REVIEW PAPER

Enhanced External Counterpulsation

Leslie Lam, FRCP, Shahid Mahmood, FACC

Mount Elizabeth Hospital
Singapore

ABSTRACT

Enhanced external counterpulsation is a noninvasive technique designed to increase myocardial perfusion and reduce cardiac workload in patients with coronary artery disease. Recent trials have documented beneficial hemodynamic effects. Stress testing and radionuclide imaging have demonstrated improvemements in functional capacity and myocardial perfusion. This procedure may be the therapeutic choice for patients with severe diffuse disease or in whom repeat revascularization is not possible. The relatively low cost of the technique makes it feasible for patients in developing countries.

(Asian Cardiovasc Thorac Ann 2003;11:92–4)

INTRODUCTION

Coronary artery disease is still a major cause of mortality worldwide. The management of coronary artery disease has been revolutionized during the last two decades. Coronary stenting, atherectomy, minimally invasive coronary bypass graft surgery, angiogenesis, and transmyocardial laser therapy are among the innovations. Many patients with coronary artery disease pose a challenge in the management of their symptoms. Primary or repeat revascularization may not be appropriate, and some may not respond to maximal medical management. In such patients, enhanced external counterpulsation (EECP) may be considered as an alternative nonpharmacologic therapy.

TECHNIQUE AND HISTORY

The procedure of EECP has evolved over time, based upon the old theory that an increase in diastolic perfusion pressure may lead to an increase in coronary blood flow by 20%–40%.[1] The concept could not initially be adopted into routine clinical practice, and by the 1980s, most cardiologists considered that the technique was inappropriate. At the same time, the first pneumatic type of counterpulsation device was being developed in China.[2] After initial encouraging results, an improved version was made in the United States, and the results of the first major study were reported in 1992.[3] The EECP technique involves sequential inflation and deflation of compression cuffs wrapped around the lower extremities. The cuffs are inflated in turn from calf to thigh to buttock, proximally during diastole, with rapid deflation of all cuffs at the beginning of systole (Figure 1). The mechanism is similar to that of intraaortic balloon pumping to augment diastolic pressure. Theoretically, by increasing venous return, EECP raises diastolic aortic pressure and cardiac output. Augmenting aortic diastolic pressure increases coronary perfusion pressure (aortic diastolic pressure minus left ventricular intracavitary pressure) and consequently coronary flow. The increases in coronary pressure and flow cause an increase in shear stress within the coronary arteries. It has been postulated that EECP stimulates endothelial-mediated intramyocardial vessel growth, or restoration of flow reserve, or a combination of both. Since the EECP response is achieved by diastolic augmentation, it is conceivable that it might not be possible to raise the diastolic pressure in patients with severe left ventricular dysfunction. In such cases, there might be no improvement or even worsening if diastolic augmentation is not greater than the systolic wave. Between 5% and 10% of the patient population may have a diastolic wave equal to or lower than the systolic wave.[2] Thus, the effectiveness of EECP is directly related to the degree of augmentation of diastolic aortic pressure (Figure 2) and can be derived from the formula:

EECP effectiveness ratio = diastolic augmented amplitude/ systolic amplitude

For reprint information contact:
Leslie Lam, FRCP Tel: 65 67321881 Fax: 65 67361652 email: cardiac@singnet.com.sg
Cardiac Centre, Mount Elizabeth Medical Centre, Singapore 228510.

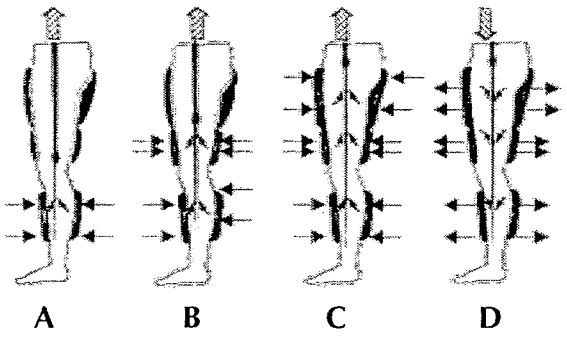

Figure 1. Enhanced external counterpulsation: inflation of the lower cuff initiates a retrograde pulse wave **(A)**, followed by inflation of the lower thigh cuff 50 msec later **(B)**, and then the upper thigh cuff **(C)**. At the end of diastole, all cuffs are deflated simultaneously to facilitate cardiac unloading **(D)**.

Normally, the therapy is given for 35 hours, in a 1- or 2-hour regimen daily. The treatment is carried out on 5 days per week for 4 to 7 weeks.

CLINICAL APPLICATION

The relief of anginal pain is one of the objectives of treating coronary artery disease. Several studies have shown the usefulness of EECP in improving exercise performance and reducing myocardial ischemia in patients with Canadian Cardiovascular Society grade 2 or 3 stable angina.[4–8] In a 5-year follow-up study of patients treated with EECP, the long-term prognosis was evaluated by Lawson and colleagues[9] who reported 64% survival without a major cardiac event. Although 61% of patients had prior revasculaization (coronary artery bypass surgery or a percutaneous intervention), it was not predictive of the response to EECP therapy. The effect may be due to increased exercise tolerance in these patients. Possibly, there is induction of myocardial collateral flow caused by increased pressure differentials between the ischemic and nonischemic regions of the myocardium through endothelial cell-mediated vessel formation.[7] In another comparative study, it was found that prior revascularization definitely improved the benefit of EECP in patients with triple-vessel disease.[10] Figure 3 shows a typical example of the improvement in stress perfusion after EECP therapy.

