Clinical Investigations

Enhanced External Counterpulsation Is Cost-Effective in Reducing Hospital Costs in Refractory Angina Patients

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ABSTRACT

Background: Enhanced external counterpulsation (EECP) is effective in the treatment of refractory angina, a condition suffered by 1.7 million Americans. Declining cardiovascular mortality and appropriate use criteria may further increase this number.

Hypothesis: EECP is hypothesized to be cost-effective in reducing hospitalizations in refractory angina patients.

Methods: The data used in this analysis were collected in phase II of the International EECP Patient Registry (IEPR-II). Data were collected on changes in Canadian Cardiovascular Society functional class, Duke Activity Status Index, and number of hospitalizations in the 6 months prior to EECP and in the 6- and 12-month intervals following EECP. Estimates of the changes in annual cost of all-cause hospitalization before and after EECP therapy were calculated by the product of the differences in hospitalization rates in the 6-month interval before and after EECP treatment and estimated hospitalization and physician charges after subtracting the average cost of EECP.

Results: Data for 1015 patients were analyzed. Hospitalization occurred in 55.2% of patients, an average of 1.7 ± 1.4 hospitalizations/patient, in the 6-month period before 35 hours of EECP; and in 24.4%, an average of 1.4 ± 1.0 hospitalizations/patient, during the 6- to 12-month period after EECP. The average hospitalization and physician charge in the US was $17 995, and the average EECP cost was $4880, yielding an annual cost savings/patient of $17 074.

Conclusions: Treatment of refractory angina patients with EECP resulted in improvement in angina and functional class accompanied by a sustained reduction in health care costs over 1 year of follow-up.

Introduction

Enhanced external counterpulsation (EECP) is a noninvasive treatment for patients with ischemic heart disease. The US Food and Drug Administration has cleared EECP for use in unstable and stable angina pectoris, acute myocardial infarction, congestive heart failure (HF), and cardiogenic shock. Currently in the United States, EECP is used mainly for the treatment of patients with end-stage coronary artery disease (CAD) with Canadian Cardiovascular Society (CCS) class III and IV angina refractory to optimal tolerated medical therapy who are poor candidates for revascularization (angioplasty or surgical therapy). The Centers for Medicare & Medicaid Services (CMS) and many insurance companies have determined to provide national coverage of EECP for patients who have been diagnosed with disabling angina (CCS class III or class IV, or equivalent classification) and who, in the opinion of a cardiologist or cardiothoracic surgeon, are not readily amenable to surgical intervention because their condition is inoperable, and/or their coronary anatomy is not readily amenable to such procedures, and/or they have comorbid conditions that can create excessive risk.

Enhanced external counterpulsation therapy uses 3 pairs of pneumatic cuffs wrapped around the lower extremities that inflate and deflate in synchrony with the cardiac cycle to produce well-demarcated hemodynamic effects. During diastole, the cuffs inflate with the R-wave of the electrocardiogram of the patient as a trigger to create a retrograde aortic flow, increasing central diastolic pressures and coronary perfusion. This external applied pressure also

Dr. John C.K. Hui is a shareholder in Vasomedical, a company marketing EECP.

The authors have no funding, financial relationships, or conflicts of interest to disclose.

Received: January 3, 2015
Accepted with revision: January 25, 2015

Published online in Wiley Online Library (wileyonlinelibrary.com)
DOI:10.1002/clc.22395

enhances blood return on the venous side and increases cardiac output by the Starling mechanism. At the beginning of systole, the applied pressure is released and the cuff deflation leaves behind an emptied peripheral vascular bed, which, by decreasing afterload impedance, decreases myocardial oxygen demand and cardiac workload. One course of EECP treatment usually consists of 1-hour daily sessions 5 days a week for 7 weeks, for a total of 35 hours.

Enhanced external counterpulsation has been shown to be highly effective in relieving angina symptoms[1,2] and improving CCS functional class,[3,4] exercise capacity,[1,5] and quality of life (QoL)[6] in patients with refractory angina. Approximately 75% of patients are responders to EECP treatment, and the benefits are often sustained from 3 to 5 years.[7,8] New insights into the mechanism of action of EECP support the hypothesis that the increased velocities of blood flow acting on the endothelium during EECP may have several pleiotropic effects mediated by shear stress–responsive gene expression.[9] Enhanced external counterpulsation has been shown to improve endothelial function[10,11]; reduce inflammatory cytokines[12,13]; promote vascular tone and function[14]; induce beneficial changes in conductance vessel compliance[15,16]; decrease oxidative stress,[14] atherosclerosis,[13] and apoptosis; mobilize endothelial cell repair precursors[17]; and recruit and develop coronary collaterals.[18,19]

