

ORIGINAL PAPER

Impact of External Counterpulsation Treatment on Emergency Department Visits and Hospitalizations in Refractory Angina Patients With Left Ventricular Dysfunction

As the overall population ages and clinicians become more adept at ameliorating the immediate consequences of acute coronary syndromes, the population of patients with refractory angina and left ventricular (LV) dysfunction has increased steadily and has been associated with a dramatic increase in health care cost. Advances in the management of acute coronary syndromes with percutaneous coronary intervention and surgical revascularization contribute to the growing number of patients with advanced coronary artery disease and LV dysfunction.¹ As the number of patients with prior revascularization increases, therapeutic options for the treatment of severe angina have become limited. Worsening symptoms that cannot be managed by mechanical revascularization result in emergency department (ED) visits, hospitalizations, and increased expense and morbidity.

Enhanced external counterpulsation (EECP) is a treatment for angina that is ideally suited for the population of patients with advanced coronary artery disease, activity-limiting symptoms, and limited options for revascularization.²⁻⁴ It improves angina and symptoms of heart failure (HF) in patients with LV dysfunction but its role in affecting ED visits and hospitalizations is unclear.^{5,6} We sought to assess the effect of EECP on subsequent ED visits and hospitalizations in patients with severe angina and LV dysfunction who were followed as part of a large patient registry—The

Patients with refractory angina and left ventricular (LV) dysfunction exert an enormous burden on health care resources primarily because of the number of recurrent emergency department (ED) visits and hospitalizations. Enhanced external counterpulsation (EECP) therapy has emerged as a treatment option for patients with angina and LV dysfunction and has been shown to improve clinical outcomes and LV function. Improvements in symptoms and laboratory assessments in these patients, however, do not necessarily correlate with a reduction in ED visits and hospitalizations. This is the first study to assess the impact of EECP therapy on ED visits and hospitalization rates at 6-month follow-up. This prospective cohort study included 450 patients with LV dysfunction (ejection fraction $\leq 40\%$) treated with EECP therapy for refractory angina. Clinical outcomes, number of all-cause ED visits, and hospitalizations within the 6 months before EECP therapy were compared with those at 6-month follow-up. Despite the unfavorable risk profile, refractory angina patients with LV dysfunction achieved a substantial reduction in all-cause ED visits and hospitalization rates at 6-month follow-up. EECP therapy appears to offer an effective adjunctive treatment option for this group of patients. (CHF. 2007;13:36-40) ©2007 Le Jacq

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International EECP Patient Registry (IEPR). The Registry methodology has been described previously.⁷

EECP therapy is a noninvasive circulatory assist device consisting of electrocardiography-gated sequential leg compression, which produces hemodynamic effects similar to those of intra-aortic balloon pump

counterpulsation.⁸ The therapy has been described previously.^{2,9} A usual course of EECP therapy consists of 35 one-hour sessions.

Methods

This study included patients with LV dysfunction (ejection fraction [EF] $\leq 40\%$) treated with EECP for refractory

angina identified from phase II of the IEPR (IEPR-II). The IEPR-II enrolled more than 2900 consecutive patients treated with EECF for chronic angina in 73 US centers between 2002 and 2004. Briefly, the IEPR-II collected patient demographics, medical history, coronary artery disease status, quality-of-life status assessed by the Duke Activity Status Index (DASI), and the number of all-cause ED visits and hospitalizations within the 6 months before EECF treatment. The DASI is a standardized assessment of functional status that correlates with maximum exercise capacity and maximum oxygen consumption.¹⁰ This quality-of-life tool is based on a scoring system that ranges from zero to a maximum of 58.2. The maximum score indicates no limitations in physical functioning with respect to personal care, ambulation, household tasks, sexual activity, or recreation.

