May 31, 2005

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Subject: External Counterpulsation (ECP) Therapy
A Formal Request for Revision of Coverage Issues Manual (20.20)

EECP® therapy, a proprietary form of external counterpulsation (ECP), commonly referred to as enhanced external counterpulsation, is a non-invasive outpatient treatment for patients with cardiovascular disease and is indicated for use in stable and unstable angina pectoris, congestive heart failure, acute myocardial infarction, and cardiogenic shock. Effective 1999, Section 20.20 (formerly 35-74) of the Coverage Issues Manual was revised to provide national Medicare coverage for external counterpulsation (ECP). The Centers for Medicare and Medicaid Services (CMS) currently covers treatment for patients who have been diagnosed with disabling stable angina (Class III or IV Canadian Cardiovascular Society or equivalent classification), who in the opinion of a cardiologist or cardiothoracic surgeon, are not readily amenable to surgical intervention because:

1. Their condition is inoperable, or at high risk of operative complications or post-operative failure;
2. Their coronary anatomy is not readily amenable to such procedures; or they have co-morbid states, which create excessive risk.

A substantial amount of additional clinical evidence has been published in peer-reviewed publications since the national coverage decision was made in 1999, some of which we have discussed in meetings with the Coverage and Analysis Group at CMS. **We are therefore formally requesting a revision of the Coverage Issues Manual to expand coverage of ECP for use in the treatment of patients with Class II angina and for use in patients with NYHA Class II/III stable heart failure symptoms with an ejection fraction ≤ 35%.** Specific coverage language is proposed in the supporting documentation attached.

HCPCS code G0166, External Counterpulsation, has been in place since the 2000 Medicare Physician Fee Schedule. When used in the hospital setting, ECP is assigned APC code 0678, External Counterpulsation.

Please feel free to contact me at 800-455-3327 ext. 154 or via email at erose@vasomedical.com if additional information is required during your review.

Sincerely,
Elizabeth (Betsy) Rose
Director, Market Development
Vasomedical Inc.

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Introduction & Overview

External counterpulsation therapy, administered with proprietary EECP® therapy systems, is a non-invasive treatment for patients with cardiovascular diseases and is indicated for use in stable and unstable angina pectoris, congestive heart failure, acute myocardial infarction, and cardiogenic shock. Vasomedical Inc., based in Westbury, NY, is the only manufacturer of EECP® therapy systems and the market-leading manufacturer of ECP products since 1995. EECP® therapy systems have been cleared by the Food and Drug Administration (FDA) on several occasions between 1989 and 2004 via 510(k) Premarket Notification Review (Appendix A).

Clinical evidence has been published in more than 50 peer-reviewed journals demonstrating that EECP® therapy provides relief of stable angina and stable congestive heart failure in selected patients in the form of:

- Improvement in symptoms
- Improvement in functional capacity
- Improvement in quality of life and health status

Angina affects 6.8 million people in the United States with 400,000 new cases of stable angina diagnosed annually. Vasomedical estimates that approximately 125-150,000 patients suffer with refractory angina inadequately relieved by medical therapy. In the United States, an estimated 20,000 patients are treated annually with EECP® therapy by approximately 800 providers. Patients treated with EECP® therapy average 66 years of age with a ten-year history of coronary artery disease. Over 80% of refractory angina patients who receive EECP® therapy complete the full course (30-35 hours) of treatment.

Treatment for chronic stable angina has two objectives as noted by the ACC guidelines:[1]

- Reduce mortality and morbid events – preventing MI and death
- Reduce symptoms of angina and occurrence of ischemia – which from the patient's perspective can be of greater concern – since anginal pain or equivalent exertional dyspnea limits activity and creates anxiety.

Treatment goals are:

- Elimination of pain
- Reduction in angina symptoms
- Results should be as complete or nearly complete elimination of anginal pain, and return to normal activity and functional capacity as close to Canadian Cardiovascular Class I as possible.

Congestive heart failure affects 5,000,000 people in the US with 550,000 new cases diagnosed each year.[2] It is estimated that of these 550,000 new patients, approximately 225,000 NYHA Class II/III patients suffer from stable CHF inadequately relieved by optimal medical therapy. Of the heart failure patients treated with EECP® therapy during clinical studies or with concomitant angina, approximately 80% completed more than 30–hours of therapy.

There are 970,000 hospital discharges for congestive heart failure, of which 720,000 (74%) are in patients over 65 years of age.[3] Hospitalization costs to the Medicare system for treating CHF are approximately $3.6 billion ($5,456 per discharge), with total direct & indirect costs to the US healthcare system estimated at $27.9 B.[4]

A significant number of clinical studies pertaining to EECP® therapy have been published in peer-reviewed journals since the current coverage decision was published in 1999. Specific to this request for expansion of coverage, data from randomized controlled trials such as the **Mu**lticenter **St**udy of **E**nhanced **E**xternal **C**ounter**p**ulsation (MUST-EECP) and the **P**rospective **E**valuation of **E**ECP in **C**ongestive **H**eart Failure (PEECH) trials, as well as data from the International EECP® Patient Registry (IEPR), demonstrate clinical benefits of EECP® therapy for patients with class II angina as well as patients with stable congestive heart failure, NYHA Class II and III, with an ejection fraction ≤ 35%. A summary of this clinical evidence by indication is attached.

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EECP® Therapy

Treatment with EECP® therapy is typically provided on an outpatient basis in 35 one-hour sessions over a period of approximately seven weeks. To receive EECP® therapy the patient lies on a treatment table and compressive cuffs (similar to large blood pressure cuffs) are securely wrapped around the patient's calves, thighs and buttocks. The patient's ECG is captured and used to control inflation and deflation of the cuffs in a synchronous fashion. The cuffs inflate in a distal to proximal sequence in late systole and deflate simultaneously in late diastole, just prior to the onset of systole.

Inflation-deflation time points are specifically adjusted to optimize therapeutic benefit. The sequential cuff inflation creates retrograde pressure waves that augment arterial diastolic pressure (increasing coronary perfusion pressure) and increases venous return to the right heart (increasing preload). Rapid, simultaneous cuff deflation decreases systemic vascular resistance, afterload and cardiac workload, thereby increasing cardiac output.

Device Name and Description
The Lumenair™ EECP® Therapy System is the most recent model in a family of EECP® therapy products manufactured by Vasomedical Inc (Figure 1). The Lumenair is comprised of two major components, a Treatment Table and a patient Cuff Set. The Treatment Table accommodates the air compressor and reservoir, a control module, a power distribution module, a microprocessor with touch screen/keyboard interface, printer, and components for acquiring and processing ECG and a finger Plethysmograph. Oxygen saturation (%SpO_2) measurement is provided by a Pulse Oximetry module. A microprocessor is used to operate and monitor the system by means of proprietary custom software, with the operator using the touch screen/keyboard interface to control its operation. The screen displays information pertinent to the operating systems, as well as treatment parameters and patient waveforms during use. The touch screen employs "hardware-less keys" which the operator touches to select a function or execute a command and the keyboard enables alphanumeric text entries. An internal disk drive is used to store data on the system and a printer is used to produce a hard copy of site and patient identification and physiologic data.

The Treatment Table frame also accommodates a mattress and other pneumatic circuits consisting of valve assemblies. The mattress contains foam and soft polyester fibers for optimal patient comfort. The valve assemblies consist of three pairs of inflation/deflation valves that open and close on command to inflate or deflate the patient Cuff Set with air.

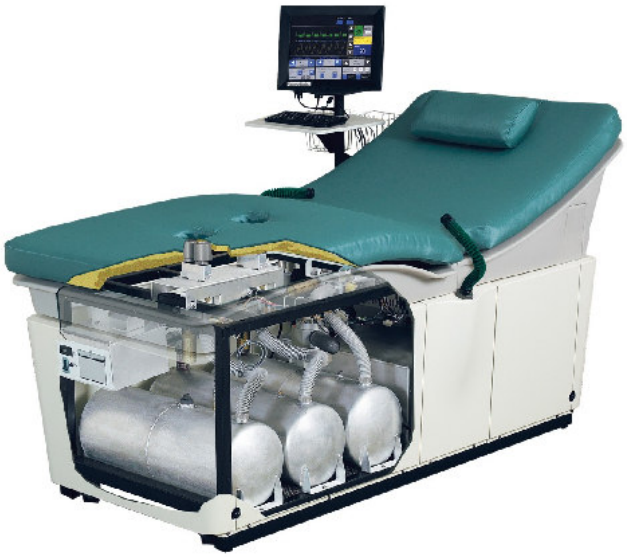

Figure 1. Lumenair™ EECP® Therapy System

Patient Selection

U.S. labeled indications for Vasomedical's EECP® therapy products specify that they are indicated for use in stable and unstable angina pectoris, congestive heart failure, acute myocardial infarction, and cardiogenic shock. EECP® therapy is a safe and effective treatment that provides immediate and sustained benefits in patients with disabling angina and angina equivalents, left ventricular dysfunction and heart failure.