The prevalence of refractory angina in the United States has been estimated to be 1.7 million, with an incidence of approximately 30 000 to 50 000 new cases each year.[20] These numbers are likely to become larger with continuing decreases in mortality rates from cardiovascular disease (CVD) and increasing numbers of patients surviving with incomplete revascularization. There are no reports on the cost-effectiveness of EECP treatment in this group of patients. Repeated hospitalizations in patients with severe angina are a major contributor to direct costs of care, and EECP has been shown extensively to be effective in improving the QoL, angina functional class, and functional capacity in refractory angina patients. The current study is a prospective observational registry study of consecutive patients undergoing ≥35 hours of EECP treatment to examine whether the benefit of EECP in improving angina class and function results in decreased all-cause hospitalization rates, alters the predictors of hospitalization, and potentially results in health care savings through a reduction in hospitalizations using a cost-benefit analysis by comparing cost savings due to the cost of EECP therapy to the reduction of subsequent repeat-hospitalization costs.

Methods

The data used in this analysis were collected in phase II of the International EECP Patient Registry (IEPR-II). Details of the registry design and patient characteristics have been described previously.[3,4] All patients signed informed written consent before entry into the Registry. The IEPR database was used to select treated patients with complete 6-month pre-EECP treatment and 12-month follow-up data. All patients completed at least the recommended 35 hours of EECP treatment over a period of ≥7 weeks. All-cause hospitalization data were collected in the 6-month period before EECP treatment and over the following 6 months after completion of the EECP courses. Changes in angina and QoL in response to EECP therapy were assessed immediately prior to treatment and at 6 to 12 months follow-up by CCS class, Duke Activity Status Index (DASI) score, and nitroglycerin (Ntg) use. Demographic predictors of hospitalization in the 6 months prior to EECP were identified using logistic regression models and compared with those 6 months following completion of EECP treatment. Statistical significance was determined at $P < 0.05$. The impact on health care costs was assessed by the proportion of patients hospitalized and the number of hospitalizations per patient in sequential 6-month periods: 6 months prior to a 35-hour course of EECP and the 6 months after completion of EECP therapy. Annual EECP hospitalization cost savings per patient was calculated by the product of estimated hospitalization and physician charges based on a sample-size weighted average of Healthcare Cost and Utilization Project (HCUP) Nationwide Inpatient Sample database[21] and the reduction of hospitalizations per year after subtracting the average cost of EECP therapy. The prevalence of refractory angina in the United States in 2008 was estimated from the American Heart Association Heart Disease and Stroke Statistics (http://www.heart.org/HEARTORG/General/Heart-and-Stroke-Association-Statistics_UCM_319064_SubHome Page.jsp) and the Incidence and Prevalence Database.[22]

Results

The IEPR data were analyzed for 1015 patients. The mean age was 67.1 ± 11.0 years; 73.3% were male. Baseline characteristics demonstrated a high risk cohort: 70.3% had prior MI, 89.8% had prior revascularization (coronary artery bypass grafting [CABG], 70.6%; percutaneous coronary intervention [PCI], 71.9%)], 23.2% had HF, 20.4% had peripheral vascular disease, 11.3% had chronic renal insufficiency, 13.8% had atrial fibrillation, and 11.8% reported a pacemaker/implantable cardioverter-defibrillator. Multivessel CAD with >70% stenosis was present in 91.7%, and only 8.2% were CABG or PCI candidates (PCI, 6.4%; CABG, 6.0%). Patients have suffered from CAD for a mean of 10.3 ± 0.8 years, and the mean left ventricular ejection fraction (LVEF) was 47.5% ± 14.4%. There was a high prevalence of risk factors: 81.3% with hypertension, 92.6% with hyperlipidemia, 43.0% with diabetes mellitus (DM), 68.5% with smoking history, and 80.4% with family history of premature CVD. Baseline medical therapy included use of antiplatelet therapy (82.4%), warfarin (11.6%), β-blockers (83.0%), statins (11.9%), angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (63.2%), calcium channel blockers (41.0%), nitrates (73.4%), and diuretics (50.1%).

In the 6 months immediately prior to EECP, 95.8% of patients were CCS III or IV; the DASI score was 11.1 ± 9.9; there was Ntg use in 70.9% (average, 8.8 ± 11.6/wk). Hospitalization occurred in 55.2% of patients, with an average of 1.7 ± 1.4 hospitalizations/patient (64.5% of patients with 1 admission, 22.0% with 2 admissions, and 13.5% with ≥3 admissions).

