Enhanced External Counterpulsation: A New Therapeutic Option for Patients Who Have Failed Coronary Angioplasty and/or Bypass Surgery

There are many patients in whom repeat (or initial) PTCA and/or CABG are not appropriate—and in whom aggressive medical therapy still fails to maintain a quality of life that patients are comfortable with. EECP is 1 of several new treatment alternatives for such patients. In our initial studies, 18 patients were treated with EECP for 1 hour daily for a total of 36 hours. All 18 patients experienced substantial improvements in anginal symptoms after EECP. Thallium-201 stress testing showed a complete resolution of ischemic defects in 12 patients (67%), a decrease in the area of ischemia in 2 patients (11%), and no change in 4 patients (22%). The long-term, sustained efficacy of EECP was confirmed in a 3-year follow-up study. One possible explanation for the improvement in perfusion that we observed is that EECP may open, or enhance the development of, collateral channels when at least 1 patent conduit (native vessel or bypass graft) is present. The importance of having such a conduit was emphasized in our most recent study of 50 patients, all of whom underwent coronary angiography before EECP.

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Each year for the past decade, hundreds of thousands of patients in the United States have undergone PTCA or CABG. Many of these patients often require repeat procedures within months or years, but in some of them there is a limit to how many repeat revascularization attempts will be attempted, based on the patient's coronary anatomy, conduit availability, left ventricular function, age, comorbidity, etc. For those patients in whom repeat (or initial) PTCA and/or CABG are not appropriate—and in whom aggressive medical therapy still fails to maintain a quality of life that patients are comfortable with—several alternative therapies have been investigated. These fall into 2 broad categories: 1) technologies to reduce angina pain by neural stimulation and 2) procedures that may enhance myocardial perfusion. Although there are several methods available to block pain associated with cardiac ischemia (sympathectomy, autotransplantation, or transcutaneous electrical nerve stimulation), the most encouraging approach may well be in direct spinal cord stimulation. Two recent studies have shown not only a decrease in angina but an improvement in exercise test parameters[1,2] after insertion of a pulse generator in the epidural space. There are 3 types of procedures currently used to increase myocardial perfusion; 2 are invasive and 1 is noninvasive. The invasive procedures include long-term intermittent intravenous therapy with urokinase[3,4] and transmy-

ABBREVIATIONS AND ACRONYMS

CABG	Coronary artery bypass graft
ECG	Electrocardiogram
EECP	Enhanced external counterpulsation
PTCA	Percutaneous transluminal angioplasty

ocardial laser revascularization,[5] an operation which utilizes the myocardial sinusoids to create new channels to deliver blood to the myocardium. Results in early studies show promise with this technique but more research is needed.

EECP: Historical Background

The other procedure that can increase myocardial perfusion and the one that this review will concentrate on is EECP, a noninvasive technique originally used over 20 years ago, the same time period that saw the introduction of the intraaortic balloon. Although external counterpulsation is not new and its initial clinical results were limited, it has been modified sufficiently in recent years to warrant reevaluation by clinicians, especially those who treat patients with chronic angina.

EECP involves the inflation of a series of compressive balloons, with compressions timed to the patient's ECG (Fig. 1). The device increases myocardial oxygen supply by increasing diastolic perfusion pressure and reduces cardiac workload by decreasing left ventricular afterload. In the early 1980s, Chinese investigators reported on their extensive experience in treating angina patients with an enhanced version of the original device using 3 cuffs, rather than the original 2, and employing sequential calf-to-thigh counterpulsation and a pneumatic, rather than hydraulic, compressing medium.[6] The new system can augment the diastolic pressure much more significantly than the previous system could. Their favorable results prompted investigators at Stony Brook to assess the efficacy of EECP in producing sustained benefits in a population of patients with chronic angina refractory to conventional therapy. Specifically, we were interested in learning whether the hemodynamic changes produced by EECP resulted in a sustained reduction in exertional ischemia and anginal symptoms, as well as an improvement in exercise tolerance. To answer this question, thallium imaging was used to document the degree of exertional myocardial ischemia before and after EECP treatment. The change in functional status after EECP was assessed by anginal diaries and symptom-limited stress testing.

