Enhanced External Counterpulsation for the Treatment of Angina Pectoris

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The treatment of refractory chronic angina pectoris presents an increasing problem for all physicians caring for patients with coronary artery disease because of the large number of individuals who have either failed multiple revascularization procedures or are not appropriate candidates for such procedures. The aim of this study was to review the safety, efficacy, and clinical applicability of a noninvasive technique (external counterpulsation) for the treatment of angina pectoris. A MEDLINE search for all English language abstracts, meeting presentations, journal articles, and reviews from 1960 through December 2005 was conducted. Of the 194 citations in the literature, 60 appeared before 1983 when the enhanced version of the technique (the one that is presently used) was first reported. Criteria for further evaluation of the 134 post-1983 citations were either (1) randomized trial, (2) observational study of at least 10 patients, or (3) investigations into possible mechanisms. Of the 134 citations, 45 were used for data extraction. Observational studies from the United States, Asia, and Europe have demonstrated improvement in symptoms, reduction in anginal episodes, better quality of life, and improved exercise performance in over 5000 patients. The only randomized study (Multicenter Study of Enhanced External Counterpulsation) confirmed these findings as well as the continuation of clinical benefits at least 1 year posttreatment. Although the mechanisms by which diastolic augmentation achieves these beneficial results are still under investigation, this is a promising noninvasive therapy in a group of patients with limited treatment options.

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Because of advances in both coronary risk factor modification and treatment of coronary artery disease, mortality from cardiovascular disease has declined drastically in the United States in the last 3 decades. Despite these gains, atherosclerotic heart disease remains the most common cause of death in the United States and in other developed countries. Not only do millions of people die of this disease but also many others continue to have anginal symptoms that interfere significantly with their quality of life *despite* aggressive anti-ischemic drug regimens combined with medical and/or surgical coronary revascularization procedures. For example, it is estimated that hundreds of thousands of patients in the United States have undergone percutaneous transluminal coronary angioplasty or coronary artery bypass graft surgery each year for the past decade, and many remain symptomatic or become symptomatic again within months or years of the original procedure. There is a limit to how many repeat revascularization attempts can be made because of the patient's coronary anatomy, conduit availability, left ventricular function, age, comorbidity, and so on.

For those patients in whom repeat (or initial) revascularization procedures are not appropriate and in whom aggressive medical therapy fails to maintain a quality of life that patients are comfortable with, several emergent therapies have been proposed. These include techniques to reduce anginal pain by neural stimulation or blockade and procedures that could potentially enhance coronary myocardial perfusion. There

are several methods available to block pain associated with cardiac ischemia, including conventional sympathectomy and 2 newer techniques popular in Europe: transcutaneous electrical nerve stimulation and spinal cord stimulation.[1] The most encouraging approach appears to be the latter, but the main drawback to spinal cord stimulation is that it is invasive.

There are also several invasive procedures currently used to increase myocardial perfusion in patients with refractory angina with varying clinical results such as transmyocardial[2,3] or percutaneous laser revascularization[3,4] (procedures that use the myocardial sinusoids to create new channels to deliver blood to the myocardium) and the still investigational angiogenic therapy for the human heart, that is, injection of an angiogenic protein such as fibroblast growth factor 1 close to the left anterior descending artery during coronary artery bypass surgery.[5] The only truly noninvasive procedure currently available for which an increase in myocardial perfusion has been reported is external counterpulsation and especially the enhanced version (EECP). This systematic review of the English language literature will focus on EECP's safety, efficacy, and applicability to current clinical practice especially as it applies to the general physician.

Methods

Data Sources

The MEDLINE database was used to identify English language abstracts, meeting presentations, reviews, and journal articles related to external counterpulsation. The main Medical Subject Headings of *assisted circulation* and *counterpulsation* were referenced with resulting citations divided into 2 periods, from 1960 to 1982 and from 1983 to 2005. This was done because of the historical development of the technique. Briefly stated, the concept of counterpulsation rests on an observation in the animal model reported in 1953 by Kantrowitz and Kantrowitz[6] that coronary blood flow could be increased significantly if the coronary artery was perfused at a higher pressure during diastole. This report led an engineer (Birtwell) to propose to a cardiac surgeon (Harken) and to colleagues at the Peter Bent Brigham Hospital that a system to implement arterial counterpulsation in humans could be developed. Studies of such a system were begun in 1957 and reported in 1961.[7] Experiments on intraaortic balloon pumping were also being conducted in Harken's laboratory at this time,[8] but this review will only focus on external counterpulsation.