Patients received 35.9 ± 2.9 hours of EECP therapy. Immediately after completion of therapy, 18.3% were CCS

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DOI:10.1002/clc.22395

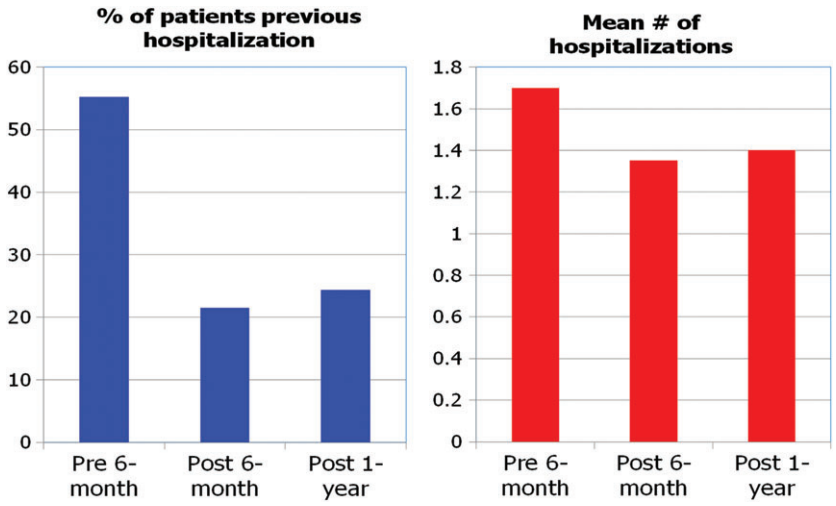

Figure 1. CCS class prior to EECP, immediately post-treatment and at 6 and 12 months post-treatment. Abbreviations: #, number; CCS, Canadian Cardiovascular Society; EECP, enhanced external counterpulsation.

III or IV and 17.8% were angina free. Post-EECP, CCS improved in 85.1% of patients (85.2% with angina reduced by ≥1 CCS class, 54.2% with angina reduced by 2 classes). The DASI score increased to 17.5 ± 12.0, Ntg decreased to 41.2% (average, 2.5 ± 6.8/wk). All-cause hospitalization during the EECP treatment period was minimal. Decompensated HF with peripheral edema or pulmonary congestion was the major concern during treatment. The patient is relatively supine during EECP treatment and the external cuffs on the lower extremities facilitate mobilization of extravascular fluid and increase venous return and right-heart and pulmonary pressures. These actions have the potential of exacerbating HF and causing pulmonary edema. Pulse oximetry is routinely employed during treatment to detect desaturation and allow timely intervention. Heart failure increased treatment concerns and was a predictor of hospitalization both before and after EECP therapy.

In the 6 months post EECP, 91 patients (9%) dropped out of the study; 19.9% of the remaining 924 patients were in CCS III or IV and 26.9% were angina free. The DASI score was 17.3 ± 12.6; Ntg was used in 45.6% (average, 5.8 ± 7.9/wk). Hospitalization occurred in 21.5% of patients, with an average of 1.35 ± 1.0 hospitalizations/patient. At 1 year post EECP treatment, 879 patients (87%) were followed. The benefits were preserved at 1 year: 21.2% were CCS III or IV and 27.6% remained angina free; the DASI score was 17.1 ± 12.6; and Ntg was used by 45.5% (average, 5.8 ± 7.9/wk). Hospitalization occurred in 24.4%, an average of 1.40 ± 1.0 hospitalizations/patient. All measures of angina, QoL, and hospitalizations were similar at 6 and 12 months post EECP and significantly improved from baseline (Figure 1). The mortality rate at 1 year post EECP was 4%.

Pre-EECP predictors of hospitalization included the effect of an increase of 10 years in age ($P = 0.002$), congestive HF ($P = 0.005$), chronic renal insufficiency ($P = 0.002$), prior PCI ($P < 0.0001$), and the length of time the patient suffered from CAD per increased year ($P = 0.013$). The odds ratios and confidence intervals are shown in the Table 1. In the

Table 1. Independent Predictors of Hospitalization

Variable	OR	95% CI	*P* Value
6 months before EECP treatment			
Effect of an increase of 10 years in age	0.863	0.756-0.985	0.002
CHF	1.533	1.091-2.155	0.005
Chronic renal insufficiency	2.249	1.408-3.593	0.002
Prior PCI	2.065	1.524-2.798	<0.0001
Duration of CAD per increased year	0.979	0.963-0.996	0.013
6 months after EECP treatment			
CHF	1.516	1.052-2.185	0.027
Prior PCI	2.195	1.478-3.259	<0.0001

Abbreviations: CAD, coronary artery disease; CHF, congestive heart failure; CI, confidence interval; EECP, enhanced external counterpulsation; OR, odds ratio; PCI, percutaneous coronary intervention.

