Short-term effects of enhanced external counterpulsation on transthoracic coronary flow velocity and reserve in patients with coronary slow flow ☆

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To the Editor:

Coronary slow flow (CSF) phenomenon, which is characterized by delayed opacification of epicardial coronary arteries in the absence of stenotic lesion, is a relatively common finding in patients undergoing routine coronary angiography and is often associated with chest pain. There are no definite treatment modalities for patients with CSF to date, and conventional antianginal therapy is of limited value in the chronic management of these patients. Enhanced external counterpulsation (EECP) has become one of the most effective noninvasive treatment methods for patients with refractory angina [1], and has been considered a new modality in management of cardiac syndrome X [2,3], whether it is effective for treating CSF remains unclear. This is a prospective study to investigate the effects of EECP on coronary flow velocity (CFV) and coronary flow reserve (CFR) assessed by transthoracic Doppler echocardiography (TTDE) in patients with CSF.

From January 2008 to October 2010, we prospectively enrolled 85 consecutive patients with angiographically documented CSF, based on thrombolysis in myocardial infarction (TIMI) frame count (TFC). Subjects with structural heart disease, atrial fibrillation or other arrhythmia that would interfere with EECP triggering were excluded. In all of the initially evaluated 85 patients, 15 were excluded for any of the above exclusion criteria, and 31 refused to participate in this study. TTDE was successfully performed in the 39 remaining patients within 1 week after coronary angiography. These patients were nonrandomly assigned to two groups according to the patients' choice by themselves. Patients in the control group received only standard medical therapy, and those in the EECP group were additionally treated with the 36 one-hour sessions of EECP. Each patient gave written informed consent to the study. Thirty-seven patients successfully completed the protocol and constituted the study population, 18 in the EECP group and 19 in the control group. TTDE examination was repeated after 8 weeks of medical/EECP therapy.

Canadian Cardiovascular Society angina class (CCS) was determined before and after completion of the study by an independent observer, who was blinded to the treatment modalities and the angiographic and echocardiographic data of the individual participants.

EECP treatment was given 1 h daily up to a total of 36 h, scheduled 6 days/week for 6 weeks. During the period of EECP treatment and the following 2 weeks, patients were instructed to continue their usual medications.

Selective coronary angiography was performed using standard Judkins technique, and all angiograms were filmed at a speed of 30 frames/s. Coronary flow was quantified objectively by observers who were blinded to the clinical details of the individual participants, using the TIMI frame count method [4]. The mean TFC for each patient was calculated by dividing the sum of the TFC of LAD, LCX and RCA by 3. All participants with a TFC greater than two standard deviations from the normal published range for the particular vessel were accepted as having CSF.

Coronary blood flow in the LAD (middle to distal) was searched by TTDE. All subjects had Doppler recordings of the LAD with an intravenous adenosine infusion at a rate of 0.14 mg/kg/min over 4 min. The spectral Doppler signals during resting and hyperemia were both recorded by TTDE over five cardiac cycles at end-expiration. Coronary diastolic peak flow velocities (DPFV) were measured at resting and after adenosine by averaging the highest 3 Doppler signals for each measurement. CFR was defined as the ratio of hyperemic to resting DPFV. Each study was analyzed by the same experienced investigator who was unaware of the treatment modalities and the angiographic data of the patients.

The two groups were similar for age, gender, cardiovascular risk factors, blood pressure, heart rate, and left ventricular function. There were no differences in characteristics for the use of medications between the two groups.

There was an excellent inverse correlation between rest DPFV and TFC for LAD ($r = -0.87$, $p < 0.001$), and CFR was inversely correlated with mean TFC ($r = -0.72$, $p < 0.001$).

After treatment, angina relief as improved at least one CCS class was detected in 14 patients in the EECP group and in 7 in the control group (77.8% vs. 36.8%, $p = 0.01$). CCS angina class significantly improved from 2.94 ± 0.73 to 1.83 ± 0.86 in the EECP group ($p < 0.001$), whereas it didn't statistically improve in the control group (2.79 ± 0.71 to 2.47 ± 0.90, $p = 0.137$).