EECP was performed by compressing the vascular beds within the muscles of the legs and thighs, including the buttocks, in a sequential manner, progressing from the calves to the lower and then upper thighs. The compression was accomplished by introducing air into 3 sets of balloons. The timing of the compression was controlled by the patient's ECG, so that increased blood flow and blood pressure would reach the coronary vessels during diastole at the time of lowest intramyocardial tension. In addition, compression of the venous bed of the lower extremities increased venous return. The external pressure was then released during systole, causing systolic unloading and decreasing cardiac workload. The net effect of increased venous return and systolic unloading caused marked increases in cardiac output as demonstrated by echocardiographic Doppler studies.[7]

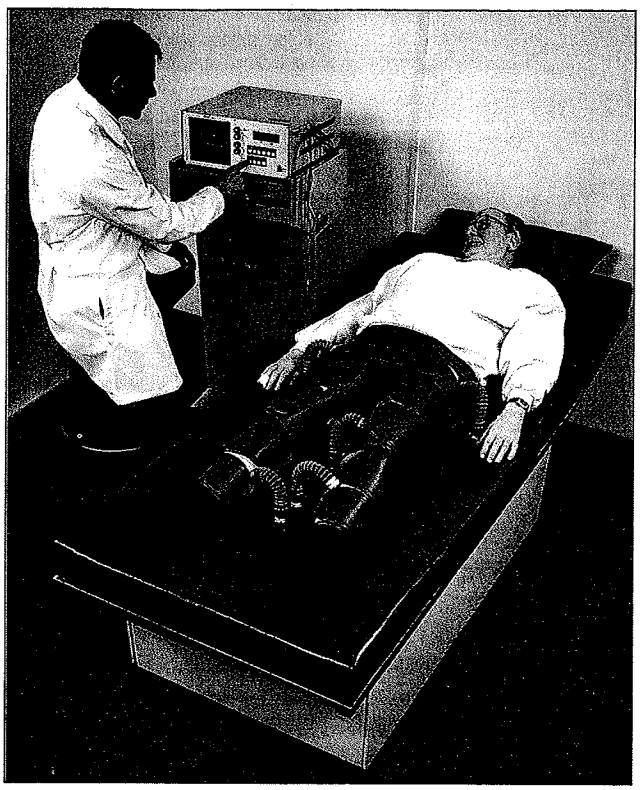

Figure 1. EECP device with ECG and finger plethysmography console. Photo courtesy of Vasomedical, Inc.

Initial Studies at Stony Brook

In our studies conducted between 1989 and 1991, 18 patients (17 men and 1 woman) were treated with EECP for 1 hour daily for a total of 36 hours.[8] The 18 patients chosen for study had chronic stable angina despite medical and surgical therapy. Other patients were excluded because of clinical congestive heart failure, aortic insufficiency, a myocardial infarction within the previous 3 months, significant ventricular ectopic activity or atrial fibrillation, nonischemic cardiomyopathy, severe occlusive peripheral vascular disease, recurrent deep vein thrombophlebitis, systemic hypertension (> 180/110 mm Hg), or a bleeding diathesis. All patients were monitored hemodynamically and clinically during treatment. Diastolic augmentation pressures were progressively increased by increasing the external compression. The highest

continued on page 16

Cohn continued from page 11

external pressure used to maximize the diastolic/systolic pressure ratio (diastolic augmentation) was 280 mm Hg. Blood pressure waveforms were continuously monitored by finger plethysmography.

Adjustments in anginal medications and other risk factor modification changes were determined by patients and their physicians during the course of the study. No other therapeutic interventions were performed during the study.