The initial external devices required blood to be led outside the body to a pump, but this was soon replaced by a totally noninvasive device marked by rigid outer housing containing water-filled bags. Sequential compression, rather than 1-stage uniform compression, was the next development under the leadership of another cardiac surgeon (Soroff). Clinical trials in patients with cardiogenic shock,[9] angina,[10] and acute myocardial infarction[11] were conducted in the United States during the 1970s and early 1980s. Treatment periods were short with results suggestive of benefit but not clearly so. At this point, interest in this technique waned (as perhaps best exemplified by the editorial of Kuhn in 1980).[12] The modern era of external counterpulsation began with modifications made in the technique by Zheng et al[13] in China that were reported in 1983. Zheng's system used compressed air with 3 sets of balloons sequentially compressing the vascular beds of the legs, thighs, and buttocks. The timing of the compression was controlled by the patient's electrocardiogram (ECG).

Since 1983 there have been 134 citations referring to external counterpulsation in the literature, of which 45 satisfied the selection criteria for this review (Table 1).[13-57] This criteria involved either (1) a randomized trial (with 3 references concerning the Multicenter Study of EECP [MUST-EECP] trial[55-57]), (2) observational clinical studies of at least 10 patients (most of the remaining references), or (3) investigations into hemodynamic effects and/or possible mechanism of action of this procedure.[19,21,25,27,31,37,48,52]

Study Selection and Data Extraction

A. Safety

Adverse effects requiring hospitalization are rare with this device, although it is occasionally

Table 1. EECP Patient Studies Between 1983 and 2005

Lead Author	Year	Reference	No. of Patients
Observational Trials (in chronological order)			
Zheng	1983	[13]	52
Kern	1985	[14]	14
Lawson	1992	[15]	18*
Lawson	1995	[16]	17*
Fricchione	1995	[17]	38*
Karim	1995	[18]	15*
Kasliwal	1996	[19]	23
Lawson	1996	[20]	27*
Lawson	1996	[21]	50*
Garlichs	1998	[22]	12
Tartaglia	1998	[23]	22
Katz	1998	[24]	13
Suresh	1998	[25]	30*
Lawson	1998	[26]	60*
Qian	1999	[27]	104
Huang	1999	[28]	14
Strobeck	1999	[29]	466†
Wu	1999	[30]	43
Masuda	1999	[31]	11
Gloth	1999	[32]	18
Werner	1999	[33]	16
Karim	1996	[34]	117
Lawson	2000	[35]	33*
Lawson	2000	[36]	2289‡
Urano	2001	[37]	12
Lawson	2001	[38]	1957‡
Barsness	2001	[39]	978†
Michaels	2001	[40]	1004†
Lawson	2001	[41]	598†
Stys	2002	[42]	175†
Holubkov	2002	[43]	323†
Lakshmi	2002	[44]	2486†
Michaels	2002	[45]	10
Linnemeeir	2003	[46]	1532†
Fitzgerald	2003	[47]	215†
Shechter	2003	[48]	20
Tartaglia	2003	[49]	25
Werner	2003	[50]	48
Michaels	2004	[51]	1097†
Dockery	2004	[52]	23
Lawson	2004	[53]	2861†
Michaels	2005	[54]	37
Randomized trial (MUST-EECP)			
Arora	1999	[55]	139
Cohn	1999	[56]	125
Arora	2002	[57]	71

*Overlapping Stony Brook populations.
†IEPR.
‡Consortium.

uncomfortable, and side effects such as skin abrasions on the legs are not uncommon. For example, in 3 large-scale observational studies cited in Table 2 in which such data were reported, the incidence of deaths or myocardial infarctions reported during the 35 to 36 hours of EECP therapy or immediately thereafter in over 3000 patients was less than 1%. In addition, no deaths or myocardial infarctions were reported in the 139 patients enrolled in the randomized MUST-EECP trial. The procedure is also well tolerated psychologically with 1 study showing a reduction in a psychosocial stress factors.[18]

B. Efficacy

Although different end points were emphasized in the various studies surveyed, one common theme was a favorable change in anginal symptoms and/or quality of life, and another theme was improvement in exercise ECG or myocardial perfusion parameters.

