The Emerging Role of Enhanced External Counterpulsation in Cardiovascular Disease Management

John E. Strobeck, MD, PhD, Robert Baklajian, MD and Joseph C. Hannon, MD
The Heart-Lung Center, Comprehensive Cardiopulmonary Care Center
Hawthorne, NJ

EECP is a unique outpatient, noninvasive treatment used to improve myocardial perfusion thereby reducing symptoms of obstructive CAD. EECP is a key component in the cardiovascular disease management program offered at The Heart-Lung Center, a comprehensive cardiopulmonary care center in Hawthorne, NJ. The center provides cost-effective preventive, educational, and diagnostic services and treatments that have been shown to provide benefits in the evidence-based literature. EECP is used to stabilize the coronary circulation in patients with severe CAD. For many of the patients with chronic progressive CAD treated at the Heart-Lung Center, EECP has contributed to stabilization when maximal medical therapy and/or invasive procedures have proven inadequate. We believe this approach will translate into a reduction in hospital ER visits, in inpatient admissions for chest pain, and of the need for and use of repeated costly and invasive forms of myocardial revascularization (PTCA and CABG). Three such cases are presented and discussed in this paper. Since EECP has demonstrated potential for stabilizing CAD, this treatment is predicted to have an emerging role as an effective cardiovascular disease management tool to help providers of cardiac care share risk for the care of chronically and seriously ill patients with managed care organizations.

The Heart-Lung Center

The Heart-Lung Center of Hawthorne, NJ is a 6,000 square foot, free-standing, cardiopulmonary care center staffed by a reconfigured and reformatted group practice specializing in outpatient cardiopulmonary disease management. By adopting this focus, the center provides:

- a full range of preventive cardiopulmonary programs (including lipid screening and therapy, a smoking cessation program, hypertension screening and treatment, cardiopulmonary rehabilitation training, and an asthma education and treatment program)
- cardiopulmonary urgent care (with EKG and hemodynamic monitoring capability for chest

Abbreviations and Acronyms

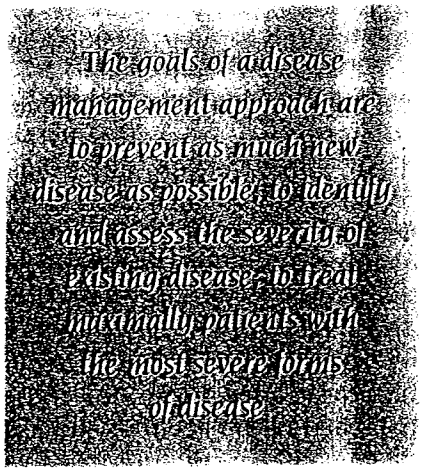
CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
EECP	Enhanced external counterpulsation
INR	International normalized ratio
LAD	Left anterior descending
LCX	Left circumflex
LV	Left ventricular
METS	Metabolic equivalents
PTCA	Percutaneous transluminal coronary angioplasty
RCA	Right coronary artery

pain triage, acute arrhythmia evaluation and treatment including cardioversion, and acute asthma/chronic obstructive pulmonary disease evaluation and treatment)
- a comprehensive cardiopulmonary consultative service
- a full range of noninvasive diagnostic services (including complete heart and vascular ultrasound, complete cardiac and non-cardiac nuclear medicine, routine and cardiopulmonary stress testing, complete pulmonary function testing, and x-ray)
- chronic infusion therapy for severe congestive heart failure patients (including intravenous dobutamine, milrinone, and diuretics for the long term stabilization of patients with the severest forms of congestive heart failure)
- EECP for patients with severe CAD to reduce anginal episodes, to improve myocardial perfusion, to reduce ER visits, and to reduce the need for invasive procedures such as cardiac catheterization, coronary interventional treatments, and CABG.

These various program elements are linked by a clinical record system making it possible to provide care that is driven by clinical and quality indicators and to track outcomes.