6 months after EECP, hospitalization predictors included congestive HF ($P = 0.027$) and prior PCI ($P < 0.0001$), as shown in the Table 1. All other pretreatment predictors were no longer significant in the post-treatment period. In addition, DM, prior CABG, white race, prior stroke or transient ischemic attack, LVEF <35%, and DASI score were not predictive of hospitalization in either time interval.

The annualized pre-EECP treatment hospitalization rate was 1.85 hospitalizations per patient per year. Post EECP, 23% of the patients were hospitalized, a mean of 1.4 ± 1.0 hospitalizations/patient in the 1 year following EECP. The post-EECP hospitalization rate was 0.63 hospitalizations per patient per year, reducing the hospitalization by 1.22 hospitalizations per patient per year (Figure 2). The average hospitalization and physician charge in the United States was $17 995, and the average EECP treatment cost was $4880, yielding an annual cost savings per patient of $17 074.[21,22] A low estimate of 30 000 refractory patients per year having

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DOI:10.1002/clc.22395

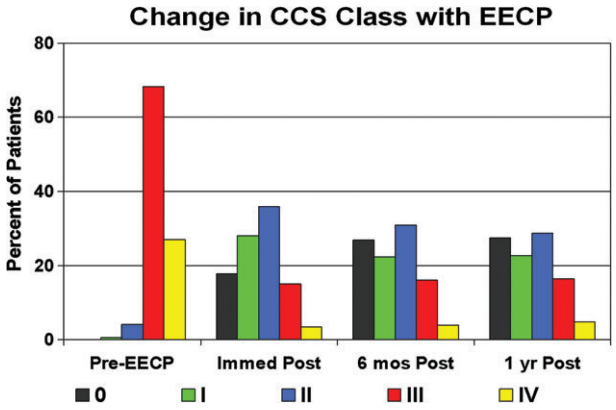

Figure 2. Percentage of patients and number of hospitalizations in the 6 months prior to and 6 and 12 months after EECP. Abbreviations: CCS, Canadian Cardiovascular Society; EECP, enhanced external counterpulsation; Immed, immediately.

been treated with EECP in the United States would translate to a reduction in hospitalization costs of approximately $512 million. A high estimate of 50 000 refractory patients having been treated with EECP would translate to an approximate total annual hospitalization cost savings of $853 million.

Discussion

Similar to exercise, EECP effectively increases shear stress, resulting in similar direct physiologic effects. An early observation was that EECP promoted a "training effect," decreasing peripheral resistance and the heart rate and blood pressure response to exercise. In subsequent physiologic studies, EECP treatment has been demonstrated to produce effects similar to exercise, with improvements in arterial stiffness, flow-mediated vasodilation, and endothelial function; increased nitric oxide; decreased lipid peroxidation; a decrease in insulin resistance and an increase in insulin sensitivity index; and an increase in vascular endothelial growth factor and muscle capillary density.[15,23–27] In clinical practice, the "passive exercise" of EECP often increasingly transitions to a more "active exercise" lifestyle as the patients are both encouraged and able to exercise with less limiting angina as treatment progresses. Some of the physiologic effects of EECP, such as a decrease in systolic blood pressure, have been demonstrated to be transient.[28] Regaining the ability to exercise and its regular practice may amplify, preserve, and extend the durability of EECP treatment. An often-unappreciated benefit of EECP therapy is the effect that the prolonged contact with health care providers (35-session course of therapy) has in promoting effective transitional care, medication compliance, patient satisfaction, and a wellness philosophy stressing beneficial lifestyle changes. This undoubtedly amplifies the benefits of EECP treatment and may play an increasing role in its choice as therapy for this group of patients as we move from a sickness/fee-for-service to a wellness/value-based model of health care.

In 2009, the United Kingdom's Health Technology Assessment Programme published a report on a systematic review and economic analysis to determine the clinical effectiveness and cost-effectiveness of EECP compared with usual care and placebo for refractory stable angina and HF.[29] The incremental cost-effectiveness ratio of EECP was £18 643 for each additional quality-adjusted life-year. The review of cost-effectiveness demonstrated that the long-term maintenance of EECP's QoL benefits is central to the estimate of its cost-effectiveness. If EECP's QoL benefits are assumed to be maintained for no more than 1 year after treatment, EECP does not appear to be cost-effective, as defined by the National Institute for Health and Clinical Excellence's cost-effectiveness threshold range (National Institute for Health and Clinical Excellence, 2004). What has not been available for evaluation is the potential cost-effectiveness of EECP in reducing medical costs (including the cost of hospitalizations, revascularization procedures, physician visits, and medicines). The presented data suggest that by impacting on medical costs as well as QoL, the cost-effectiveness of EECP may have been underestimated in prior analyses.

