attenuation of myocardium ischemic injury. To assess the effect of EAP on myocardial metabolism, we screened SUV changes pre- and at 3 days post-PCI in 40 patients with left anterior descendant coronary disease by PET/CT imaging. Our data revealed significantly increased SUV in the anterior wall in the EAP group compared to control, providing evidence to support the beneficial effects of EAP by reducing myocardial metabolism after PCI. It was reasonable to deduce that EAP prior to PCI may attenuate early myocardial injury, enhance the resolution of early inflammatory response and improve the myocardial metabolism at early stage, which led to the subsequent improvements in cardiac function and the reduction in MACCE rate in patients undergoing PCI during a 24-month follow-up. Moreover, multivariate analysis

Fig. 3. Representative PET/CT imaging in two patients with left anterior descendant coronary stenosis at pre-PCI and at 3 days after PCI. A. Rest myocardial metabolism PET images (top two rows) and representative transverse section from a cardiac CT scan (bottom) obtained from a 56-year-old man in the EAP group and a 58-year-old man in the control group. PET/CT reveals focal uptake in the anterior wall of myocardium (white arrows). B. The standardized update value (SUV) of the anterior, but not posterior, wall increased significantly in patients receiving EAP compared to control (n = 40, P = 0.039). EAP = electroacupuncture pretreatment; PCI = percutaneous coronary intervention; PET/CT = positron emission tomography/computed tomography.
showed that EAP was associated with decreased likelihood of MACCE, which further indicated that EAP pretreatment as an independent factor might reduce the MACCE rate in patients undergoing PCI.

In the “real-world”, patients enduring complex coronary artery disease often have significant co-morbidities such as hypertension, peripheral vascular disease (e.g., arteriosclerotic occlusion), or peripheral circulatory disturbances (e.g., diabetes mellitus). Such patients are clearly ineligible for remote ischemic preconditioning prior to PCI. In the present trial, EAP was safely used in 24.5% patients with diabetes and 47.1% of patients with hypertension, suggesting the safe use of EAP for patients with the above-noted co-morbidities.

We recognize the limitations of our present trial. Our main results found that EAP prior to PCI reduced the incidence of myocardial infarction after PCI, in which the serum cTnI level was reduced in patients with complex coronary lesions. However, the difference of cardiac function and MACCE rate in subgroups was not analyzed due to the relatively small patient sample size. It must be emphasized here that the subgroups in our study consisted of patients with complex coronary lesions that were prone to develop severe myocardial injury, therefore they should have pronounced treatment effects, if any, that are easier to detect. In addition to that, the protective effects of EAP in different pathological conditions, such as those with diabetes and hypertension, need further investigations, and the detailed underlying mechanisms should also be explored.

In conclusion, the present multi-center trial provides the first evidence that EA prior to PCI significantly reduces peri-procedural cardiac injury and MACCE rate at 24 month follow-up after PCI. EAP can be safely and non-invasively employed in patients with relatively complex coronary lesions, hypertension, or diabetes. Our data strongly indicate that this simple maneuver may be considered in all patients undergoing PCI procedure after large clinical trials are needed to clarify whether those effects can be translated into improved clinical outcome.

Disclosures

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Conflict of interest statement

The authors have no conflict of interests to declare.
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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ijcard.2015.05.043.

References

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