Coronary Artery Disease Management

Disease management of patients with obstructive CAD involves providing them with the cost-effective preventive, educational and diagnostic services and treatments described in evidence-based literature. The goals of a disease management approach are to prevent as much new disease as possible; to identify and assess the severity of existing disease; to treat maximally patients with the most severe forms of disease. As a result, chronic disease is stabilized, thus producing the maximal therapeutic benefit at the lowest possible cost for the longest period of time. Disease stabilization in the CAD patient should result in a reduction of coronary events, a reduction of ER visits and hospitalizations for chest pain, a reduction of anginal episodes and nitroglycerin consumption, an improvement in myocardial perfusion, and an improvement in functional status. For many Heart-Lung Center patients with chronic progressive CAD, the availability of EECP has contributed to stabilization when they otherwise would have required invasive revascularization procedures. As with any treatment involving patients with chronic CAD, appropriate case selection is important:



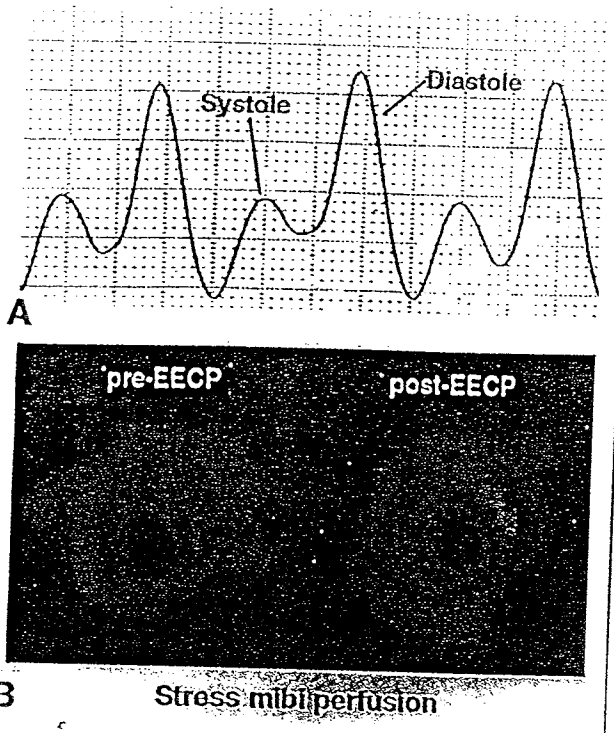
- Patients with left main CAD and no patent bypass grafts to the left coronary system are not treated with EECP. These patients still require CABG surgery.
- Patients who have undergone at least one prior revascularization procedure (PTCA, stent, or CABG) and are in need of another are good candidates as long as at least one open conduit (graft or native vessel) connecting to the distal coronary bed is present.
- Patients with single- or double-vessel CAD unsuitable for PTCA or stent implantation are also good candidates
- Patients with triple-vessel disease of a diffuse nature with unsatisfactory distal bypass target vessels are also good candidates as long as at least one artery does not have a severe proximal obstruction.
- Patients, however, with evidence of an abdominal aortic aneurysm, severe ileofemoral occlusive disease, or evidence of deep vein thrombosis in the lower extremities are not good candidates for EECP. Caution also is advised for patients with a left ventricular ejection fraction less than 30%.

When used in this fashion, the disease-stabilizing benefits of EECP allow the cardiologist to confidently accept some of the risk for coronary events and for myocardial revascularization that exists in these patients, particularly Medicare patients. Many managed care organizations are developing case rates or risk-sharing arrangements with cardiologists and cardiac surgeons to care for patients with CAD over specified periods of time (episodes of care). In these arrangements, the physicians share risk for cardiac events, outpatient or inpatient care, and all procedures required to stabilize patients after initial contact (which may be a myocardial infarction, PTCA, or a CABG). EECP represents the only outpatient, adjunctive treatment, other than maximal medical therapy, available to stabilize these patients and prevent them from needing more invasive, costly, inpatient treatments.

The most recent trial comparing medical therapy to revascularization therapy (PTCA or CABG) was the Asymptomatic Cardiac Ischemia Pilot Study.[1,2] Patients in this trial were randomized to one of two medical therapy groups (diltiazem and