Patients that may benefit from EECP® Therapy

Patients that may benefit from EECP® therapy include patients with stable angina or angina equivalents, CCSC Class II-IV **AND** patients with stable congestive heart failure, NYHA Class II/III with EF≤ 35% who:

- Respond inadequately to or do not tolerate medical therapy
- Restrict their activities to avoid symptoms
- Are unwilling to undergo additional invasive revascularization procedures
- Have LVD (EF≤35%)
- Have co-morbid conditions that increase the risk of revascularization procedures (e.g. diabetes, heart failure, pulmonary disease, renal function)
- Have coronary anatomy unsuitable for surgical or catheter-based revascularization
- Are considered inoperable or at high risk of operative/interventional complications
- Suffer with microvascular angina (Cardiac Syndrome X)
- Are elderly patients at high risk for morbidity and mortality associated with invasive coronary interventions.

Status of FDA Approvals

External counterpulsation devices are so-called Class III pre-amendment devices; as such devices were in interstate commerce prior to the enactment of the Medical Device Amendments and have not been reclassified by the FDA since. FDA 510(k) marketing clearances pertinent to Vasomedical EECP® therapy systems and their indications for use include the following:

510(k) Number	Date Granted	Device Name	Indications for Use	Comment
K882401	03/03/1989	Stony Brook Model EECP® MC-1		Pertains to the precursor model of Vasomedical's first commercial product
K940264	02/23/1995	Vasogenics EECP® MC-2	Stable and unstable angina, acute myocardial infarction, cardiogenic shock	Vasomedical's first commercial product (Vasogenics was acquired by Vasomedical, Inc.)
K003469	12/06/2000	EECP® Therapy System Model TS3	Stable and unstable angina, acute myocardial infarction, cardiogenic shock	Vasomedical's 2nd generation EECP® therapy system
K020857	06/14/2002	EECP® Therapy System Model TS3 with Pulse Oximetry	Stable and unstable angina, **congestive heart failure**, acute myocardial infarction, cardiogenic shock	Added congestive heart failure to labeled indication for use; modified device to incorporate pulse oximetry
K033617	03/01/2004	EECP® Therapy Systems Model TS4 with/without Pulse Oximetry Model TS3 with/without Pulse Oximetry Model MC-2	Stable and unstable angina, congestive heart failure, acute myocardial infarction, cardiogenic shock	Vasomedical's 3rd generation EECP® therapy system; modified contraindications and precautions

Appendix (A) contains copies of the 510(k) memorandums.

Mechanisms of Action

The specific mechanisms of action of EECP® therapy are not yet precisely known. However, clinical studies continue to identify components of the hemodynamic, neurohormonal and other physiological cascades initiated by the sequential cuff inflation and simultaneous cuff deflation during treatment. Improvement of endothelial function, promotion of collateral vessels and enhancement of ventricular function are all thought to be contributing factors (Figure 2).

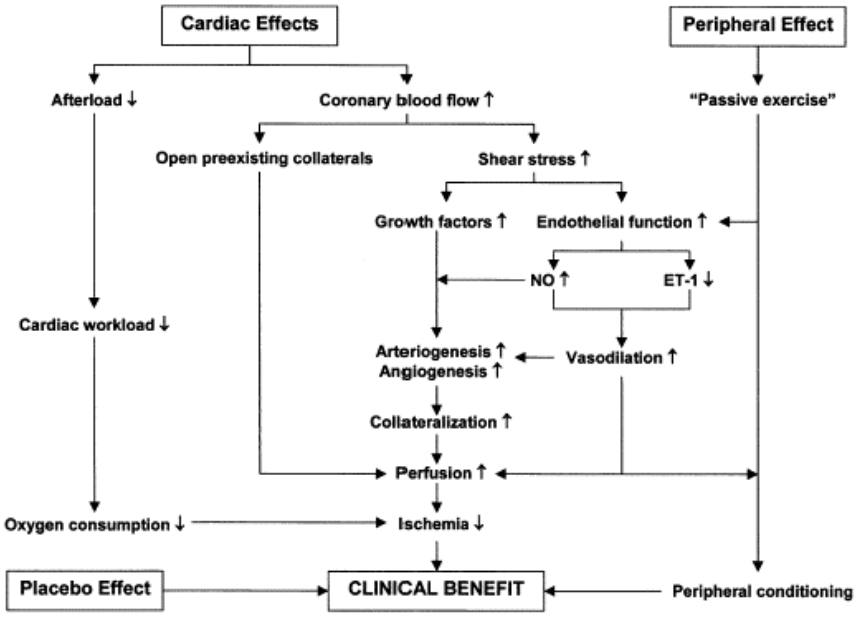

Figure 2. Mechanisms of Action of EECP® Therapy

Growing evidence supports the hypothesis that improvement in endothelial function represents an important mechanism supporting the clinical benefit observed with EECP® therapy.[5] EECP® therapy-induced increases in blood flow enhance endothelial shear stress, providing a stimulus resulting in increased endothelial nitric oxide levels, and reduced endothelin-1 levels, and vasodilatation. EECP® therapy also increases coronary collateral perfusion by opening pre-existing collateral channels, and potentially inducing arteriogenesis and angiogenesis.

EECP® therapy also produces effects mediated through arterial diastolic augmentation. The retrograde arterial pressure wave increases coronary perfusion pressure, creating a gradient between ischemic and non–ischemic areas of the myocardium that may recruit latent conduits and enhance myocardial perfusion. Increased endothelial shear stress releases growth factors.

Bonetti et al suggested that mechanisms contributing to the clinical benefit of EECP® therapy include improvement in endothelial function, promotion of collateralization, enhancement of ventricular function and peripheral effects similar to those observed in response to physical exercise.[6]

In a study evaluating the effects of EECP® therapy using reactive hyperemic–peripheral arterial tonometry (RH-PAT) as a measure of peripheral endothelial function, Bonetti et al conclude, that EECP® therapy is associated with an acute improvement in peripheral endothelial function, as is demonstrated by the acute increase in the RH-PAT index observed in response to therapy on the first three study days. Moreover, the significant difference between RH-PAT indices before the course of EECP® therapy and at one-month follow-up suggests that EECP® therapy also exerts a beneficial medium-term effect on endothelial function. [7]

Other Possible Mechanisms of Action

Effects on Nitric Oxide, Atrial Natriuretic Peptide and Brain Natriuretic Peptide

Urano et al also reported the effects of EECP® therapy on levels of atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) pre- and post-EECP® therapy in a pilot study of 12 patients with CAD.[8] While there were no significant changes in ANP, the plasma level of BNP significantly decreased following treatment (65 ± 33 vs. 56 ± 33 pg/mL, $p<0.05$, pre- vs. post-treatment). Plasma BNP levels positively correlated with improvement in diastolic function as evidenced by left ventricular end diastolic pressures [LVEDP] ($r = 0.44$, $p<0.05$) and negatively correlated with peak filling rates [PFR] ($r = -0.47$, $p<0.02$).

Similarly, Masuda et al, reported the effects of EECP® therapy on levels of nitric oxide (NO) and neurohormonal factors (ANP and BNP).[9] NO increased following completion of EECP® therapy, reaching a significantly greater level at 1 month ($p<0.02$) as compared to baseline. At 1 week following completion of EECP® therapy, both ANP ($p<0.02$) and BNP ($p<0.05$) had significantly decreased compared to baseline.

Hemodynamic Effects of EECP® Therapy

Studies have shown that the hemodynamics of EECP® therapy closely resemble those of the intraaortic balloon pump (IABP), long held as the "gold standard" for circulatory support of hemodynamically compromised patients. The magnitude of diastolic augmentation that can be achieved with EECP® therapy was found comparable to and often greater than that of the IABP resulting in improved coronary blood flow with decreased cardiac workload. Michaels et al in a landmark study using invasive measurement techniques during cardiac catheterization, demonstrated the hemodynamics of EECP® therapy in the central vasculature:

"Treatment with EECP® therapy unequivocally and significantly increases central aortic and intracoronary diastolic pressure and intracoronary blood flow velocity. Mean aortic and intracoronary pressure is increased, and left ventricular systolic unloading occurs during EECP® therapy (Figure 3)."[10]

A study by Taguchi suggests that the benefits of EECP® therapy compared to intra aortic balloon counterpulsation include an increase in coronary blood flow by diastolic augmentation, but with a positive effect on venous return with an increased preload and cardiac index.[11]