After initiation of EECF therapy, data were collected prospectively on anginal status according to the Canadian Cardiovascular Society Classification (CCSC), medication use, quality of life, and adverse clinical events including all-cause ED visits and hospitalizations. Clinical outcomes and number of all-cause ED visits and hospitalizations within the 6 months before EECF therapy were compared with those at 6-month follow-up from the initiation of EECF treatments. All patients gave written informed consent before the procedure. The protocol was approved by the University of Pittsburgh's Institutional Review Board Research Conduct and Compliance Office, and the study was approved by the Institutional Review Board of each participating center. The investigation conforms to the principles outlined in the Declaration of Helsinki.

Statistical Analyses

Baseline characteristics are shown for categorical variables as the proportion of patients reporting and as mean and SD for continuous variables. Changes in continuous variables were analyzed by paired *t* tests. Event rates at 6 months

Table 1. Characteristics of Patients With LVEF \leq 40% Prior to EECF Therapy (n=450)

Age, mean \pm SD, y	69 \pm 11
Male sex, %	81
Prior myocardial infarction, %	86
Prior CABG, %	75
Prior PCI, %	69
Hypertension, %	80
Hyperlipidemia, %	92
Smoking history, %	71
Diabetes, %	42
Peripheral vascular disease, %	22
History of congestive heart failure, %	49
LVEF, mean \pm SD, %	30 \pm 8
At least 1 ED visit 6 months before EECF, %	44
At least 1 hospitalization 6 months before EECF, %	58

LVEF indicates left ventricular ejection fraction; EECF, enhanced external counterpulsation; CABG, coronary artery bypass graft surgery; PCI, percutaneous coronary intervention; and ED, emergency department.

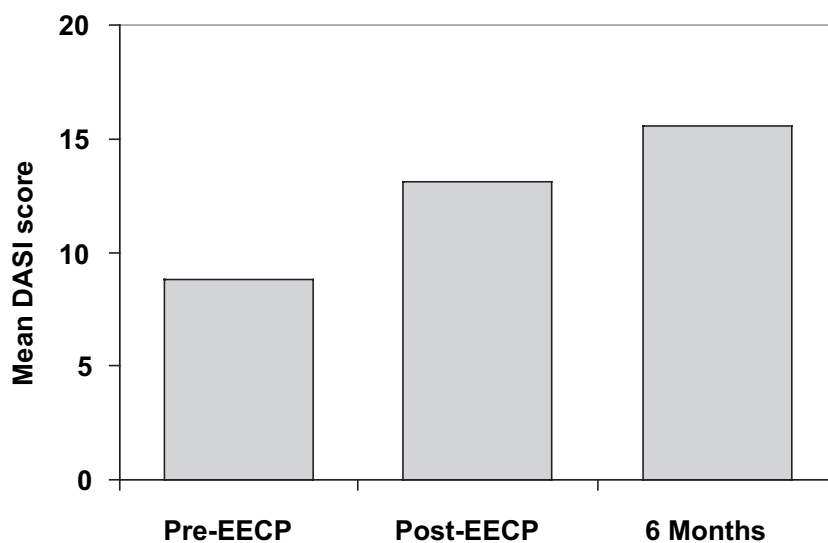


Figure 1. Duke Activity Status Index (DASI) pre-enhanced external counterpulsation (EECF), post-EECF, and at 6 months.

were determined from Kaplan-Meier survival analysis.

Results

The IEPR-II enrolled 2917 patients between 2002 and 2004. Of these, 450 patients had refractory angina, LV dysfunction, and complete data on ED visits and hospitalizations before EECF treatment and were included in this study. Four patients who died during the initial treatment period were excluded. Eighty-one percent of patients provided data at 6-month follow-up.