FIGURE 1

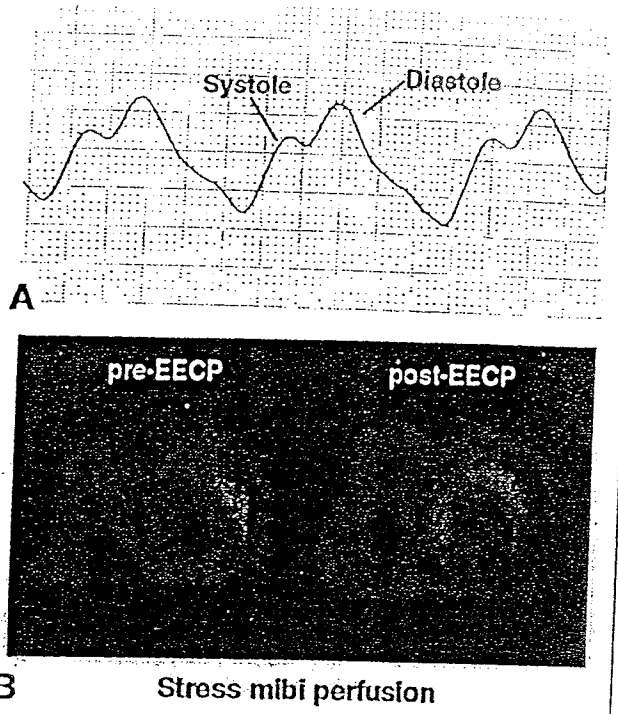
Plethysmogram during EECP



A. The upper panel demonstrates the simultaneously recorded EKG rhythm strip and the finger plethysmogram during EECP of the patient described in Case I. This pattern was representative of all this patients's EECP treatments. The ratio of diastolic volume to systolic volume demonstrated is 2.4, indicating optimal diastolic augmentation. B. The lower panel depicts the composite stress scintigrams of this patient pre-EECP (1/10/97) and post EECP (5/27/97) displayed in a polar format. Note the markedly improved anteroseptal and inferior wall perfusion in the post EECP™ stress scintigram.

FIGURE 2

Plethysmogram during EECP



A. The upper panel demonstrates the simultaneously recorded EKG rhythm strip and the finger plethysmogram during EECP of the patient described in Case II. This pattern was representative of all this patient's EECP treatments. The ratio of diastolic volume to systolic volume demonstrated is 1.3, indicating optimal diastolic augmentation. B. The lower panel depicts the composite stress scintigrams of this patient pre EECP (1/20/97) and post EECP (5/23/97) displayed in a polar format. Note the markedly improved antero-septal and inferior wall perfusion in the post EECP stress scintigram.

isosorbide dinitrate or nifedipine and atenolol) or revascularization therapy. Dosages of medications were titrated until patients had unwanted side effects and then back-titrated to a steady state level controlling symptoms. The average dose of diltiazem and isosorbide dinitrate used was 179 mg/day and 71 mg/day respectively and the average dose of nifedipine and atenolol was 47 mg/day and 51 mg/day, respectively. Results of the trial indicate that the revascularization therapy eliminated ischemia more commonly after 12 weeks and one year than did either medical treatment strategy.

Other factors important in producing maximal antiischemia therapy include:

- Lowering blood pressure to acceptable clinical levels;
- Curtailing or stopping smoking;
- Including weight reduction and programmed physical therapy as part of medical therapy;
- Lowering lipids (cholesterol and LDL) to levels acceptable by the National Cholesterol Education Program guidelines usually with a "statin" drug;
- Achieving good blood sugar control for diabetics, bringing triglycerides to normal or near normal levels;
- Using an angiotensin-converting enzyme inhibitor in patients with ischemic heart disease if the ejection fraction is less than 40%;
- Continuing β-blocker therapy in patients after high risk myocardial infarction; and

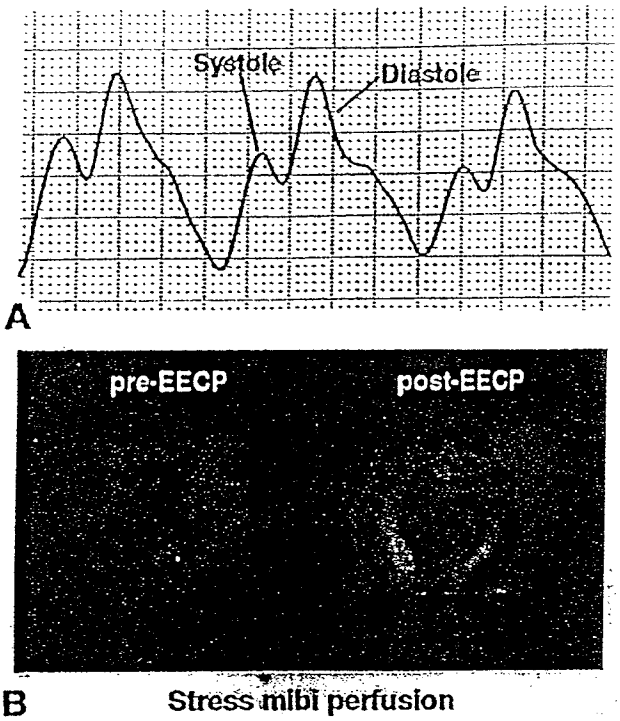
- Considering an antioxidant such as Vitamin E as part of baseline therapy.[1]