Observational studies

The Stony Brook study reported in 1992[15] was the initial prospective observational study with the enhanced device reported in the United States. Patient selection and reasons for exclusion are typical of all the other observational studies cited. The 18 patients enrolled in this study had chronic stable angina despite medical or surgical therapy or both and evidence of exertional ischemia on thallium-201 perfusion imaging. Other patients were excluded because of overt congestive heart failure, aortic insufficiency, a myocardial infarction within the previous 3 months, arrhythmias that prevent suitable ECG triggering such as frequent ventricular ectopic activity or atrial fibrillation, severe occlusive peripheral vascular disease, recurrent deep vein thrombosis, systemic hypertension (>180/110 mm Hg), or a bleeding diathesis. After completing the course of 36 hours of outpatient EECP therapy (an empiric number derived from the Chinese studies of Zhengs et al[13]), patients underwent a thallium-201 stress test (with usual medication continued); exercise duration was the same as that during baseline testing so as to provide a comparison of imaging test results. In addition, a maximal stress test was performed less than a week after EECP treatment to assess exercise tolerance. All 18 patients experienced substantial improvements in anginal symptoms after EECP. Thallium-201 stress testing (performed to the same exercise duration before and after EECP) 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

Table 2. Effect of EECP in 3 Large Observational Trials

	EECP International Consortium (n = 2289) [36]	IEPR (n = 978) [39]	International Study (n = 175) [40]
Beneficial effect: improvement in at least 1 anginal class	73%	81%	85%
Serious adverse effect (death/MI)	0.7% (8/8)	0.6% (2/4)	0

(22%). Thus, 14 of 18 patients had a reduction in myocardial ischemia after EECP as assessed by thallium-201 imaging ($P < .01$).

In this Stony Brook study (as in the other observational studies), patients served as their own controls; thus, a placebo effect cannot be ruled out. In addition, because the course of coronary artery disease is largely unpredictable, it is possible (but not probable) that regression of disease could occur over the 6- to 7-week trial period in a group of patients whose angina had been disabling or progressive over a period of months or years. The enrolled patients did not undergo any new therapy, such as diet, lipid reduction, or smoking cessation, during the study. Dosages of antianginal medications remained the same (or decreased) over the course of the study. Because the study cohort was predominantly male, no definitive conclusions regarding efficacy in women could be made. EECP was well tolerated by these 18 patients, and none withdrew after enrollment.

Protocols similar to the one used in the Stony Brook patients were also used in several other studies from a variety of countries and reported in a variety of medical journals. Thus, Karim et al[17] reported significant improvement in perfusion imaging and exercise tolerance in 38 Indonesian patients who also had a decrease in anginal symptoms. Kasliwal et al[19] reported a decline in the number of anginal episodes and an increase in left ventricular myocardial function determined by echocardiology in 23 Indian patients. In the United States, Tartaglia et al[23] reported increased exercise tolerance and prolongation of time to ST depression in 22 patients, as well as in radionuclide perfusion scores and functional class,[49] whereas Michaels et al[54] found clinical and exercise improvement but no changes in radionuclide measurements, and Glothen and Oken[32] reported improvement in anginal functional class in 18 patients.

As impressive as the data from these small studies are the reports from several large cooperative multicenter ventures. For example, Strobeck et al,[29] Lawson et al,[38] and Barsness et al[39] reported data from the International EECP Registry (IEPR) centered at the University of Pittsburgh. These investigators found improvement in anginal class and decrease in nitroglycerin use in 466, 1957, and 978 patients, respectively. The report of Barsness involving 43 centers found that 81% of patients reported improvement of at least one anginal class immediately after the last treatment[39] (Table 2). Even with ejection fractions less than 35% and a history of congestive failure,[29,38] many patients were still able to complete the treatment course with good results.

In more recent studies, the IEPR investigators found that improvement in anginal symptoms and quality of life were sustained for 2 years, and quality of life were sustained 2 years posttreatment,[51] that even patients with left main disease who were not operated on could be helped,[53] that diabetic patients had similar degrees of improvement as did nondiabetics,[46] and that EECP also is efficacious as initial therapy, that is, in those patients who chose not to have invasive revascularization procedures.[47] Another large observational study[40] enrolled 175 patients in 7 countries in the United States, Europe, and Asia and specifically compared radionuclide stress testing before and after therapy. In the 4 centers performing post-EECP radionuclide stress tests to the same level of exercise, 81 of 97 patients (83%) had improved perfusion images, whereas in the 3 centers using maximal exercise testing, 42 of 78 (54%) showed improvement. Improvement in anginal functional class was reported in 85% of patients. The EECP Clinical Consortium (a forerunner of the IEPR) enrolled 3788 patients from 1997 to 2000 with complete follow-up data available in 2289 patients from 84 centers.[36] The average Canadian Cardiovascular Society (CCS)