The mean age of the patients was 69 \pm 11 years; the mean duration of clinical coronary artery disease was 13.8 \pm 9.5 years. Due to the extent and severity of disease, LV dysfunction, comorbid conditions, prior interventions, and high risk-benefit ratio, 98% of patients were not candidates for further revascularization. Angina was severe (class III-IV) in 93% of patients and 50% of the patients had a history of HF. There was a high prevalence of cardiac risk factors, including 81% with a family history of premature

Myocardial infarction (MI)	0.7
CABG	0.2
PCI	1.2
MI/CABG/PCI	1.8
Unstable angina	4.0
Congestive heart failure	2.6
Skin breakdown	4.9
Musculoskeletal	2.3

LVEF indicates left ventricular ejection fraction; EECP, enhanced external counterpulsation; CABG, coronary artery bypass grafting surgery; and PCI, percutaneous coronary intervention. *Values are expressed as percentage.

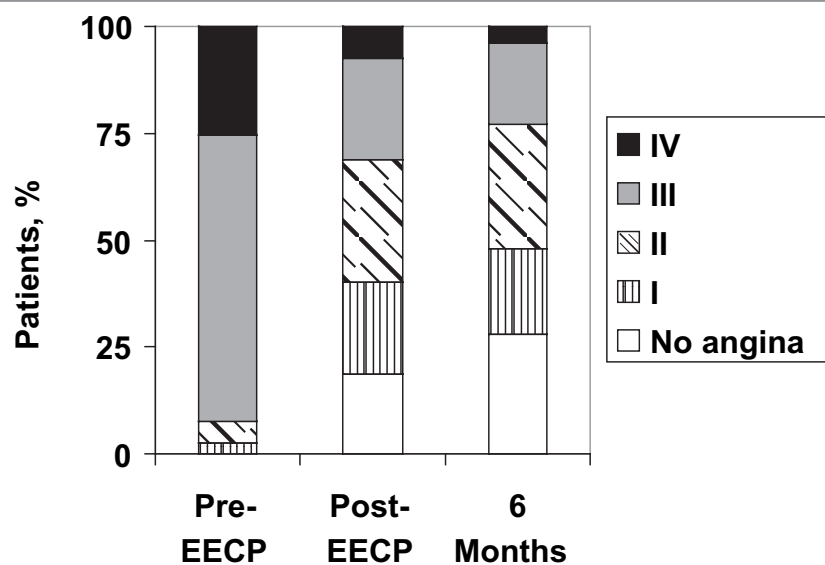


Figure 2. Angina class pre-enhanced external counterpulsation (EECP), post-EECP, and at 6 months.

atherosclerotic cardiovascular disease. The mean LVEF was $30\% \pm 8\%$, which was not particularly low for an EF population in terms of HF studies. Forty-four percent of patients had at least one ED visit and 58% had at least 1 hospitalization in the 6 months before EECP therapy (Table I). Quality of life was very poor, with a mean DASI score of 9.9 ± 8.6 at baseline.

Patients underwent a mean of 31.2 ± 10.0 hours of EECP, with 78% completing a 35-hour course of therapy. Eight percent stopped due to a clinical event, and 14% stopped due to patient preference. Major adverse cardiovascular event (MACE) (myocardial infarction, coronary artery bypass graft surgery [CABG], percutaneous coronary intervention, death) rates occurring

during the course of EECP therapy were 0.7%, 0.2%, 1.2%, and 0.0%, respectively, for a total MACE rate of 1.8%. HF exacerbation or new HF was reported in 2.6% of patients (Table II).

After completion of EECP therapy, angina decreased by at least 1 class in 72% of patients, 19% reported no angina, and only 2% had an increase in angina class ($P < .001$). The mean number of weekly angina episodes decreased by 7 ± 14 episodes from 11.4 ± 16.9 to 3.8 ± 10.9 ($P < .001$). Of those taking nitroglycerin on an as-needed basis, 43% discontinued nitroglycerin use after EECP therapy. Quality of life, as assessed by the DASI score, improved with a mean increase in score of 4.8 ± 9.0 , from 9.9 ± 8.6 to 14.8 ± 11.0 ($P < .001$) (Figure 1).