However, in spite of current maximal antiischemia therapy for chronic CAD there is still a need for an outpatient adjunctive treatment to improve myocardial perfusion so that more costly, invasive revascularization can be avoided. EECP represents the first method of this type to be developed, validated, and used in a widespread fashion.

Case Studies

I. A 27-year-old man who had a history of familial hyperlipidemia with an episode of associated pancreatitis, began developing exertional angina pectoris in September 1996. He was referred for evaluation in January 1997, at which time he underwent an isotope stress test. At 6 METS he exhibited a hypotensive blood pressure response, chest pressure, and 1.5–2.0 mm horizontal ST depression in the lateral leads of the electrocardiogram. Sestamibi scintigraphy revealed a large inferolateral perfusion defect with partial reperfusion and a moderate area of hypoperfusion of the mid to distal anterior wall with partial reperfusion on rest images. The patient underwent cardiac catheterization and coronary angiography, which revealed 100% occlusion of the mid-RCA with small right to right collateral vessels, 95% proximal stenosis and 100% mid-LAD coronary artery occlusion with early collateral development to the LAD from the distal LCX coronary artery, and a 95% proximal stenosis of a small marginal branch of the dominant LCX. The LCX also provided collateral vessel connections to the distal RCA. The left ventricular ejection fraction was 40%, and the left ventricular end-diastolic pressure was 24 mm Hg. As a result of his young age, considerable discussion occurred between the patient, his family, cardiologists, and cardiac surgeons regarding CABG as the revascularization method of choice. The final choice of the patient was to explore non-surgical methods of revascularization first. He was not found to be a good candidate for coronary interventional therapy because of his two chronic total occlusions (RCA and LAD) and the small caliber of the marginal vessel, which was narrowed by 95%. He was offered EECP as another revascularization method and he elected to undergo 35 one-hour treatments over a 7 week period, which began in January 1997. During EECP, his ratio of diastolic volume to systolic volume as measured by finger plethysmography consistently ranged from 2.0–2.4. His medical therapy consisted of Imdur® 60 mg/day, diltiazem 120 mg/day, metoprolol 100 mg/day, Lipitor® 10 mg/day, and aspirin 325 mg/day. He was advised to increase the amount of his regular physical

FIGURE 3



A. The upper panel demonstrates the simultaneously recorded EKG rhythm strip and the finger plethysmogram during EECP of the patient described in Case III. This pattern was representative of all this patient's EECP treatments. The ratio of diastolic volume to systolic volume demonstrated is 2.2, indicating optimal diastolic augmentation. B. The lower panel depicts the composite stress scintigrams of this patient pre EECP (3/06/97) and post EECP (6/10/97) displayed in a polar format. Note the markedly improved anterior, septal and lateral wall perfusion in the post EECP stress scintigram.

activity during the treatment period and by the third week of therapy he reported a marked decrease in his frequency of angina. By the conclusion of the 7 week course of therapy his angina was completely eliminated at normal levels of exertion. In May 1997, he underwent repeat isotope stress testing with sestamibi at the same workload as the pre EECP stress test, which showed a marked improvement in myocardial perfusion in both the anterior and inferolateral regions during stress when compared to the study of January 1997 (Fig. 1). The patient will undergo a follow up isotope stress test in 6 months to determine the durability of the improvement in myocardial perfusion.

This case is a graphic example of a potential role for EECP as an alternative, outpatient treatment for myocardial revascularization. Repeat treatments with EECP are possible if myocardial perfusion further deteriorates over time.