A paper by Bondesson and colleagues of Sweden compared hospital utilization and costs for spinal-cord stimulation (SCS) and EECP for refractory angina pectoris.[30] There were 35 patients in the SCS group and 38 in the EECP group. The collected data were divided into 3 time periods. The first period covered the first year preceding treatment, the second was the treatment period, and the third was divided into 1 to 12 months and 13 to 24 months after treatment. In Sweden, the mean number of days spent in hospital due to refractory angina was 3.58, using data from the country's national registry of cardiovascular disease in 2009. During the pretreatment period, 23% of SCS patients had acute cardiac-related hospital admission, averaging 7.03 ± 9.55 days per admission, vs 26% in the EECP group, with 5.82 ± 8.24 days per admission, with no significant differences between groups. During the treatment period, with an average of 5.89 months spent waiting and undergoing treatment, there was a 3% admission rate with 0.4 hospital days per admission in the SCS group, and a 16% admission rate in the EECP group with an average of 1.03 days per admission. There were no significant differences between groups. The hospitalization admissions did not change significantly during the 1-year and 2-year follow-up periods, but the hospitalization days reduced to 4.89 ± 8.15 days ($P < 0.0001$ compared with pretreatment) and 4.74 ± 8.70 days ($P < 0.001$) in the SCS group, and 3.94 ± 9.10 days ($P < 0.004$) and 3.03 ± 9.74 ($P = 0.104$) in the EECP group, respectively.

In 2006, using data from the IEPR, in a cohort of 450 refractory angina patients with LVEF $\leq$40%, Soran and colleagues reported that 44% had $\geq$1 emergency department (ED) visits and 58% had $\geq$1 hospitalizations in the 6 months before EECP therapy.[31] The proportion of patients reporting $\geq$1 ED visits in the 6 months after the start of EECP treatment was 11.8%, with 23.5% of patients reporting $\geq$1 hospital admissions. The mean number of ED visits per patient deceased from 0.9 ± 2.0 pre-EECP to 0.2 ± 0.7 at 6 months post-EECP ($P < 0.001$), and hospitalizations were reduced from 1.1 ± 1.7 to 0.3 ± 0.7 ($P < 0.001$). These results are in agreement with the results of this study, given that refractory angina patients with reduced LVEF are often associated with more extensive disease and an increased ischemic burden. We have not reported ED visits in the

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DOI:10.1002/clc.22395

current study because there is a large overlap between ED visits and hospital admission.

Angina alone is a poor predictor of mortality. Although it clearly affects QoL and function, survival is more closely related to other variables, such as LV function, extent and severity of CAD and the candidacy for revascularization, arrhythmias, and comorbid conditions such as renal failure and DM. Most patients treated with EECP have end-stage CAD. Risk factors that were prevalent in the study cohort that would substantially increase the risk of mortality include LV dysfunction, extensive CAD, DM as a comorbid condition, and lack of revascularization candidacy. For end-stage CAD, annual mortality is estimated to exceed 5%.[32]

Study Limitations

The current study is a prospective study using data from refractory angina patients enrolled consecutively in EECP treatment centers. Because of the nature of the treatment, randomization and double blinding were impractical. The lack of a control group is a study limitation. It is assumed that drop-out was random, and thus the reported rates are a simple percentage of those reporting. The further details of hospitalization are not available for analysis. It should be noted that this was a voluntary registry with no payments to investigators or patients, minimizing the bias of subsidized studies but placing a substantial unreimbursed administrative burden on collaborating investigators. Although the durability and consistency of effect suggests a true treatment benefit, the potential cost savings appears clear regardless of the potential mechanism.

Conclusion

Treatment of end-stage CAD patients with a course of EECP resulted in substantial improvement in QoL. The QoL improvement was accompanied by a sustained reduction in health care costs over 1 year of cost follow-up. Enhanced external counterpulsation improved CCS angina class in refractory angina patients and decreased hospitalization rates in the 6 months post treatment. After EECP, hospitalization in PCI patients may reflect restenosis and the need for repeat revascularization. Most factors predicting hospitalization pre-EECP are not predictive of hospitalization post-EECP. This suggests that EECP broadly benefits refractory angina patients regardless of baseline demographics or comorbidity. Appropriate use of EECP in refractory angina patients could result in a substantial decrease in hospital costs at an attractive cost-effectiveness ratio.

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DOI:10.1002/clc.22395