Six months after initiating EECP therapy, improvements in angina, quality of life, and nitroglycerin use were maintained (Figure 2). MACE rates at 6 months included 5.3% death, 1.9% myocardial infarction, 0.5% CABG, and 3.7% percutaneous coronary intervention, for a total MACE rate of 10.6%. HF exacerbation or new HF was reported in 3.1% of patients. The proportion of patients reporting at least 1 ED visit in the 6 months after the start of treatment was 11.8%, and the proportion of patients reporting at least 1 hospital admission was 23.5% (Figure 3). The mean number of ED visits per patient decreased from 0.9 ± 2.0 pre-EECP to 0.2 ± 0.7 at 6 months ($P < .001$), and hospitalizations were reduced from 1.1 ± 1.7 to 0.3 ± 0.7 ($P < .001$).

β -blocker, calcium blocker, angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, antiplatelet, diuretic, and hypolipidemic medication use were similar at baseline and at 6-month follow-up (Table III).

Discussion

This is a prospective, observational study in which the occurrences of all-cause hospitalizations and ED visits during the 6 months following therapy are compared with the all-cause hospitalizations and ED visits in the 6 months before therapy in the same patients.

This cohort of patients with refractory angina and LV dysfunction are characterized by long-standing multi-vessel coronary artery disease, a high prevalence of coronary disease risk factors, and severe angina unresponsive to medical therapy. In addition, they are not amenable to conventional invasive revascularization.¹¹ These study results show that EECP therapy is well tolerated in these patients with severe angina and LV dysfunction, and lasting improvements in angina symptoms and quality of life are achieved in the majority of patients. These observations are consistent with data from a randomized controlled trial and several prospective trials that assessed the effects of EECP therapy in patients with chronic angina and preserved LV function.¹²⁻¹⁵

Recently, EECP therapy has emerged as a treatment option for patients with refractory angina and LV dysfunction.¹⁶ It has been shown to improve both angina and stress myocardial perfusion and reduce ischemia in patients with coronary artery disease.^{17,18} Modes of action studies have shown that EECP therapy increases arteriogenic factors, improves endothelial function, and enhances vascular reactivity.¹⁹⁻²⁴ Improvements observed in symptoms and laboratory tests, however, do not necessarily correlate with a reduction in ED visits and hospitalizations during the management of refractory angina patients with LV dysfunction. This study is the first to report the possible impact of EECP therapy on all-cause ED visits and hospitalization rates at 6-month follow-up.

There are an estimated 300,000 to 900,000 patients in the United States who have refractory angina on maximal medical treatment, with 25,000 to 75,000 new cases diagnosed each year.^{25,26} The epidemiology of refractory angina pectoris and LV dysfunction is not clearly defined, however. Patients with refractory angina and LV dysfunction have greater disability and are hospitalized more frequently than patients with all forms of cancer combined. Therefore, patients with refractory angina and LV dysfunction impose a serious health burden. New treatment regimens that can be used as an adjunct to the current therapies may lessen the burden of hospitalization and improve clinical outcomes.

Recently, Mukherjee and colleagues²⁷ showed that patients who are ineligible for traditional methods of revascularization had a hospitalization rate of 1.3 per patient per year, with a rehospitalization rate of 128%. It is estimated that patients with angina and LV dysfunction average 2.1 hospitalizations annually.²⁷ In our study, the mean number of all cause-hospitalization was 1.1±1.7 in the 6 months before EECP therapy, which is just about equal to the rate of 2.1 hospitalizations annually. Six months after initiating EECP therapy, the mean

Table III. Medication Use at Baseline and at 6 Months After EECP Treatment

MEDICATION TYPE	PRE-EECP, %	AT 6 MONTHS, %
β-Blocker	81	76
Calcium channel blocker	32	32
Angiotensin-converting enzyme inhibitor	58	57
Angiotensin receptor blocker	16	17
Antiplatelet	83	83
Diuretic	66	66
Lipid-lowering	80	82

EECP indicates enhanced external counterpulsation.