After completing the course of EECP therapy, patients underwent a thallium-201 stress test (with their usual medications continued). Although exercise duration was the same as that during baseline testing (so as to provide a valid comparison of imaging test results), a maximal symptom-limited stress test was also performed within 1 week of cessation of EECP treatment to assess exercise tolerance.

All 18 patients experienced substantial improvements in anginal symptoms after EECP; 16 were completely free of angina during the usual activities of daily living. Thallium-201 stress testing showed a complete resolution of ischemic defects in 12 patients (67%), a decrease in the area of ischemia in 2 patients (11%), and no change in 4 patients (22%). Thus, 14 patients had a reduction in myocardial ischemia after EECP as assessed by thallium-201 imaging ($p < 0.01$).

Comparison of maximal stress test results before and after EECP showed that EECP produced a 19% increase in exercise duration (from 8.14 ± 0.71 to 9.72 ± 0.77 minutes, $p < 0.005$) without a significant change in double product (from 22,062 ± 1,664 to 22,816 ± 1,653 mm Hg x bpm). Subgroup analysis of the 14 patients who showed improvement in their thallium-201 scans after EECP revealed increases in both exercise duration (from 8.58 ± 0.66 to 10.44 ± 0.59 minutes, $p < 0.001$) and double product (from 21,827 ± 2,044 to 24,842 ± 1,707mm Hg x bpm, $p < 0.01$) during maximal stress testing after EECP.

Subsequent Studies at Stony Brook

The long-term, sustained efficacy of EECP was confirmed in a follow-up study.[9] We successfully contacted 17 of the 18 patients who underwent EECP therapy in our earlier study. At a mean follow-up of 3 years, 13 patients (72%) reported the continued absence of limiting angina; also, no myocardial infarctions or other ischemic events had occurred in these patients. Furthermore, repeat thallium-201 stress testing, performed in 10 of the 14 originally