In the EECP group, rest DPFV, hyperemic DPFV and CFR were significantly increased after therapy (20.23 ± 4.47 vs. 24.12 ± 4.40, $p = 0.007$; 40.82 ± 15.57 vs. 57.93 ± 14.88, $p < 0.001$; and 1.96 ± 0.41 vs. 2.42 ± 0.52, $p < 0.001$), whereas in the control group, those variables were not statistically increased after therapy (21.26 ± 4.48 vs. 21.91 ± 4.23, $p = 0.299$; 43.73 ± 14.42 vs. 46.17 ± 13.91, $p = 0.214$; and 2.02 ± 0.32 vs. 2.10 ± 0.44, $p = 0.395$).

This is the first study undertaken to investigate the effects of EECP on coronary blood flow in patients with CSF. Our results indicated that EECP is effective for improving coronary flow velocity, as shown by the

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increased resting and hyperemic DPFV and CFR measured by TTDE after EECP therapy. The improvement in coronary blood flow is consistent with angina relief.

The correlations between CFV measured by TTDE and angiographic TFC have not been fully elucidated in patients with CSF. Our present study demonstrated that there was an excellent inverse correlation between resting DPFV and TFC for LAD, and CFR was inversely correlated with mean TFC, which are consistent with the results reported by Caliskan et al. [5]. These results suggested that CFV and CFR measured by TTDE could be reliable indices for assessing patients with CSF.

The mechanisms responsible for improving coronary blood flow of EECP are unclear. As an effective noninvasive treatment method for patients with coronary artery disease, EECP has been proved to exert various beneficial effects on cardiovascular system, such as increasing coronary perfusion pressure and the arterial wall shear stress, improving endothelial function, decreasing inflammation, promoting vascular remodeling, triggering angiogenesis, improving microvascular dysfunction, and ameliorating blood rheology [6]. All these effects may help to improve coronary flow in patients with CSF.

We should acknowledge some limitations of this study. It is not a randomized and sham-controlled study for practical reasons, although the baseline data between groups were comparable. The second limitation is the lack of repeat angiographic measurements after therapy. In addition, long-term follow-up studies powered on clinical outcomes are warranted to confirm the efficacy of EECP for treatment of CSF.

In conclusion, EECP is effective for improving coronary flow velocity and coronary flow reserve in patients with coronary slow flow. EECP may be considered an effective new therapeutic modality in the management of coronary slow flow, and larger randomized and sham-controlled clinical studies are warranted to confirm the findings of this study.

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Cardiopulmonary exercise testing for the assessment of exercise capacity in patients with cardiac syndrome X

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Patients with cardiac syndrome X (CSX) often have a reduced exercise capacity and many complain of extreme fatigue during mild exertion and/or after prolonged chest pain episodes [1]. It is not known, however, whether this reduced exercise tolerance and symptoms of fatigue correlate with exercise capacity, as assessed objectively by cardiopulmonary exercise testing (CPET). CPET is known to be useful for the clinical assessment of patients with heart failure and has more recently been shown to be able to detect functional cardiovascular abnormalities in patients with coronary artery disease [2–4].

In the present study we assessed the relationship among fatigue and CPET responses in CSX patients and control individuals. We studied 31 patients (mean age 54 ± 7 years, 28 women) with CSX and 30 apparently healthy subjects (mean age 51 ± 6 years, 24 women) recruited among the medical and nursing staff in our institution. A standardized questionnaire was administered to all participants to obtain information regarding conventional cardiovascular risk factors and pharmacological treatment. All participants were also asked to complete a validated 11-item self-rating fatigue questionnaire [5]. Fatigue scores ranged from 0 (no fatigue symptoms) to 11 points (severe fatigue) and patients were prospectively subdivided into two subgroups, low fatigue score (0–4 points) and high fatigue score (5–11 points) [5]. All subjects enrolled underwent a CPET. Peak oxygen uptake (VO_2) was defined as the average value obtained during the last 30 seconds of exercise. The anaerobic threshold (AT) was determined by the V-slope method [2]. The study protocol was approved by the local Ethics Committee. All participants signed written informed consent before study entry.

Results are presented as mean ± 1 standard deviation and as percentages for categorical data. Analysis of normality was performed

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