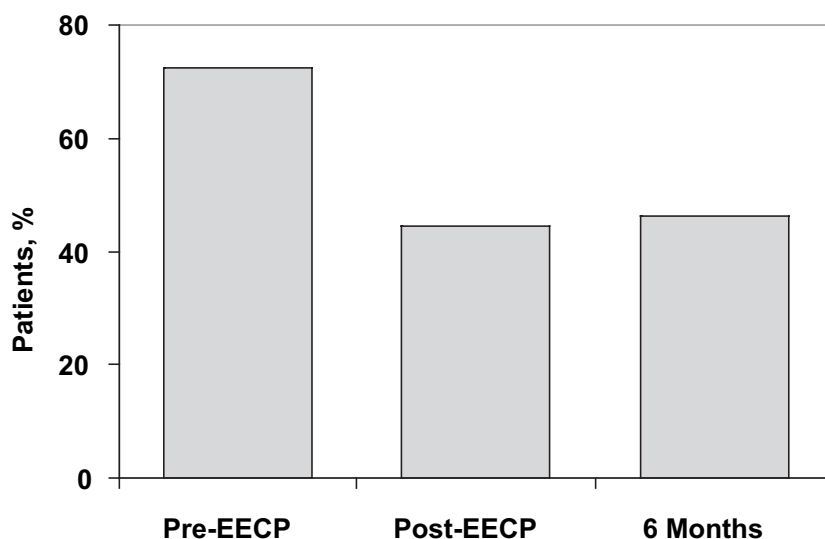


Figure 3. Nitroglycerin use pre-enhanced external counterpulsation (EECP), post-EECP, and at 6 months.

number of hospitalizations was significantly reduced from 1.1±1.7 to 0.3±0.7 ($P < .001$). This study was not a randomized controlled trial, but the results should be considered in light of the nature of the patients recruited. These patients have exhausted nearly all treatment options and, from a patient perspective, the treatment worked while others had failed. There is a paucity of randomized controlled trials showing that alternative, more expensive, or invasive treatments that might be considered for these patients, including high-risk repeat revascularization, spinal cord stimulation, left stellate ganglion blockade, thoracic sympathectomy, and myocardial laser revascularization, are effective. Murray and associates²⁸ assessed the impact of spinal cord stimulation on the need for acute admissions for

chest pain in patients with refractory angina pectoris. Implantation of spinal cord stimulation led to a decrease in the rate of admissions per patient from 0.97 per year to 0.27 per year. They did not report the mean EF of their cohort. While the reduction appears similar to results obtained in our study, their data reported admission rates for chest pain-related hospitalizations while ours reported all-cause hospitalizations, typically a more frequent occurrence in these patients.

This study explored the benefits of adjunctive therapy in a group of patients who would normally experience severe activity-limiting symptoms and low quality of life. EECP therapy, however, was not without cost in terms of financial resources required or the potential for reversible dermal injury such as blisters. Therefore, it

is imperative to know whether EECP therapy in this group of patients was any more beneficial than in a controlled group.

A limitation of this study is the lack of a control group to assess the outcomes. While difficult to perform in patients who have exhausted nearly all treatment options, a randomized clinical trial would provide a more rigorous

evaluation of the impact of EECP therapy on all-cause and cardiovascular hospitalization and ED visits.

Conclusions

Despite an unfavorable risk profile, refractory angina patients with LV dysfunction achieved a substantial reduction in rates of ED visits and hospitalizations at 6-month follow-up

compared with the 6 months before treatment. EECP therapy offers an effective adjunctive treatment option for this group of patients and may lessen the health care burden that comes with frequent ED visits and hospitalizations.

Disclosure: Dr Soran serves on the Speakers' Bureau of Vasomedical, Inc.

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