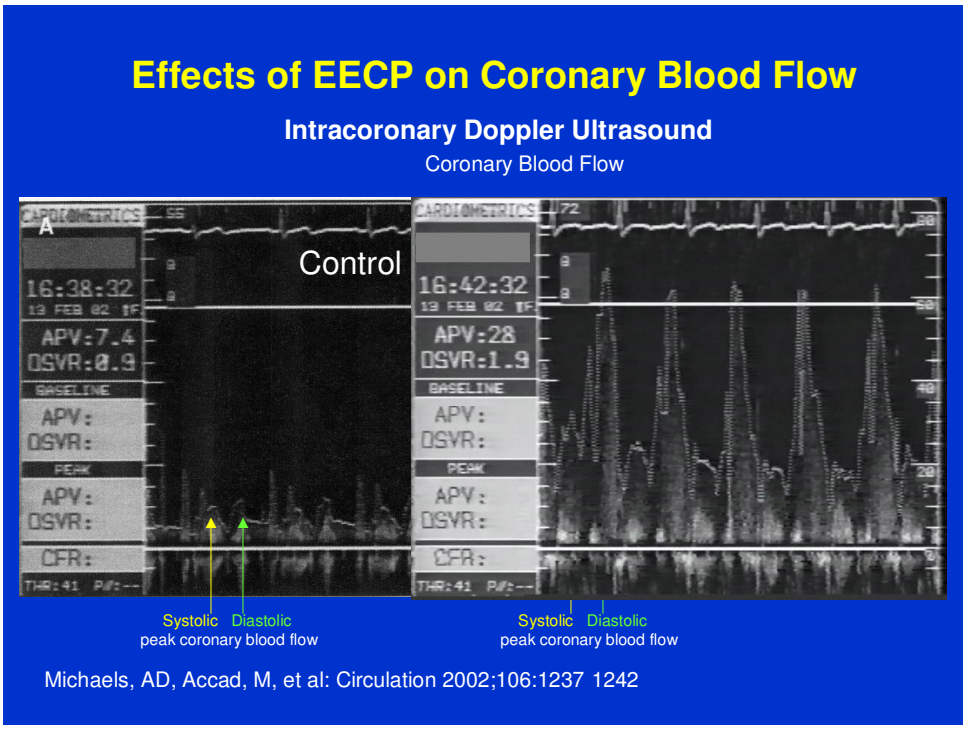

Figure 3. Effects of EECP on Coronary Blood Flow

Angina

Angina affects 6.8 million people in the United States with 400,000 new cases of stable angina diagnosed annually. Vasomedical estimates approximately 125-150,000 patients suffer with refractory angina inadequately relieved by medical therapy. In the United States, an estimated 20,000 patients are treated annually with EECP® therapy by approximately 800 providers. Patients treated with EECP® therapy average 66 years of age with a ten-year history of coronary artery disease. Over 80% of refractory angina patients who receive EECP® therapy complete the full course of treatment (30-35 hours).

Treatment for chronic stable angina has two objectives as noted by the ACC guidelines:[12]

- Reduce mortality and morbid events – preventing MI and death
- Reduce symptoms of angina and occurrence of ischemia – which from the patient's perspective can be of greater concern- angina pain or equivalent exertional dyspnea limits activity and creates anxiety.

Treatment goals are:

- Elimination of pain
- Reduction of angina symptoms
- Results should be as complete or nearly complete elimination of anginal pain, and return to normal activity and functional capacity as close to Canadian Cardiovascular Class I as possible.

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Clinical Data Summary for Class II Angina Indication
Multicenter Study of Enhanced External Counterpulsation (MUST-EECP)

The effects of EECP® therapy on exercise-induced myocardial ischemia and angina were evaluated in a prospective, multicenter, randomized, double-blind study conducted in 139 patients with angina and documented coronary artery disease (CAD).[13] Patients were randomized to active EECP® therapy (300 mmHg applied pressure) or sham-EECP® therapy (70 mmHg applied pressure)(Figure 4). Patients enrolled were evaluated according to Canadian Cardiovascular Society Classification (CCSC) for angina and included patients with Class I (25%), Class II (50%), and Class III (25%) angina. The treatment effect was measured by changes in exercise treadmill parameters (exercise duration, time to ≥ 1mm ST-segment depression) and symptoms (frequency of anginal episodes and nitroglycerin use).

The MUST-EECP trial had pre specified parameters including:

- Exercise ability determined by exercise duration using a standardized or modified Bruce protocol and time to ST-segment depression.
- Clinical status defined as frequency of anginal episodes, intake of oral nitroglycerin, and medication use.
- Adverse experiences which were evaluated through physician exam, laboratory testing and daily questions.

Statistical analysis was performed using a two-sided t-test @ $p \leq 0.05$. Testing for significance used ANOVA for continuous variables and Chi-square for non-continuous variables.

Figure 4 illustrates the study path followed by patients entered into the MUST-EECP trial and reports what happened to patients as they progressed through the study.

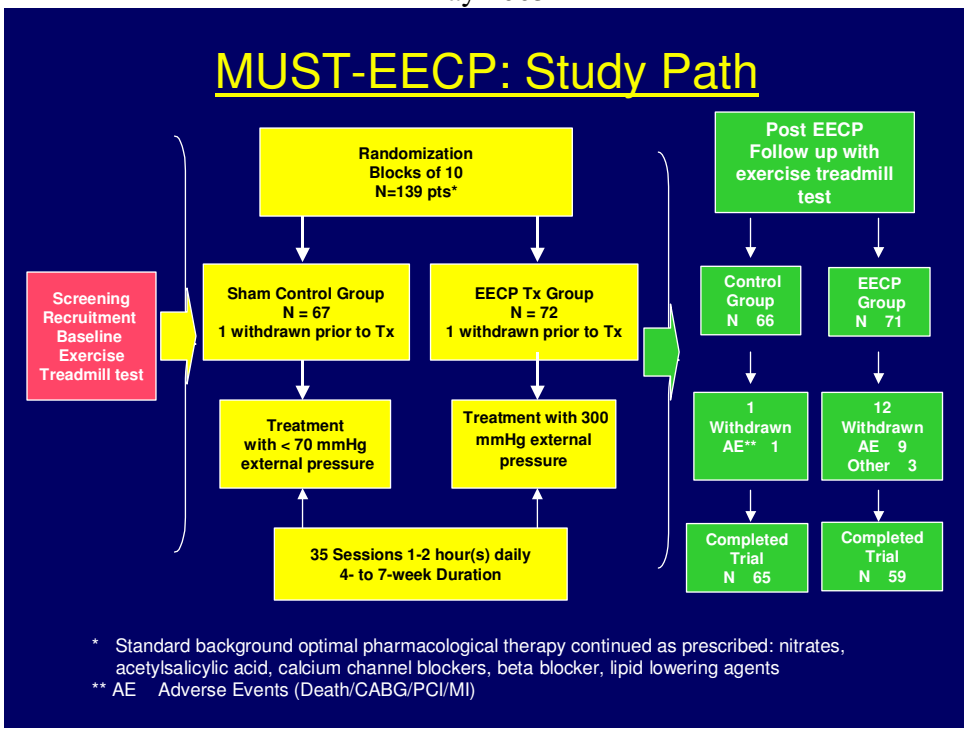

Figure 4. Patient Disposition in MUST-EECP

MUST-EECP Summary of Results

Results from the trial demonstrated that, as compared to the sham-EECP® treatment group, patients in the active group demonstrated a significant improvement in time to ≥1-mm ST-segment depression (p=0.01).

JACC Vol. 33, No. 7, 1999
June 1999:1833–40

Table 2. Exercise Treadmill Test

	Inactive CP				Active CP				Between-Group
	n	Pre-CP	Post-CP	p Value	n	Pre-CP	Post-CP	p Value	p Value
Exercise duration (s)	58	432 ± 22	464 ± 22	< 0.03	57	426 ± 20	470 ± 20	< 0.001	< 0.31
Time to ≥1-mm ST-segment depression (s)	56	326 ± 21	330 ± 20	< 0.74	56	337 ± 18	379 ± 18	< 0.002	= 0.01

Duration in seconds, mean ± SEM.
Pre-CP: baseline, before counterpulsation; Post-CP: follow-up, postcounterpulsation. p values are computed based on adjusted change in duration from baseline to follow-up.

Moreover, there was also a significant between-group difference in angina counts.

Table 3. Angina Counts

			Improvement			Worsening				p
		Median	50+%	25%–49%	0%–24%	1%–25%	26%–50%	51%–100%	100+%	Value
Intention to treat										
Inactive CP	66	0%	21	3	28	2	2	4	6	
Active CP	71	−20%	32	1	33	0	0	2	3	< 0.05
≥34 sessions										
Inactive CP	59	0%	19	2	24	0	2	5	7	
Active CP	57	−50%	29	1	23	0	0	0	4	< 0.02

Categories of change are expressed in percent versus baseline. Daily average of self-reported episodes of angina pectoris are computed over three 24-h periods. p values are calculated for between-group differences using a Cochran-Mantel-Haenszel chi-square test for ordered categories stratified by treatment center.

Exercise duration increased in both groups and was not significantly different between groups. Nitroglycerin usage decreased in the active-EECP group compared to baseline, but was not significantly different between groups.

MUST-EECP Summary of Results of Sub-group Analysis by CCS Class

Consistent with the results in the MUST-EECP trial study population overall presented for the original national coverage decision, the results of a sub-group analysis in patients with Class II angina were comparable to results in patients overall (CCS Class I, II and III patients). Appendix (B) has a summary of the MUST-EECP trial data.

As compared to the sham-EECP® treatment group, EECP® treated patients demonstrated a significant improvement in time to ≥1-mm ST-segment depression (p=0.01)(Figure 5), with a trend towards a significant reduction in the number of anginal episodes (p=0.044) (Figure 7).

Compared to controls, Class II angina patients undergoing EECP® therapy experienced increased time to ischemia on exercise and decreased frequency of angina episodes.

Compared to baseline, Class II angina patients experienced an increase in total exercise duration (Figure 6), an increase in time to ischemia on exercise, and a decrease in angina episodes.