anginal class before treatment was 2.78 compared with 1.81 after treatment ($P < .001$). The greater the impairment at baseline, the greater the degree of improvement. Overall improvement in at least 1 angina class was reported in 74% of patients. Although the results from the various observational trials—both large and small—were encouraging in the extremely symptomatic populations studied, it cannot be emphasized strongly enough that by definition the observational studies lacked a suitable control group. This was one of the reasons a randomized multicenter trial was begun in 1995. Its goal was measuring the effect of EECP versus placebo on both symptoms and various exercise parameters.

Randomized trial

The MUST-EECP was a randomized, placebo (sham)-controlled, multicenter trial designed to evaluate EECP in patients with angina and documented coronary artery disease.[55] Treatment effect was determined by comparing changes in exercise treadmill test parameters (exercise duration and time ≥1-mm ST segment depression) and symptoms (frequency of anginal episodes and nitroglycerin use). The MUST-EECP trial was conducted at 7 medical centers in the United States, with the Core Laboratory and Data Coordinating Center at the State University of New York at Stony Brook and the Data and Safety Monitoring Committee located at the University of Florida in Gainesville.

Approximately 500 patients with chronic stable angina were considered for inclusion, of whom 139 were randomized between May 1995 and May 1997.

Main reasons for nonenrollment included failure to satisfy inclusion/exclusion criteria and patient refusal. To be eligible, patients had to meet the following inclusion criteria: between 21 and 81 years of age; symptoms consistent with CCS angina levels I, II, or III; documented evidence of coronary artery disease; and positive exercise test result for ischemia.

Evidence of coronary artery disease required at least one of the following criteria: angiographically proven stenosis greater than 70% in at least one major coronary artery; history of myocardial infarction (MI) documented by characteristic creatine kinase elevation and development of Q waves on ECG; or positive result of nuclear exercise stress test for infarction or ischemia.

Exclusion criteria were similar to those cited earlier. Before a patient underwent randomization, medical history, physical examination, and a baseline treadmill test were performed. The baseline treadmill test used a standard or a modified Bruce protocol and was performed within 4 weeks of treatment initiation. All medications (except on-demand nitroglycerin) remained unchanged for the duration of the study. Once randomized, patients underwent 35 hours of either active counterpulsation (EECP) or inactive counterpulsation (sham). Within 1 week of completion of 35 treatment sessions, a posttreatment exercise test was performed. Baseline and posttreatment treadmill tests were performed by personnel who were blinded to whether the patient was in the active or inactive counterpulsation group.

Tracings of each treadmill test from each study center were sent to the core laboratory, where exercise duration (in seconds) and time ≥1-mm ST-segment depression (in seconds) were confirmed by personnel unaware of both treatment assignment of each patient and whether the treadmill test was baseline or after treatment. Diaries were evaluated for frequency of angina episodes and nitroglycerin use.

Table 3. Effect of EECP in the randomized MUST-EECP trial

	Active Treatment	Sham Treatment	*P*
Improvement in exercise parameters: change in time to 1 mm ST depression (s)*	37 ± 1	−4 ± 12	<.01
Improvement in symptoms:			
Change in daily anginal episodes from baseline*	0.15 ± 0.3	−0.01 ± 0.3	<.05
Continued reduction in symptoms 1 y later (%)†	70	37	<.01

*[55].
†[56].

There was no significant difference between groups in change in exercise duration from baseline to after treatment, but time to ≥1-mm ST-segment depression was 337 ± 18 seconds at baseline 379 ± 18 seconds after treatment in the EECP group. In the sham group, time to ≥1 mm ST-segment depression was 326 ± 21 seconds at baseline and 330 ± 20 seconds after treatment. There was a significant difference between groups in change in time to exercise-induced ischemia from baseline to after treatment (Table 3).