II. This patient is a 72-year-old male with a history of hypertension, non-insulin dependent diabetes mellitus, triple-vessel CAD, chronic atrial fibrillation, gout and stable angina who was self-referred for evaluation in January 1997. The patient had undergone cardiac catheterization in 1986, which showed 85% LAD stenosis, 100% LCX stenosis, and 40%–50% stenosis of the mid-RCA. At that time he was offered CABG and he refused. He was treated medically until September 1996, when he experienced a change in his anginal pattern. In October 1996, he underwent a thallium stress test, which showed a new inferior fixed defect and evidence of apical ischemia. This finding suggested progression of disease in the right coronary artery but an echocardiogram done in October 1996, showed normal LV function and no regional wall motion abnormalities to suggest previous inferior infarction. He was advised to undergo repeat catheterization, but again the patient refused, feeling his symptom pattern change was not severe enough to warrant further invasive testing. Upon evaluation, he was found to be a good candidate for EECP. He underwent a pre EECP isotope stress test, which revealed severe hypoperfusion of the inferior wall and apex at 6 METS with near complete reperfusion on rest images. His blood pressure response to stress was normal, but he did experience chest pressure at peak stress. The EKG showed right bundle branch block and atrial fibrillation throughout. His atrial fibrillation, however, was well controlled and his ventricular rate was consistently in the 60–75/min range at rest. Arterial Doppler studies of the lower extremities showed biphasic and monophasic waveforms distally despite the absence of significant plaque accumulation. His warfarin dose was adjusted to an INR of 2.0 to prevent any intramuscular hemorrhage from the barotrauma of the pneumatic cuffs. He initially received 35 sessions of EECP, but because his diastolic to systolic volume ratio measured by finger plethysmography during treatment was consistently 0.8:1.0, it was decided to extend his course of treatment by an additional 10 treatments.(Recent studies by Suresh et al[4] showed that the optimal ratio is 1.5:2.0.) Following a total of 45 treatments with EECP the patient underwent a repeat isotope stress test. Stress perfusion images were obtained at the same workload as the pre EECP stress test and revealed a marked improvement in myocardial perfusion in the inferior wall and apex. The patient returned to normal physical activity with no chest pain symptoms or nitroglycerin consumption since completion. His current medical regimen includes nifedipine 30 mg/day, propranolol 80 mg/day, isosorbide dinitrate 60 mg/day, warfarin 5 mg/day, and glyburide 5 mg/day.

This case demonstrates the safety and efficacy of EECP in improving myocardial perfusion in a diabetic patient with chronic atrial fibrillation on warfarin and in whom the initial level of diastolic augmentation was found to be suboptimal. Typically the presence of ileofemoral occlusive disease reduces the degree of diastolic augmentation that may be achieved with EECP, but this case shows that the distensibility of the peripheral vasculature (i.e., loss of triphasic flow patterns) also plays a role in determining the ratio of diastolic to systolic volume measured during EECP (Fig. 2).

III. The third patient is a 72-year-old male with a history of triple-vessel CAD, previous myocardial infarctions in 1974 and 1995, previous CABG x 5 in 1984, ischemic cardiomyopathy with left ventricular ejection fraction of 20%, progressive angina pectoris with minimal exertion, non-insulin dependent diabetes mellitus, paroxysmal atrial fibrillation, and chronic ventricular ectopy who was referred for consideration of EECP. He had undergone repeat cardiac catheterization in June 1995, because of an acute non-Q wave myocardial infarction that revealed an occluded saphenous vein graft to the posterior descending and postero-lateral branches of the RCA, an occluded vein graft to the diagonal branch of the LAD, a patent left internal mammary artery graft to the LCX and a patent right internal mammary artery to the LAD. The proximal portions of all three native coronary arteries were 100% occluded and collaterals were present from the distal LAD to the RCA. The patient required cholesystectomy in October 1996, which was complicated by