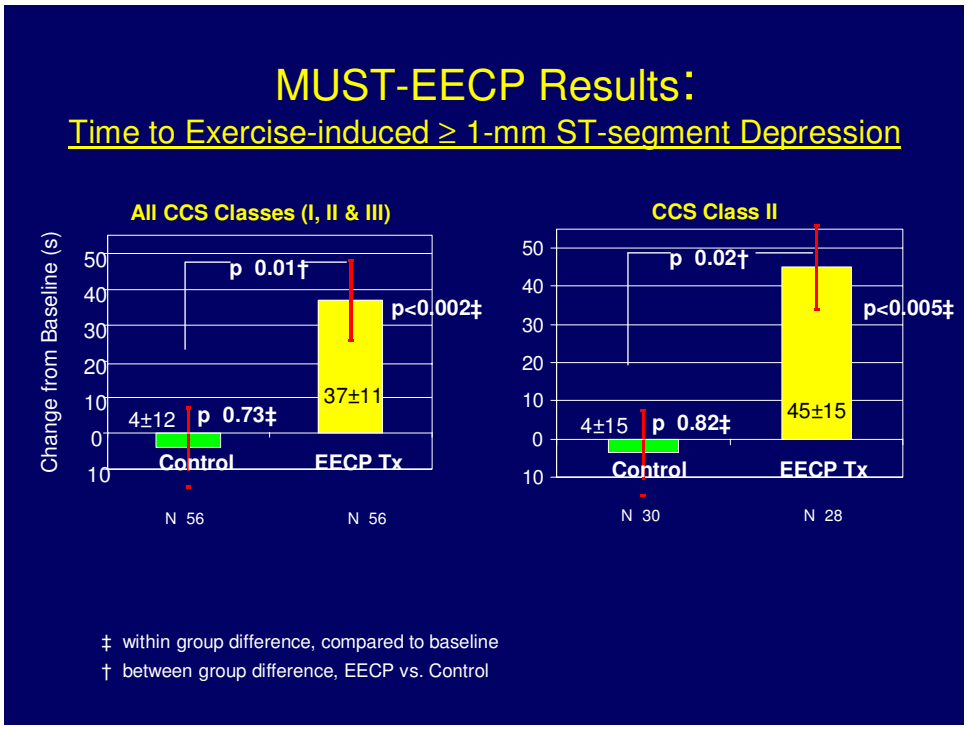

Figure 5. MUST-EECP Results: Exercise Induced ≥1 mm ST-Segment Depression

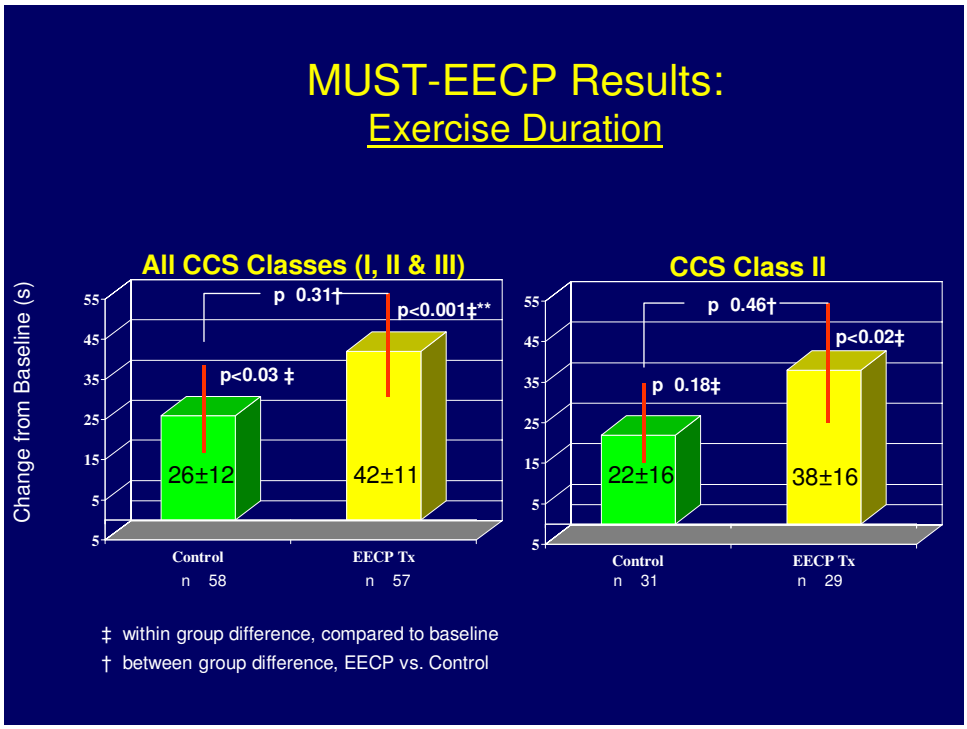

Figure 6. MUST-EECP Results: Exercise Duration

MUST-EECP Results:
Frequency of Angina Episodes

Comparison of the mean number of episodes between baseline and the last week of treatment

All CCS Classes (I, II & III)									
		Improvement			Worsening				P*
% Changes	N	50+%	25-49%	0-24%	1 25%	26 50%	50 100%	100+%	
Control	66	21	3	28	2	2	4	6	<0.05
EECP Tx	71	32	1	33	0	0	2	3	
CCS Class II									
Control	34	14	1	10	2	2	1	4	<0.04
EECP Tx	35	19	1	11	2	0	1	1	

* between group difference, EECP vs. Control

Figure 7. MUST-EECP Results: Frequency of Angina Episodes

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Summary of Two-Year Outcomes After Enhanced External Counterpulsation for Stable Angina Pectoris (from the International EECP Patient Registry [IEPR]) Results[14]

The International EECP Patient Registry is a University of Pittsburgh Epidemiology Data Center-based registry prospectively enrolling consecutive chronic stable angina patients from voluntarily participating EECP® therapy provider sites. Initiated in January 1998, the IEPR enrolled greater than 5,000 patients from more than 100 centers in a first phase of enrollment completed in 2001. Criteria for entry into the registry include patient consent, presenting for EECP® therapy because of angina, and completion of more than 1 hour of EECP® treatment.

Pre treatment data collection included demographics, medical history, symptom status, medication use, coronary disease status and quality of life assessments prior to initiating EECP® therapy. Following EECP® treatment, data are collected on symptom status, medication use, adverse clinical events, additional interventions and quality of life assessments. Long term follow-up is obtained at subsequent visits or by phone interviews at 6 months, 1, 2, and 3 years after their last EECP® treatment.

The data presented here appeared in a peer-reviewed publication reporting the outcomes in a cohort of 1,097 patients from 28 sites with 2-year follow-up data with greater than 85% compliance (Figure 8). Data analysis was performed using the "intention to treat" principle.

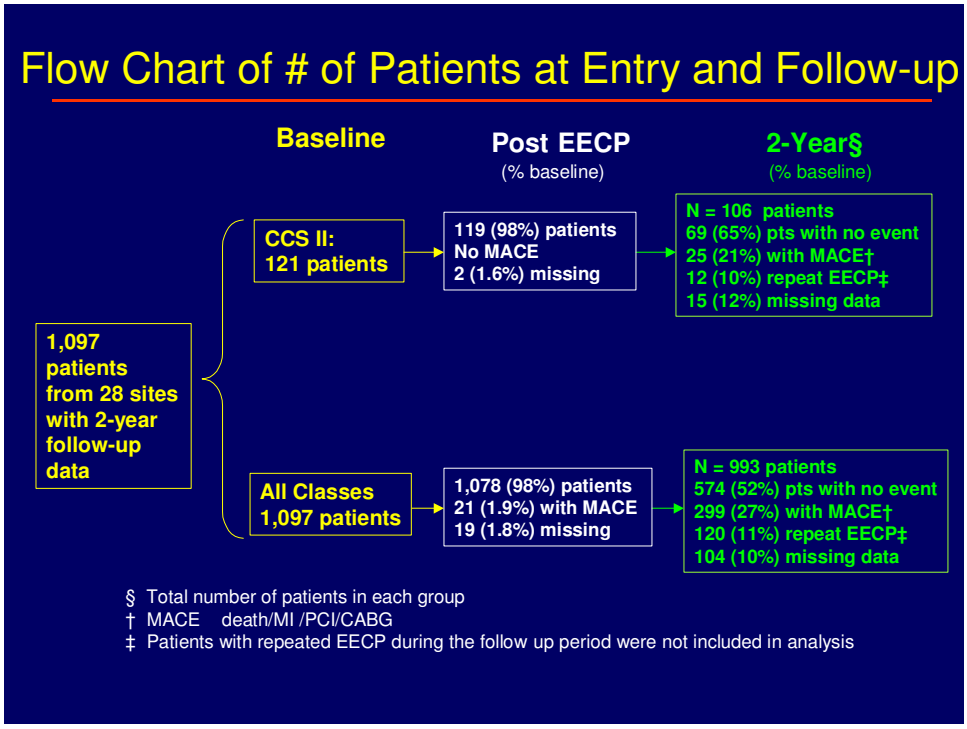

Figure 8. Two-Year Outcomes from IEPR

Analysis of the change in functional classification revealed a significant change in the percentage of patients with improvement of ≥1 angina class. Immediately following EECP® therapy, 73% of all classes of patients had an improvement of ≥ 1 angina class (Figure 9a). Within the patient subgroup with Class II angina (121 patients, 11%), 52.9% had improvement of at least 1 angina class, p<0.01(Figure 9b). The between group difference between patients with Class II and all Classes was statistically significant, p<0.05.