In patients who completed 34 sessions or more, angina counts were 0.72 ± 0.14 at baseline and 0.57 ± 0.38 after treatment in the EECP group and 0.77 ± 0.14 at baseline and 0.76 ± 0.22 after treatment in the sham group. The difference between groups in the change in angina counts from baseline was statistically significant (Table 3). A similar number of patients in each group showed a 0% to 25% level of improvement, but more patients reported greater than 50% improvement in angina frequency, and fewer worsened in the EECP group compared with the sham group ($P < .05$). Nitroglycerin use was similar in both groups.

The MUST-EECP trial confirmed the conclusions of the observational studies: EECP can reduce exercise-induced ischemia in patients with symptomatic coronary artery disease. The lack of significant treatment effect on exercise duration, despite reduction in other measures of ischemia, has been seen in other clinical trials involving antianginal agents and may be because of a fixed exercise duration in patients heavily medicated with antianginal drugs, especially β blockers. Just as the observational studies reported improvement in symptoms, the randomized trial demonstrated a trend toward angina reduction after treatment with EECP in the intention-to-treat analysis. This trend reached statistical significance when the analysis included only those subjects completing at least 34 sessions. This latter observation confirms the prior experience that a certain number of treatment hours are required to maximize the antianginal benefit of this device.

Effect of Treatment on Prognosis

Follow-up studies from the Stony Brook series were published at means of 3[16] and 5 years[38] after completion of treatment. Of the first 33 patients studied, 4 died 1 to 5 years after therapy. Only 9 other patients required interim hospitalization for acute ischemic events, leaving 20 of the original 33 without new events 4 to 7 years after EECP treatment, which is an impressive accomplishment. Most of the new events occurred in the 7 patients (of the 33) who had not responded satisfactorily to the initial therapy. Karim et al[34] also reported 5 years of follow-up data in their Indonesian patients. They treated 117 patients between 1992 and 1999, with a follow-up from 1 to 6 years. There were 5 deaths and only 4 other acute events. (A control group of 198 patients had a significantly greater event rate, but the criteria for enrollment in the control group were unclear.) The IEPR reported 1-year follow-up data on 589 patients: death occurred in 3 patients, with major cardiac events requiring hospitalization in 94 other patients (a total of 17% of the original cohort).[42,43] Two-year follow-up of 1097 patients showed 9 deaths with 40% requiring hospitaliztion.[51] Long-term follow-up data are not yet available from the EECP consortium patients except for a subset of patients with a history of heart failure[38] who were less likely to maintain their angina reduction than nonfailure subjects 6 months after treatment. In the randomized MUST-EECP trial, 2 different prognostic protocols have demonstrated the same result: an improvement in quality of life that has persisted up to 1 year posttreatment.[56,57] One protocol used follow-up questionnaires administered by nurse clinicians at each site. As seen in Table 3, 70% of actively treated patients reported persistent improvement compared with 37% in the sham group ($P < .01$). The other protocol used more sophisticated and comprehensive questionnaires (the SF-36 and QLI-HF instruments). All instruments showed better results in the active versus sham patients, with 3 questionnaires achieving statistically significant intergroup differences. Perhaps, the most striking was the observation that the favorable 1-year follow-up data were dramatically similar to the initial posttreatment results in the actively treated patients.

Hemodynamic Effects

The acute hemodynamic effects of an enhanced version of the external counterpulsation device

were first demonstrated invasively by Kern et al[14] in 1985 and later noninvasively by Suresh et al in 1998.[25] Using finger plethysmography to measure the amplitude and area of the peak diastolic and peak systolic pressure waves, Suresh et al found that an "effectiveness ratio" of 1.5 to 2 (the peak diastolic amplitude divided by the peak systolic amplitude) was associated with an optimal enhancement of diastolic retrograde aortic flow. More recently, Michaels et al[45] were able to invasively demonstrate the beneficial acute effects of EECP on intracoronary and left ventricular hemodynamics in 10 patients studied with Doppler flow measurements during cardiac catheterization. Arterial stiffness is, however, not altered.[52]

Attempts to confirm a relationship between the effectiveness ratios established by Suresh et al and clinical benefits have generally been successful. For example Michaels et al[41] and Lakshami et al,[44] using the IEPR data base, reported that patients with the greatest increase in the ratio had the greatest reduction in angina class at 6 months follow-up, yet investigators have noted that some patients with lower ratios also demonstrated clinical improvement.

