Enhanced external counterpulsation improves systolic function by echocardiography in patients with coronary artery disease

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The clinical benefits of enhanced external counterpulsation (EECP) for patients with refractory angina pectoris have been well established.[1-5] The mechanisms by which this clinical benefit occurs, however, has not yet been clearly elucidated. Improved systolic and diastolic function by way of recruitment of coronary collateral vasculature is one plausible mechanism. EECP is a noninvasive technique that provides augmentation of diastolic coronary blood flow similar to the intraaortic balloon pump and uses the serial inflation of 3 sets of cuffs that wrap around the calves, thighs, and buttocks. Inflation and deflation is timed to the patient's electrocardiogram, and the arterial pressure waveform is monitored noninvasively. The overall hemodynamic effect is to provide diastolic augmentation and thus increase coronary perfusion pressure and to increase venous return and, subsequently, cardiac output.[6,7] This therapy is also presently being explored as a treatment for patients with congestive heart failure and left ventricular dysfunction.[8-10]

METHODS

We examined 14 consecutive patients with coronary artery disease and refractory angina pectoris. Patients selected for EECP treatment were eligible if they met the following criteria: (1) age between 21 and 81 years; (2) symptoms consistent with Canadian Cardiovascular Society Classification angina levels I, II or III; (3) documented evidence of coronary artery disease; and (4) exercise treadmill test (ETT) positive for ischemia. Patients were excluded if they had medical conditions that contraindicated EECP or that might interfere with study. The subjects received 35 hours of EECP treatment (Figure 1). All patients underwent resting and dobutamine stress echocardiography (DSE) before and after EECP therapy. Two-dimensional and Doppler echocardiography examinations were performed with Acuson Sequoia machines (Mountain View, CA) equipped with a variable-frequency phased-array transducer (2.5 to 3.5 to 4.0 MHz). One physician blinded to the echocardiographic examination results estimated the measurements. Consequently, coded 2 dimensions and Doppler echocardiography were recorded on s-VHS videotape. Two readers examined all tracings, and a average of 5 cardiac cycles was used to minimize differences during the breath cycle. We measured left ventricular systolic function and left ventricular diastolic function parameters. Left ventricular ejection fraction (LVEF) was measured by Simpson's rule at rest and at peak stress. In addition, we investigated multiple diastolic parameters including isovolumic relaxation time, peak mitral velocity of E- and A-waves, and E/A ratio. Isovolumic relaxation time was recorded as the interval between aortic closure and mitral opening click.

STUDY PROTOCOL

Resting and DSE was performed before and after 35 1-hourly sessions of EECP. On the day of examination, the patients abstained from nitrates and β-blockers. A perfuser was used to ensure continuous intravenous infusion of dobutamine starting at a dose of 5 μg/kg body weight/min. The dose was increased by 10 μg/kg body weight/min every 3 minutes to obtain doses of 20, 30, and a maximum of 40 μg/kg body weight/min to obtain the desired heart rate (220.0 − age × 0.85). Images were obtained before starting the infusion (resting), before each incremental increase, at the end of infusion, and after 2 and 6 minutes of recovery (postinfusion). At the end of study, 0.25-mg doses of atropine were administered as needed to achieve the desired

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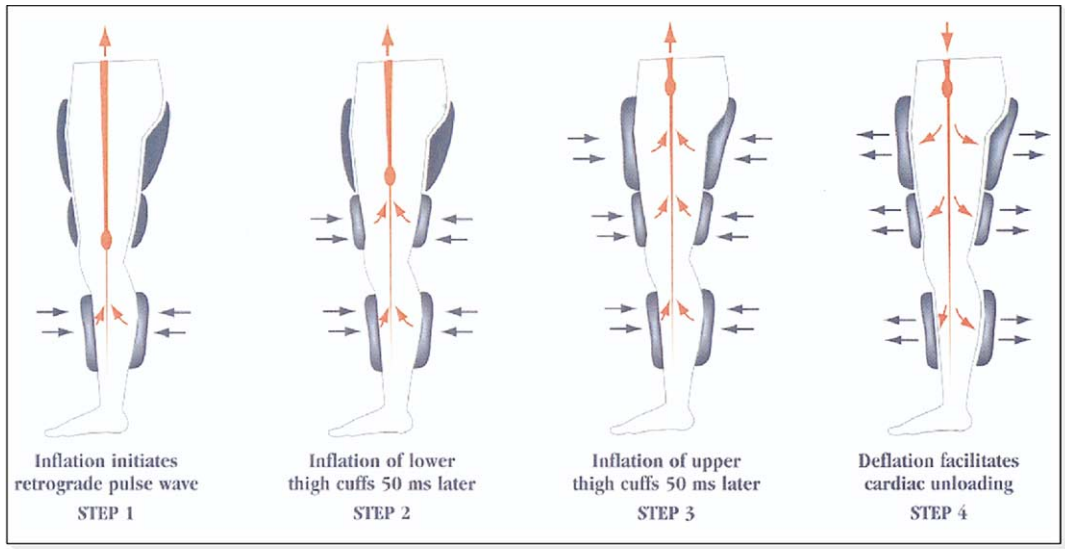

Fig 1 Principles of EECP. Series of three cuffs inflate—timed with the cardiac cycle—at the calf, thigh and buttock levels.

heart rate. The local ethics committee at our institution approved the study protocol. Written informed consent form was obtained from all the patients.