IEPR: % distribution of CCS Class
Immediately after EECP

	All Classes		CCSC II*	
	Baseline	Post-EECP	Baseline	Post EECP
# of Patients (N)	1,097	1,078	121	119
No Angina (%)	0	14.0	0	15.1
Class I (%)	2.0	21.3	0	37.8
Class II (%)	11.0	38.1	100	43.7
Class III (%)	61.4	20.1	0	0.0
Class IV (%)	25.6	6.7	0	3.4
% of patients with improvement of ≥ 1 class angina class		73.0**		52.9**

* Between group d fference, CCSC II vs. A C asses, p<0.05
**W th n group d fference, p<0.01

Figure 9a. Percent Distribution of CCS Class Immediately Post-EECP

IEPR Results: % distribution of CCS at 2-Year Follow-up
Excludes Patients with MACE and Repeat EECP treatment

	All Classes		CCSC II§	
	Baseline	2-Year	Baseline	2 Year
# of Patients	1,097	574	121	69
No Angina	0	29.3	0	39.1
Class I	2.0	21.8	0	30.4
Class II	11.0	28.6	100	23.2
Class III	61.4	16.4	0	4.4
Class IV	25.6	4.0	0	2.9
% of patients with improvement of ≥ 1 class angina class		80.7**		69.6**

** W th n group d fference, p<0.01
§ Between group d fference, p NS

Figure 9b. Percent Distribution of CCS Class at 2-Year Follow-Up

There were also highly significant changes observed in the number of angina episodes per week experienced by patients immediately following and at two years post-treatment compared to baseline ($p<0.001$) at both time points (Figure 10). This analysis also revealed differences between the study population overall compared to Class II only at baseline and immediately post-treatment that were not present at two years post-treatment.

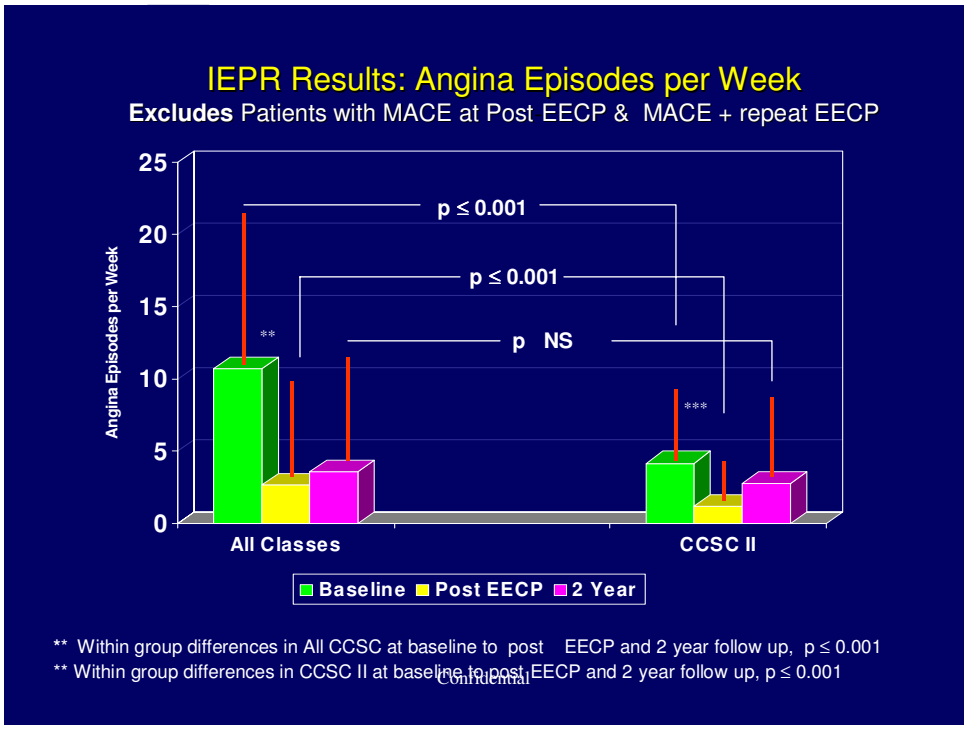

Figure 10. IEPR Results: Angina Episodes per Week

Additionally, changes in Quality of Life measures showed a significant improvement from baseline both in all patients and in the Class II patients for all three quality of life measures at both time points following EECP® therapy (Figure 11).

IEPR Results: Changes in Quality of Life

	All Classes‡	CCSC II‡
Immediately post-EECP		
# of patients	1,050	117
Health Improved (%)	53.6	52.1
Quality of life improved (%)	54.9	54.7
Satisfaction improved (%)	58.0	50.9
2 years follow-up		
Excludes Patients with MACE at Post EECP and MACE + repeat EECP		
# of patients	574	67
Health Improved (%)	47.2	43.3
Quality of life improved (%)	51.0	47.8
Satisfaction improved (%)	52.0	43.3

All values are mean ± standard deviation (N # of patients in each cohort). MACE is defined as death/MI/CABG/PCI

‡ There is a significant improvement from baseline in both groups for all 3 of their QoL measures at each time point. There is no significant between group difference in improvement in QoL.

Figure 11. IEPR Results: Changes in Quality of Life

Special note should be made that the results noted at two years post-treatment are those seen only in patients who did not experience MACE or repeat EECP® therapy during the follow-up period.

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Adverse Events

EECP® therapy was well tolerated in all angina patient populations evaluated. Cardiac events such as unstable angina, congestive heart failure, myocardial infarction, CABG or PCI are within expected ranges in patients with advanced CAD undergoing or following treatment with EECP® therapy. It should be noted that these patients were predominantly not candidates for revascularization due to extensive coronary artery disease, significant co-morbidities, and histories of myocardial infarction or CHF. (Figure 12).

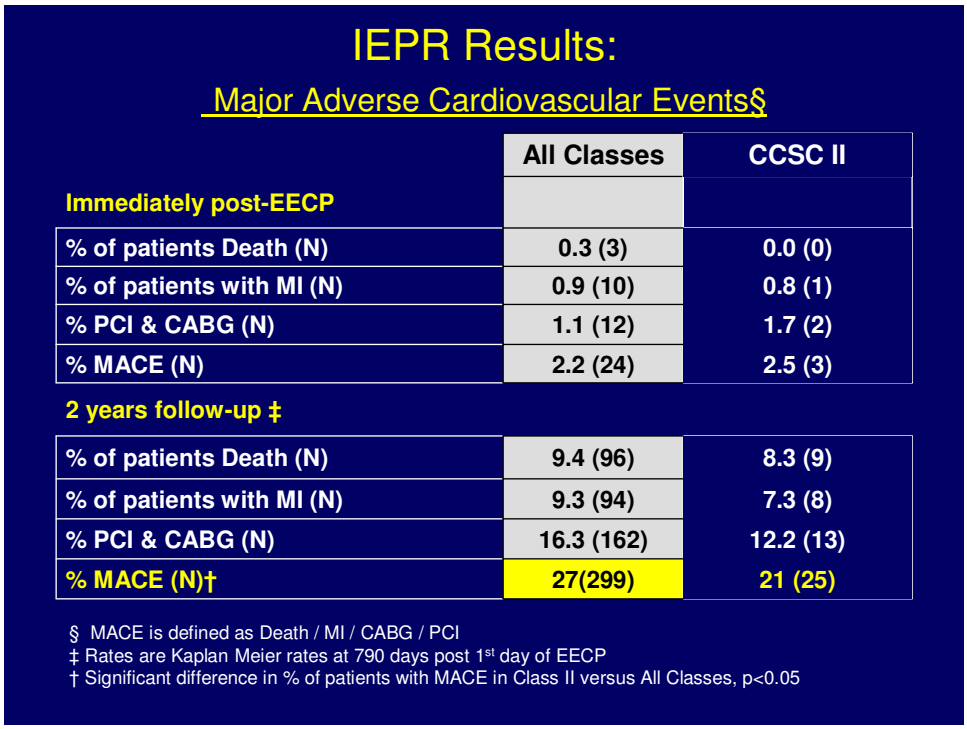


Figure 12. IEPR Results: Major Adverse Cardiovascular Events

In the IEPR, noncardiac medical events were reported by 5.4% of patients. Adverse events associated with EECP® therapy are generally limited to minor skin irritation and nonspecific musculo-skeletal complaints.

In conclusion, this subgroup analysis of the two-year outcomes data from the IEPR demonstrates overall results in CCS Class II patients comparable to results in patients of all classes for 1) a significant increase in the percentage of patients with Class II angina achieving improvement by ≥ 1 angina class immediately post EECP® therapy, 2) a decrease in angina episodes and 3) a significant improvement in Quality of Life measures.

Details from the Multicenter Study of Enhanced Counterpulsation (MUST-EECP) and the Two-Year Outcomes After Enhanced External Counterpulsation for Stable Angina Pectoris (from the International EECP Patient Registry) are attached in Appendix B.

Cost Utility Analysis

A decision analysis prepared for Vasomedical by Aequitas[15] was designed to evaluate the cost-effectiveness of EECP® therapy plus guideline-compliant medical therapy for chronic stable angina by comparing its clinical benefits, in particular, improvement in angina class and health-related quality of life (HRQOL) to patients who were treated with medication alone.