Because diastolic augmentation and systolic unloading are the major features of both the internal and external counterpulsation devices, it was noteworthy—but not that surprising—when the degree of diastolic augmentation achieved with EECP was similar to that of intraaortic balloon counterpulsation (the current "gold standard) in a Doppler study measuring internal mammary artery flow with both techniques in the same patient.[24] One difference between the 2 techniques is the increase in venous return during EECP, which results in a greater improvement in cardiac output but could also theoretically worsen heart failure. Several groups—including the IEPR investigators[29,38]—have not found this to be as worrisome as first feared, and in fact, a future application for this device might well be as adjunctive therapy for heart failure patients.[58]

Possible Mechanisms of Action

Several mechanisms of action have been postulated to explain both the short- and long-term benefits seen with EECP. These include beneficial effects on endothelial function, coronary collateralization, left ventricular function, and even the peripheral circulation.[48,59] They are not mutually exclusive. A relationship between improved endothelial function and collateral formation is suggested by several studies. For example, improvement in myocardial perfusion using N-13 ammonia positron emission tomography scanning was reported by Masuda et al[31] in 11 Japanese patients. Nitric oxide production was enhanced in this study, as it was in 18 Chinese patients reported by Qian et al,[27] suggesting coronary vasodilation resulted from enhanced endothelial function that in turn was induced by EECP therapy. Reduction in a potent vasoconstrictor (serum endothelin—1) in these studies also indicates a vasodilator effect. Urano et al[37] measured atrial and brain natriuretic peptide levels before and after EECP therapy. The latter decreased along with improvement in myocardial perfusion and exercise performance. The production of these various vasoactive and neurohumoral substances—perhaps associated with the increased shear forces produced by EECP—may diminish or stabilize atheromatous plaques in coronary arteries and/or help form new collateral vessels or open previously present channels. Anatomic data confirming this collateralization in humans have not yet been reported in more than an anecdotal manner, but there is some encouraging animal data to suggest it may have validity.[60]

Clinical Applicability

Physicians treating cardiac patients want to know first and foremost whether this procedure "works" and if it is safe. If so, which patients would benefit most from this procedure by being referred to appropriate treatment centers? When the federal government approved Medicare reimbursement for coronary patients, it specified its use in patients with chronic "angina refractory to conventional medical and/or anginal therapy," and this still defines its status at the present time. Some private insurers will also consider reimbursement for those patients whose coronary anatomy is unsuitable for revascularization procedures, a policy that appears reasonable based on this review. As noted earlier, common limitations include patients with arrhythmias (especially atrial fibrillation and

frequent ventricular extra systoles that prevent triggering and severe peripheral vascular disease and/or aortic regurgitation that prevents adequate counterpulsation). Other exclusion criteria reflect possible complications related to the high pressures created in the legs (severe systolic hypertension, history of thrombolphlebits, recent MI, etc). Werner et al[50] estimated that as many as two thirds of possible candidates may not meet inclusion criteria, and a third of the treated patients may find therapy too time-consuming. This German study highlights some practical limitations of EECP therapy.

In the United States alone, there are probably hundreds of thousands of patients who fit the Medicare guidelines and who do not have the exclusion criteria cited above (as well as others noted earlier in the review) and therefore are suitable candidates for EECP. Our experience at Stony Brook has allowed us to further identify those patients who would benefit most from EECP based on coronary angiographic studies. Our findings suggest that at least one open conduit is necessary for improvement in symptoms whether native vessel or bypass graft. Fifty consecutive patients were studied[21] in this analysis, with improvement in radionuclide stress perfusion seen in 80% of the overall group and in 93% of those with a patent conduit. Prior surgical revascularization also improves clinical benefits.[26]

Conclusions

Although there are no panaceas for the treatment of refractory angina, a systematic review of the recent medical literature suggests that EECP appears to be an efficacious and clinically reasonable approach to help manage patients with chronic stable angina who are refractory to conventional measures. Because of its proven ability to noninvasively use the beneficial effects of diastolic augmentation on the coronary circulation, it has been advocated as therapy in selected patients—especially before using an invasive procedure such as transmyocardial revascularization that has an appreciable morbidity and mortality.[61] The American College of Cardiology/American Heart Association's 2002 Guideline Update for the Management of Chronic Stable Agina[62] recommends laser revascularization therapy, EECP, and spinal cord stimulation as class 2 alternative therapies for chronic refractory angina patients. Although the latter 2 therapies are both limited by a paucity of randomized trial data, the general physician should consider that EECP (unlike spinal cord stimulation) is a noninvasive, outpatient procedure with little risk of adverse events.

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