The diastolic augmentation produced by EECP greatly increases pulsatile shear stress on the intima. Multiple endothelial responses to stress have been reported, including expression of platelet-derived growth factors A and B along with fibroblast growth factor-2, which result in structural changes in blood vessels.[8] In addition, activation of pathways affecting actin cytoskeleton leads to endothelial cell migration. Whether or not angiogenesis or vasculogenesis is produced by EECP is still a subject of controversy, however, it has an effect on endothelial function. Initial data suggest that during EECP treatment, levels of

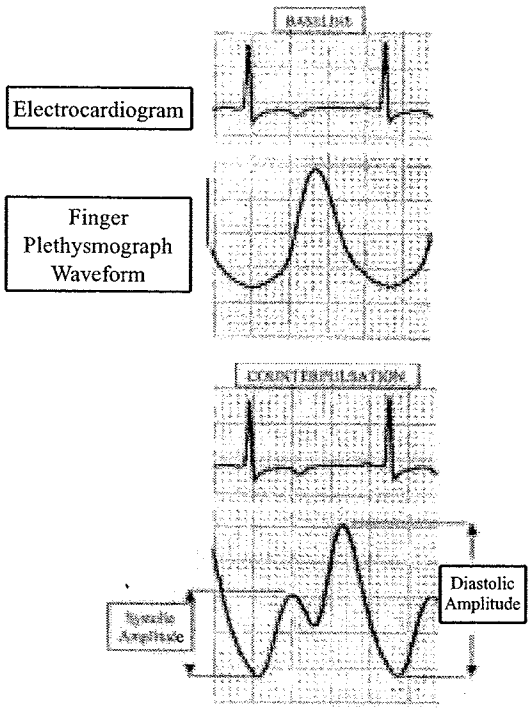

Figure 2. Electrocardiograms and pressure waveforms before and during enhanced external counterpulsation: at the onset of diastole, venous return is increased due to peripheral cuff pressure, leading to a higher diastolic waveform amplitude.

vascular endothelial growth factors and nitric oxide are raised, while those of endothelin are lowered.[12]

Improved technology has made it possible to quantify coronary perfusion and flow reserve. In a recent study, Masuda and colleagues[13] evaluated myocardial perfusion in patients, using N^{13}-ammonia positron emission tomography. The quantification was made at rest and after dipyridamole infusion, before and after therapy. Myocardial perfusion and flow reserve improved after treatment with EECP. Increased nitric oxide levels were also observed, which related to an increase of endothelial nitric oxide synthase.[13] A multicenter study on EECP in males demonstrated a significant improvement in exercise duration, without a change in the double product.[14] It was postulated that improved perfusion post-EECP is not related to a change in oxygen demand but to collaterals or angiogenesis; in 175 patients, no worsening of perfusion was reported.[14] However, in our experience with EECP, we noticed a mild worsening of perfusion in a few patients who had improved exercise capacity after EECP. Interestingly, a greater degree of improvement in perfusion was noted in patients who had undergone prior angioplasty.[14] This suggests that use of EECP in patients who have undergone an intervention may reduce the risk of restenosis. A well-controlled trial is warranted to evaluate this potential benefit. At least one study has demonstrated the safety of EECP one month after interventional procedures.[15]

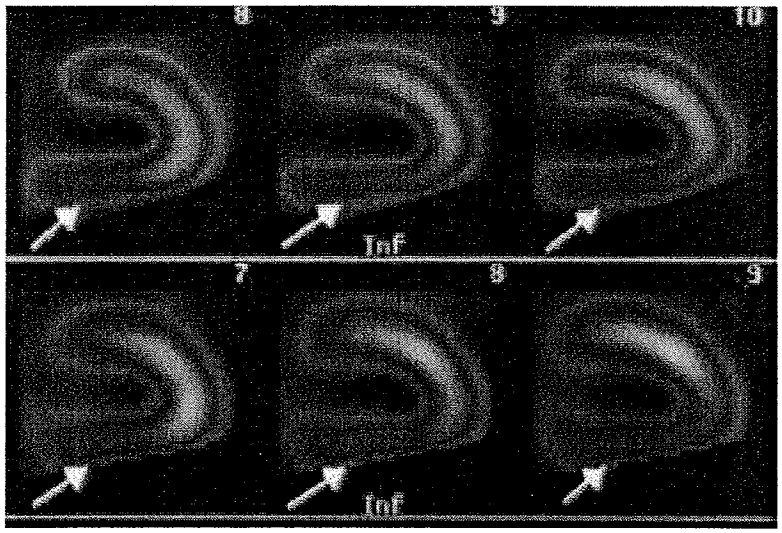

Figure 3. Myocardial perfusion images: stress perfusion tomographic slices before **(A)** and after **(B)** enhanced external counterpulsation. This patient had prior coronary bypass grafting. Substantial improvement in the inferior wall is obvious. Exercise capacity improved by 55 sec, and left ventricular function improved by 5%.

Although the current results of EECP appear promising, more studies are required to establish its role in the management of coronary artery disease. Further studies are needed to confirm whether levels of endothelial-derived factors are altered by EECP treatment. If proven, long-term benefit may occur through restoration of the vascular response to oxygen demand or improved flow autoregulation. In the United States, EECP therapy is now covered under Medicare. Nevertheless, contraindications for the technique (uncontrolled heart failure, severe pulmonary hypertension, uncontrolled systemic hypertension, aortic insufficiency, coagulopathy, thrombophlebitis, and uncontrolled arrhythmias) should be born in mind. The cost of treating angina refractory to medical therapy or revascularization is too high. In developing countries, the choices are further limited due to lack of technology. Potentially, EECP is a simple, noninvasive, cost-effective, and beneficial mode of treating such patients.

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