The analytical framework of the cost-utility analysis (CUA) model was predicated upon the evidence supporting an association between anginal functional grades and measures of HRQOL. Several studies have demonstrated a correlation between the severity of angina and HRQOL using various validated assessment tools specific for angina or coronary artery disease, such as the Duke Activity Status Index, the Seattle Angina Questionnaire, and the Quality of Life Index-Cardiac Version III.[16,17,18,19]

Because the calculation of quality-adjusted survival relies on the duration of time spent in various health states, it was hypothesized that a reduction in the time spent in states associated with greater morbidity, and therefore, lower quality of life, would result in superior outcomes for EECP® therapy in terms of cost-utility when compared to medical therapy alone.[20]

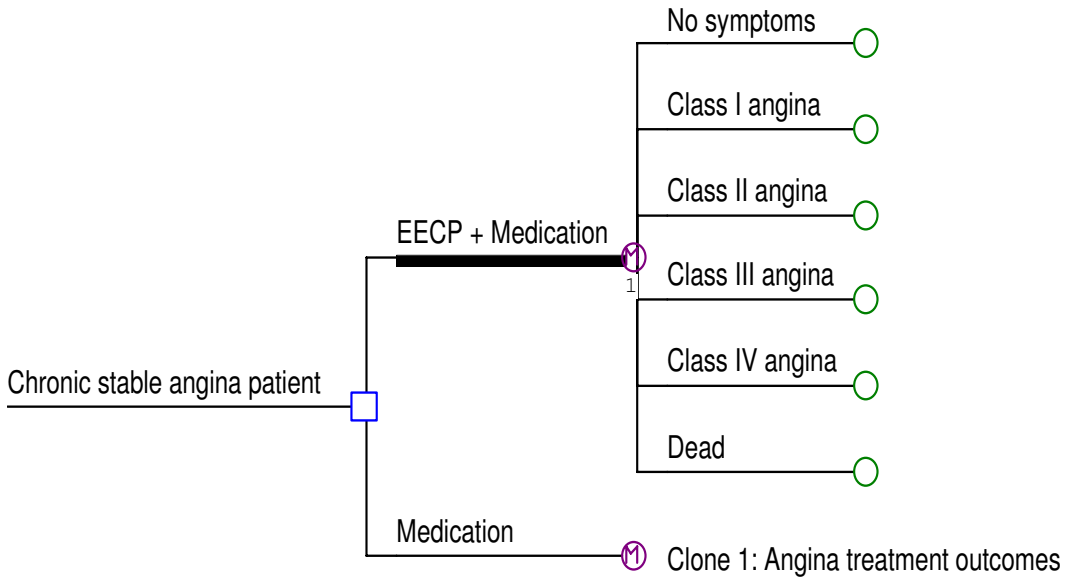
The outcomes of the cohort receiving medical therapy alone were modeled using data from the Mediators of Social Support Study (MOSS), a prospective, observational study by Kandzari et al (2001), which compared the outcomes of long-term survival, QoL, resource use, and costs among advanced CAD patients (total n=1189) treated with medications, percutaneous coronary angioplasty (PTCA), or coronary artery bypass grafting (CABG).[21]

Economic Analysis

Using the Decision Analysis by TreeAge Professional (DATAPro™) software[22], a CUA decision tree was constructed to simulate the outcomes of patients undergoing EECP® therapy plus ACC/AHA guideline-compliant medical therapy or ACC/AHA guideline-compliant medical therapy alone for the treatment of chronic, stable angina (Figure 13). The outcomes of the comparator therapies were measured in terms of costs and quality-adjusted life years (QALYs). In the baseline CUA, the latter outcome was calculated over a period of two years as the sum of the estimated quality-adjusted time spent in various health states (No Symptoms, CCS Class I, Class II, Class III, and Class IV angina, and death). Using Markov processes and these outcomes, an incremental cost-effectiveness ratio (ICER) was derived by the following formula, which estimated the incremental cost per QALY gained:

$$\frac{\text{(Cost of Treatment A – Cost of Treatment B)}}{\text{(QALYs for Treatment A – QALYs for Treatment B)}}$$

Figure 13.
Cost Utility Analysis Decision Tree for EECP® Therapy Versus Medical Therapy



The ICER represents the added cost per unit of added benefit of an option, relative to the next less expensive choice, and permits the decision maker to account for the availability of less expensive options when selecting an appropriate strategy.[23] By standard definition, a strategy was considered dominant if the alternative strategy resulted in better overall effectiveness at the same or lower cost.[24]

Results

The results of the analysis showed that EECP® therapy with standard ACC/AHA guideline-compliant medical therapy is a cost-effective strategy for the treatment of patients with chronic stable angina (Figure 14). When compared to standard medical therapy alone, the ICER of the EECP® strategy was $3,126 per QALY and fell well below the customary willingness-to-pay (WTP) threshold of $50,000-$100,000 per QALY. Sensitivity analyses showed that the ICER of this strategy relative to medical therapy alone appeared to be most sensitive to changes in the transition probabilities for the Class III and Class IV angina states (See Appendix C). This reflected and further supported the observation in published clinical studies that patients with more severe grades of angina bear greater deficits in QoL and higher costs of care. Therefore, therapies that improve angina class, as recommended by the ACC/AHA may also result in favorable economic outcomes. Given its low ICER and beneficial impact on angina severity and quality-adjusted survival, compared to medical therapy alone, EECP® therapy plus standard ACC/AHA guideline-compliant medical therapy is a superior option for the treatment of chronic stable angina.

Figure 14. Cost-Effectiveness Analysis: EECP® Therapy Plus Medical Therapy Versus Medical Therapy Alone

Strategy	Cost	Incremental Cost	Efficacy (QALYs)	Incremental Efficacy (QALY)	C/E	Incremental C/E per QALY
Medication	$10,709	-	1.31		$8,195	
EECP + Medication	$11,554	$845	1.58	0.27	$7,326	$3,126

C/E = Cost/Effectiveness

QALYs – Quality Adjusted Life Years

Discussion

There is general consensus that improvement in angina class is beneficial. The ACC and the AHA recommend that for most patients with chronic stable angina, the goals of treatment should be complete, or nearly complete, elimination of anginal chest pain and to return to normal activities and CCS Class I functional capacity.[25]

Until recently, however, the predictive value of angina functional grades in the context of health outcomes had not been extensively explored. In a recent prospective, population-based trial, the Appropriateness of Coronary Revascularization (ACRE) study, higher CCS angina class was associated with higher coronary angioplasty and bypass graft rates ($P<0.001$ and $P=0.03$, respectively) and higher probabilities of all-cause death and nonfatal myocardial infarction (log rank $P<0.001$).[26] Other studies have demonstrated that patients with more severe angina bear a greater risk for perioperative cardiac complications,[27] perioperative mortality, [28] and ischemic stroke.[29]

The results of the cost utility analysis using the Markov Model reveals that EECP® therapy and guideline-compliant medical therapy yields a $3,126 cost per QALY at 2 years compared to medication therapy alone. The authors concluded that EECP® therapy for treatment of chronic stable angina was highly cost-effective, as patients experienced fewer MACE, less use of rescue nitrates and better quality of life (Appendix C).

Heart Failure

Congestive heart failure affects 5,000,000 people in the US with 550,000 new cases diagnosed each year.[30] It is estimated that of these 550,000 new patients, approximately 225,000 Class II/III patients suffer from stable CHF inadequately relieved by optimal medical therapy. Of heart failure patients treated with EECP® therapy during clinical studies or with concomitant angina, approximately 80% completed therapy.

The primary manifestations of this clinical syndrome are dyspnea and fatigue resulting from any functional or structural cardiac disorder impairing the ability of the ventricle to fill or eject blood. Coronary artery disease is the underlying cause of CHF in about two-thirds of patients with left ventricular dysfunction. The remainder have non-ischemic etiology, which may or may not have an identifiable cause (e.g. hypertension, idiopathic dilated cardiomyopathy).

This disorder is the underlying reason for 12-15 million physician office visits and 6.5 million hospital days each year. Nearly 300,000 patients die of CHF as a primary diagnosis or secondary diagnosis each year, and the number of deaths has increased despite advances in treatment.[31] It is estimated that the hospital costs to treat CHF to the Medicare system are approximately $3.6 billion ($5,456 per discharge) with total direct & indirect healthcare costs estimated at $27.9 B[32]. There are 970,000 hospital discharges for congestive heart failure, 720,000 (74%) occur in patients over 65 years of age. [33]

Causes of Heart Failure

- Ischemic heart disease
- Myocardial infarction
- Valvular disease
- Dilated cardiomyopathy
- Hypertension
- Atrial fibrillation[34]

Risk Factors

- Age
- Male gender (under 75 years of age)
- Myocardial infarction
- Ischemic heart disease
- Hypertension
- Left ventricular hypertrophy
- Left ventricular dilatation
- Diabetes
- Atrial fibrillation

- Genetic markers
- Increased plasma natriuretic peptides[35]

Congestive heart failure is a progressive disease reflected in a decline in the pumping efficiency of the heart and a worsening of symptoms. A number of predisposing conditions can lead to heart failure. Prognosis for patients with CHF is poor with mortality rates of 50-80% within five years of diagnosis.