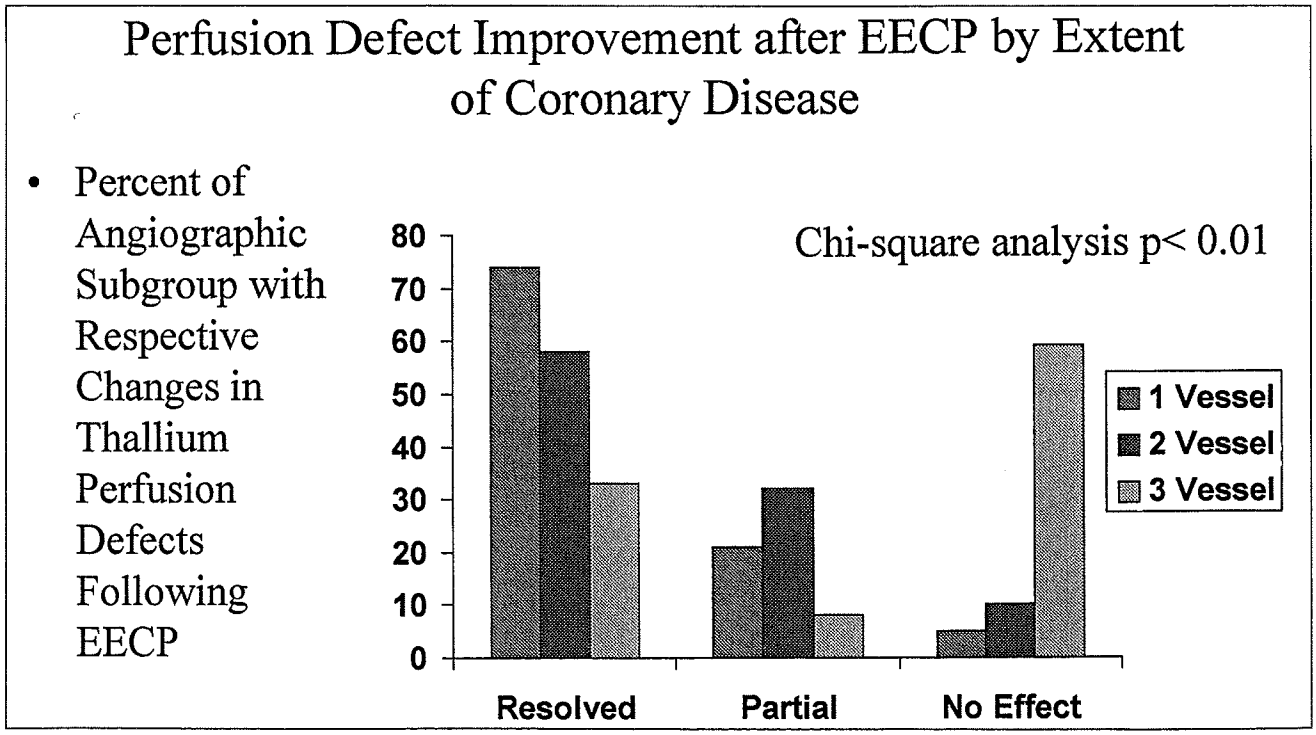

Figure 2. Relation of extent of coronary disease to results of radionuclide stress testing after EECP. Patients are divided into groups with 1-, 2-, and 3-vessel "residual" disease (e.g., a patient with 1 of 3 patent grafts has 2-vessel "residual" disease). Postcounterpulsation therapy stress perfusion deficits are shown as either resolved, partial improvement, or no effect compared with pretherapy baseline. The percentage with each type of response is shown in relation to the extent of residual disease. Reproduced with permission.[10]

continued on page 21

Cohn continued from page 16

improved patients, again showed improvement from the pre-EECP test in 8 patients and worsening in only 2 patients.

In our most recent report, we evaluated the angiographic features that seemed to predict the best clinical result.[10] Fifty patients formed the study group—almost evenly divided into subgroups with 1-, 2-, or 3-vessel "residual" disease, a definition somewhat different from the traditional meaning of the term (see Fig. 2). Patients with at least 1 open conduit (i.e., the 1- and 2-vessel residual disease subgroup) fared best. Thus, while perfusion defects improved in 95% of patients (18 of 19) with residual 1-vessel coronary artery disease and in 90% of patients (17 of 19) with residual 2-vessel coronary artery disease, in those with stenotic grafts and 3-vessel disease improvement was seen in only 42% (5 of 12).

That many of our patients improved after EECP was gratifying, but the mechanism responsible for that improvement remains speculative. The increase in exercise time could be due, in part, to a training effect,[11] but this could not explain the thallium findings. One possible explanation for the improvement in perfusion that we observed is that EECP may open, or enhance the development of, collateral channels. Such a mechanism may also explain the relative lack of efficacy of EECP in patients with severe or diffuse "residual" 3-vessel coronary artery disease. As noted above, at least 1 open conduit may be necessary to achieve a beneficial effect. In our studies, EECP was well-tolerated by all patients. No patient withdrew after enrollment, and no complications of EECP occurred.

Future Studies

Even though these results indicate that 3 years after the initiation of EECP therapy, beneficial effects—both subjective and objective—were demonstrable in patients with chronic refractory angina, our studies lacked a suitable control group. Accordingly, we enlarged our data base to include patients from other hospitals. Specifically, a multicenter trial was begun in 1995 with the goal of enrolling 120 patients to measure the effect of EECP versus placebo on symptoms and various exercise parameters measured pre- and posttreatment. For entry into the study, all patients had to have documented coronary artery disease and positive exercise tests, as well as chronic angina, and be free of the exclusion criteria mentioned earlier. The protocol calls for either "active treatment" (full pulsation), or "inactive treatment" (weak pulsation). Enrollment will be completed in 1997. Until these results are available, Stony Brook is the only reliable source of data on American patients who have failed PTCA and/or CABG and who have been treated with EECP. With nearly 100 patients treated as part of research protocols, or in our recently opened clinical unit, our results suggest that EECP may be potentially useful for many chronic angina patients who desire a better quality of life.

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