recurrent angina and congestive heart failure. After discharge from the hospital in November 1996 the patient was referred for EECP. Echocardiography showed biatrial and biventricular dilation with moderately severe mitral regurgitation and an LV ejection fraction of 20%. The patient remained on medical therapy with stable angina until he was able to start EECP in March 1997. A pre-EECP isotope stress test revealed marked LV dilation and severe hypoperfusion of the inferior wall with mild reperfusion on rest images. In addition there were large fixed defects of the anterior wall; lateral wall, and septum with no reperfusion on rest images. The patient received 35 treatments with EECP. EECP was very effective in producing diastolic augmentation, despite evidence by arterial doppler examination of diffuse plaque in all major proximal vessels evaluated bilaterally. Arterial waveforms were uniformly triphasic in all vessels. Typically the ratio of diastolic volume to systolic volume measured by finger plethysmography was 1.7:2.0 in this patient throughout the 35 treatments. The patient's INR was lowered to 2.0 during treatment by reducing the Coumadin dose. Typically O_2 saturation levels measured by pulse oximetry were 95%–96% pre EECP and 98%–99% during EECP. In no case did O_2 saturation levels decline during the hour of treatment. The patient had no complaints of shortness of breath or signs of orthopnea during treatment to suggest the development of pulmonary congestion. He did require treatment with procainamide during his course of EECP to reduce the frequency of unifocal ventricular ectopy, which made his treatment more uncomfortable due to vigorous leg compression after a compensatory pause. His functional status and chest pain pattern markedly improved during and after EECP. The post EECP isotope stress test showed persistent LV dilation with an improved LV ejection fraction of 36% and marked improvement in the perfusion of the anterior, lateral, septal, and inferior walls during stress compared to the pre EECP stress images. His current medication regimen includes digoxin 0.125 mg/day, enalapril maleate 20 mg/day, furosemide 80 mg/day, potassium bicarbonate 25 mEq/day, chlorpropamide 250 mg/day, aspirin 81 mg/day, warfarin 3 mg/day, and ranitidine 300 mg/day (Fig. 3).

This patient with severe ischemic heart disease and LV dysfunction benefited from 35 treatments of EECP due to the high level of diastolic augmentation and systolic unloading. This case demonstrates the safety and efficacy of EECP in patients with ischemic LV dysfunction. There was no aggravation of heart failure or pulmonary congestion during treatments. Post EECP the patient's functional status markedly improved. The response of this patient raises the possibility that EECP may have efficacy in patients with congestive heart failure, particularly those with an ischemic etiology.

The experience of The Heart-Lung Center with EECP treatments in 45 patients is being prepared for later publication. In summary, of the 45 patients treated from April 1996, to the present, one patient could not finish the treatment due to aggravation of spinal osteoarthritis, three patients with severe triple-vessel CAD did not respond to the initial 35 treatments and required a second course of 10–35 treatments and one patient developed a progressive chest pain pattern requiring repeat catheterization prior to finishing EECP but did not require a revascularization procedure. He successfully resumed EECP and finished his course of 35 treatments with no recurrence of chest pain. The remainder of the patients responded favorably to EECP with a reduction of symptoms and an improvement in stress myocardial perfusion. Only one patient (the patient described above who needed catheterization) was admitted to the hospital for a cardiac event in the 15 months since treatments began. Long term follow up is planned with careful tracking of clinical outcomes.

Future Directions

EECP, the most striking externally-applied mechanical stimulus producing demonstrable coronary vasodilation in patients with obstructive CAD, is actively being studied in a number of centers. It has been used successfully in the unstable angina patient as an adjunct to revascularization.[5] Other studies are planned to evaluate its safety and efficacy in the treatment of patients with systolic left ventricular dysfunction, particularly those with complicating mitral regurgitation. The full scope of the usefulness of EECP is still unclear and needs further evaluation. Theoretically, the vasodilating effects of diastolic blood pressure augmentation could be beneficial in other vascular beds besides the coronary vascular bed. If this hypothesis is borne out with rigorous investigation, one might propose the following for future research:

- EECP should be studied in patients with hypotension or shock to stabilize hemodynamics post-infarction or post-revascularization in either the inpatient or cardiac outpatient setting.
- EECP should be studied in patients who have received thrombolytics to improve myocardial perfusion and prevent reocclusion.

- EECP should be studied in patients with systolic LV dysfunction to improve afterload reduction, restore diuretic responsiveness, improve patient functional status, reduce pulmonary congestion, reduce mitral regurgitation, induce neurohormonal withdrawal, or possibly serve as a "bridge to transplantation."
- EECP is likely to emerge from controlled outcomes studies as a primary form of outpatient coronary revascularization to be used instead of more costly and invasive inpatient methods such as PTCA or CABG. This use will establish its role as a CAD management tool for physicians and managed care organizations involved in sharing the risk of care of these patients over specified periods of time.

We are convinced that EECP research is beginning and will be a fertile area from many perspectives including therapeutic cardiac benefits, cost effectiveness, resource utilization and applications for improved blood flow to other vascular beds. We invite all interested physicians to participate in the National EECP Patient Registry and help this work move forward. •

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