The majority of patients with CHF are classified by functional symptoms and are found in the early classes, however this is not a static state and there is a frequent shift between NYHA classes. Given the prevalence of early stage disease (70% Class I/II), a large number of patients are treated and monitored by primary care physicians and as they progress to Class III/IV NYHA are more likely to be seen by a cardiologist and/or heart failure specialist (Figure 15). The ACC/AHA developed a staging classification to identify 4 stages of CHF recognizing established risk factors and structural prerequisites for the development of CHF and the therapeutic interventions performed (Figure 16).[36]

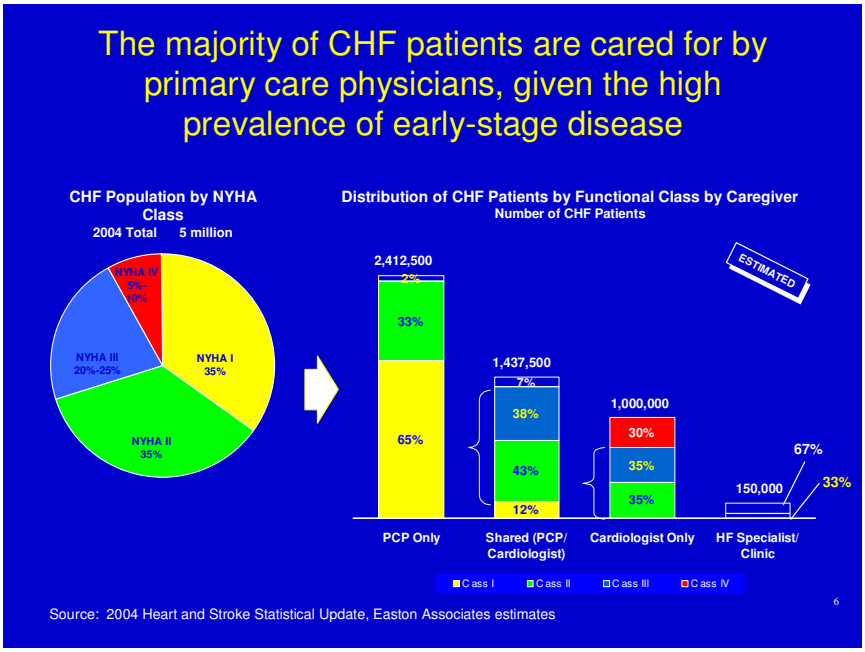


Figure 15. Distribution of CHF Patients by Functional Class by Physician

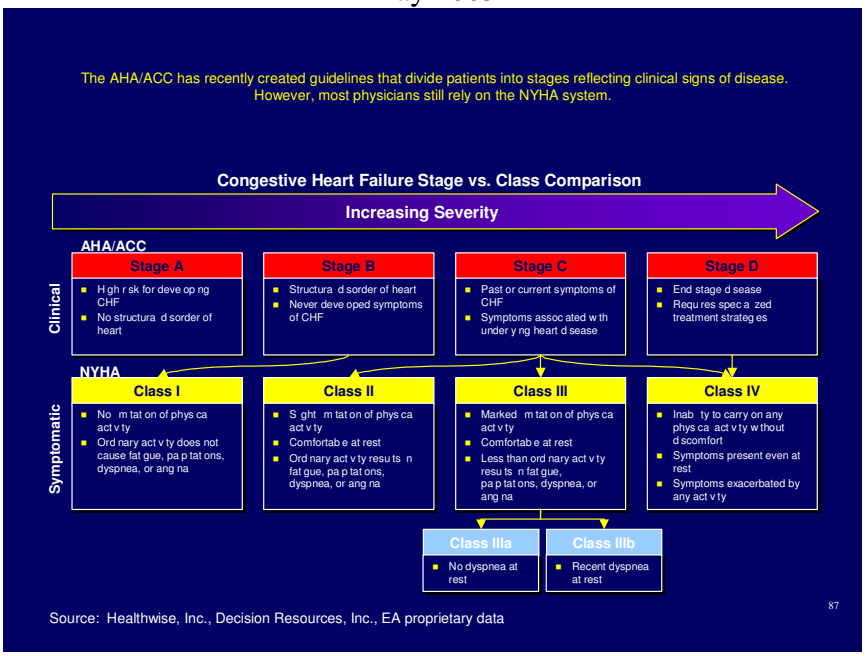


Figure 16. Congestive Heart Failure Stages

Current Treatment Options

The goals of heart failure treatment are to prolong active life and improve or maintain the quality of life by improving symptoms, retarding disease progression, reducing major morbidity and subsequent disability, and avoiding iatrogenic adverse effects of management.[37]

Guideline-compliant pharmacologic therapy includes four types of drugs: a diuretic, ACE inhibitor, beta-blocker and digitalis. Additional drug therapy can include nitrates, antihypertensives, antiplatelets, antiarrhythmics and anticoagulants as required by the patient's condition as published. We understand that the current ACC/AHA guidelines for CHF are undergoing revision. [38]

Coronary revascularization and implantable cardioverter-defibrillators are recommended for management of concomitant diseases in patients with CHF and coronary disease without angina, and in patients with CHF who have a history of sudden cardiac death, ventricular fibrillation, or ventricular tachycardia respectively. Current practice includes biventricular pacemakers, which have recently been shown to benefit selected patients with dysynchronous ventricular contraction (QRS duration > ~130 msec).

Summary of Clinical Data Supporting Expansion to Class II/III CHF Indication
Early Studies

Observational studies of patients enrolled in the International EECP® Patient Registry [IEPR] with angina and a history of CHF or with left ventricular dysfunction were completed at 1 and 2-year follow-up.[39,40] In the IEPR 1-year outcomes study, 355 of the 2,358 patients enrolled from January 1998-January 2002, who had a history of CHF and systolic dysfunction (LVEF≤35%) were studied, with 84% (N=298) completing the 1-year follow-up. As noted in Figure 17, ninety percent of patients at baseline had Class III/IV angina, whereas immediately post-EECP® therapy, only 34% of patients remained in Class III/IV. Angina class was improved by greater than 1 CCS class in 72.2% of patients, comparing baseline to immediately post-EECP® therapy. A sustained improvement in angina status was seen at 1-year with an improvement in angina class seen in 75.8% of patients comparing baseline to 1-year post-EECP® therapy. Improvements in the number of angina episodes per week and the amount of nitroglycerine required were also seen (Figures 17 and 18).

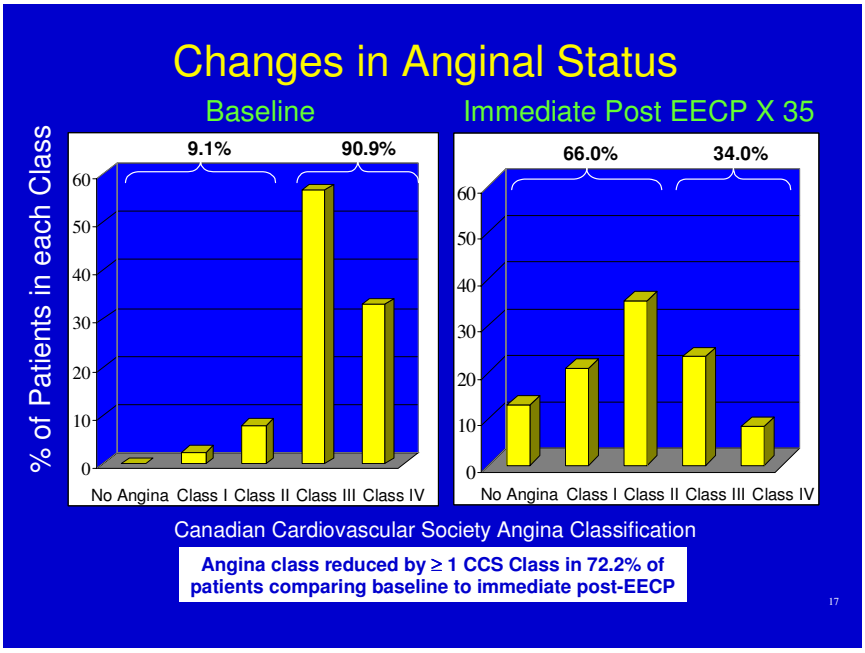


Figure 17. IEPR Studies in Patients with Angina & CHF: Changes in Anginal Status

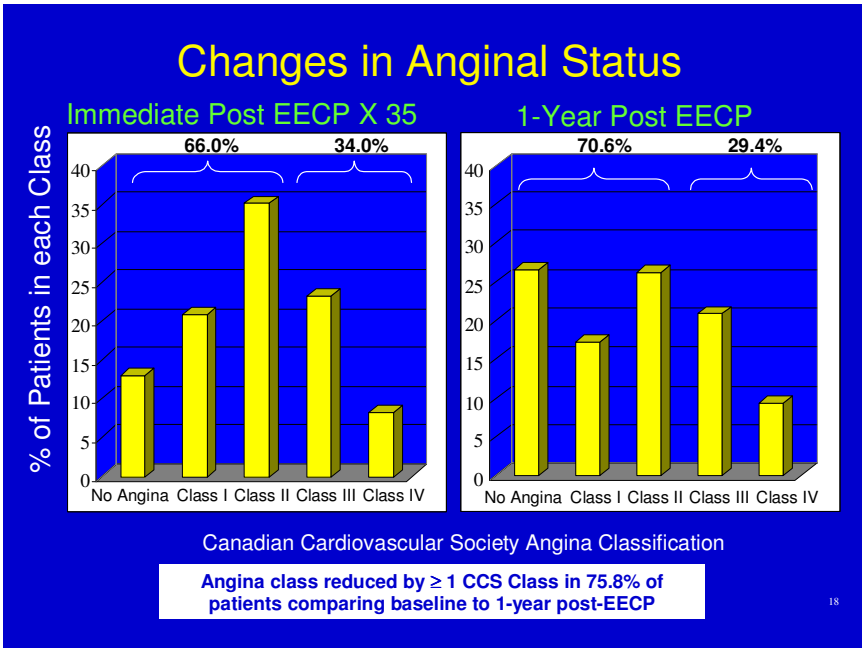


Figure 18. IEPR Studies in Patients with Angina & CHF: Changes in Anginal Status at 1-Year

Major adverse cardiovascular events defined as death, myocardial infarction, PCI or CABG, during treatment and at the 1 year follow-up were within expected ranges given the severity of cardiac disease seen in these patients with angina and concomitant CHF (Figure 19).