STATISTICAL ANALYSIS

SAS (Cary, NC) software was used to analyze the data. This was a nonprobability example. All variables were presented as mean ± SD. To determine if pre-EECP and post-EECP values were significantly different, paired Student *t* test was performed.

RESULTS

All patients experienced an increase in LVEF at both rest and peak stress as a result of EECP treatment. Mean resting LVEF increased from 47.2% before EECP to 52.1% after EECP ($P < 0.000001$) (Figures 2 and 3). Mean peak stress LVEF increased from 65.3% before EECP to 70.3% after EECP ($P < 0.000001$). No statistically significant difference was observed for any of the diastolic parameters (Tables I through III). The mean highest dobutamine dose used in DSE was 25 μg/kg body weight/min + 5 μg/(+ SD).

DISCUSSION

Together with earlier reported results of improved hemodynamic parameters,[7-12] our findings suggest improved systolic function contributing to the benefit with EECP. EECP has been shown to

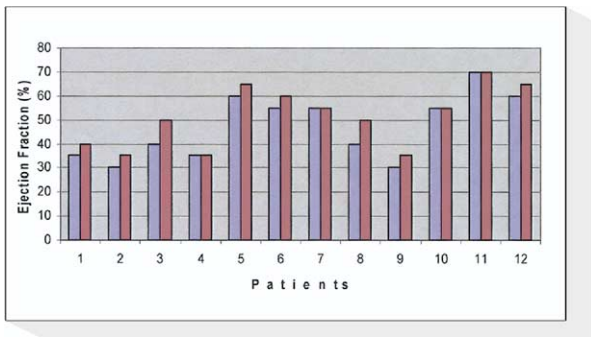

Fig 2 Visual estimate. Resting LVEF, before and after EECP.

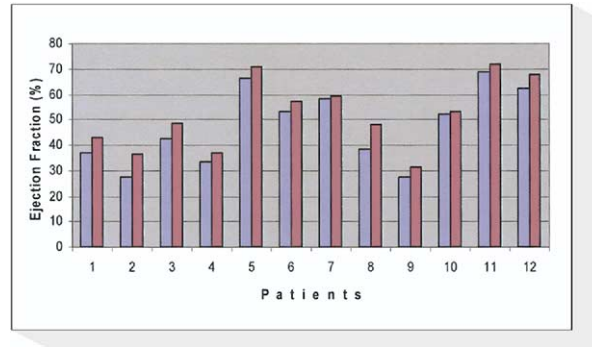

Fig 3 Simpson's rule. Resting LVEF, before and after EECP.

Table I
Left ventricular diastolic function values at rest and peak stress

	Pre-EECP	Post-EECP	*P* value
IVRT (ms)	82.5 ± 16.7	76.6 ± 20.2	NS
E-wave (cm/s)	0.77 ± 16.7	0.76 ± 0.24	NS
A-wave (cm/s)	1.05 ± 0.29	1.07 ± 0.31	NS
E/A	0.83 ± 0.15	0.73 ± 0.07	NS

EECP, Enhanced external counterpulsation, *IVRT,* isovolumic relaxation time; *NS,* not significant.
Values presented as mean ± SD.

Table II
Left ventricular systolic function: average LVEF by visual estimate

	Rest	Peak
Pre-EECP (%)	47.1 ± 14.9	63.6 ± 14.2
Post-EECP (%)	51.2 ± 12.6	68.1 ± 14.1
P value	.000001	.000001

EECP, Enhanced external counterpulsation; *LVEF,* left ventricular ejection fraction.
Values presented as mean ± SD.

Table III
Left ventricular systolic function: average LVEF by Simpson's rule

	Rest	Peak
Pre-EECP (%)	47.2 ± 14.9	65.3 ± 15.4
Post-EECP (%)	52.1 ± 13.8	70.3 ± 15.0
P value	.000001	.000001

EECP, Enhanced external counterpulsation; *LVEF,* left ventricular ejection fraction,
Values presented as mean ± SD.

decrease afterload and promote venous return, thereby enhancing cardiac output by up to 25%.[11-14] Indirect evidence of improvement of ventricular function was demonstrated in 2 smaller studies in patients in whom decreased atrial natriuretic factor and brain natriuretic peptide plasma levels were decreased in patients with stable angina pectoris. In a study by Urano et al[12] in patients with stable refractory angina, EECP treatment did not alter systolic LV function, but it did significantly improve parameters of diastolic ventricular function. However, in the present study we did not see a difference in these parameters. Another study[10] of 8 patients with severely impaired LVEF (mean 25%) showed an increase in EF (up to 29%) associated with a significant decrease in resting heart rate after EECP treatment. The present study demonstrated that even in the presence of normal to mild left ventricular dysfunction, EECP augmented EF from 47% to 52% at rest and from 65% to 70% at peak exercise without alteration in systolic blood pressure and heart rate. Therefore, EECP treatment may have a positive effect on systolic function, but its effect on diastolic function must be elaborated in larger studies. Preliminary data from clinical studies show that EECP represents a safe and effective treatment in patients with impaired left ventricular function.[8-10] The salutatory response seen in these studies may in part have been mediated by augmenting systolic function.

LIMITATIONS

The results, conclusions, and impact of this study are tempered by its limitations, namely small population size and no parallel control intervention (eg, clinic visits without EECP). The echocardiograph readers were blinded to the name, date, and whether the study was performed before versus after EECP.

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