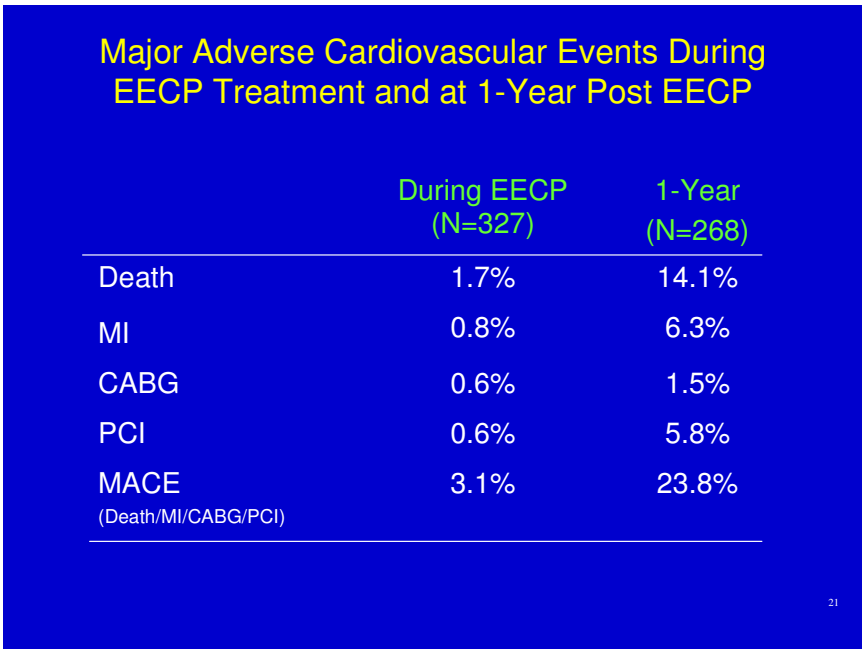


Figure 19. IEPR Results: MACE in Patients with Angina and History of CHF

A 2-year outcomes study of IEPR patients with impaired left ventricular dysfunction defined as having an ejection fraction of less than or equal to 35% was completed with 363 patients (7%) of 5,000 enrolled in the IEPR from January 1998 to June 2001. Eighty-one percent of the 363 patients completed a full course of EECP® therapy.

Immediately post-EECP® therapy, 77% of patients improved more than 1 angina class, 15.6% had no angina post treatment ($p<0.001$) (Figure 20). During EECP® therapy, heart failure exacerbations or worsening heart failure events were reported to be 5.4%.

At 2 years, 265 patients completed follow-up and 55% of patients had sustained improvement in angina class (Figure 21). Quality of Life (Figure 22) measures using the Likert scale indicated that 58% of patients improved their QoL post-EECP® therapy compared to baseline and at 2-year follow-up, 63% improved compared to baseline ($p<0.001$).

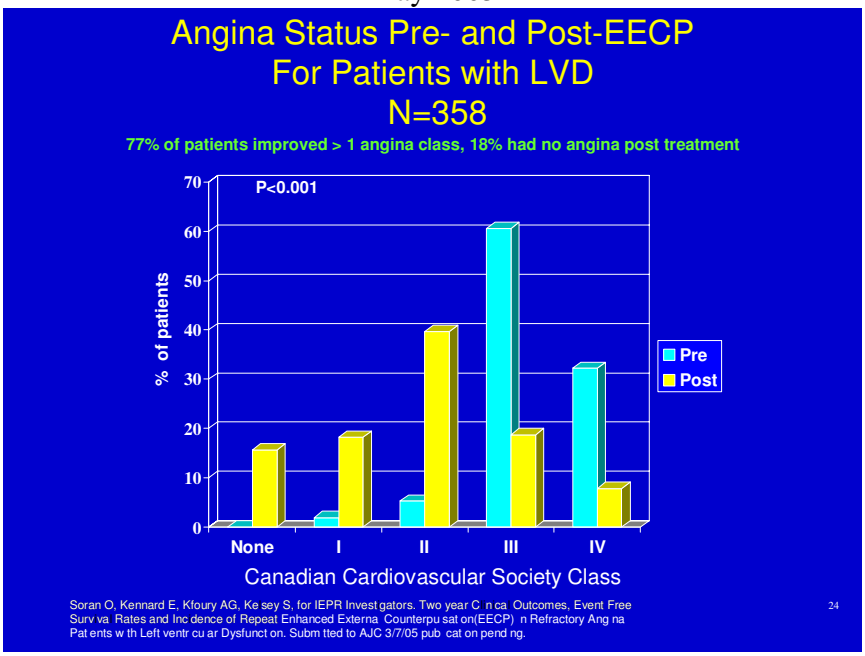


Figure 20. IEPR 2-Year Outcomes Angina Status Immediately Post-EECP

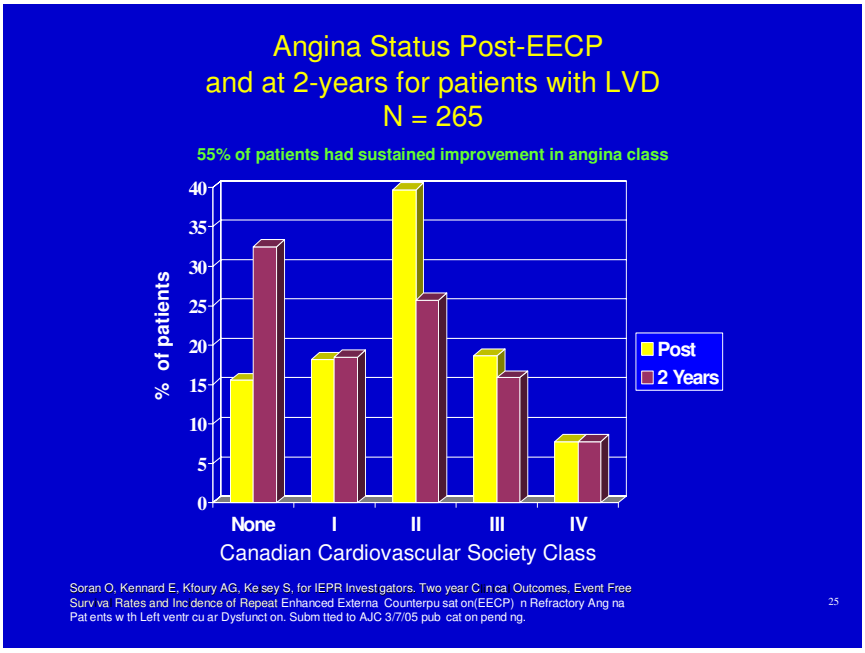


Figure 21. IEPR 2-Year Outcomes Angina Status at 2-Years Post-EECP

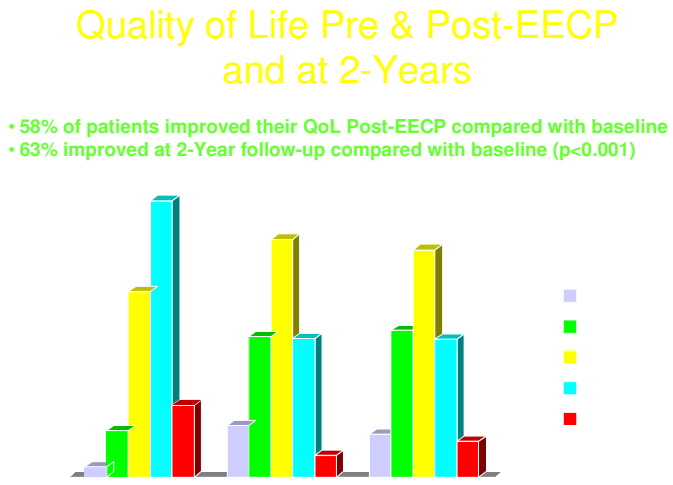


Figure 22. IEPR Results: Quality of Life in Patients with LVD

Adverse Events
Major adverse events during EECP® therapy as well as at the 1-year and 2-year follow-up were within expectations given the severity of concomitant disease in both study groups. At 2-years, 70% of patients had event-free survival.

Results
The 2-year results were similar to the 1-year outcomes as a reduction in angina was seen is the majority of treated patients. The angina improvement observed immediately post-EECP® therapy in the heart failure patients was sustained in 76% of patients at 1 year and 55% at the 2- year follow-up.

Multicenter Feasibility Study of EECP® Therapy in CHF

A multicenter feasibility study conducted with 26 patients demonstrated that, with careful patient selection and monitoring, EECP® therapy was well tolerated in euvolemic, stable heart failure patients.[41] EECP® therapy appeared safe when applied as an adjunctive therapy to medical therapy in this patient population. Efficacy data suggested that EECP® therapy may improve exercise capacity, functional status, and enhance QoL in the short term and for six months post therapy.

Although a small study, statistically significant improvements in exercise duration (Figure 23) and peak oxygen uptake (Figure 24) were observed in both ischemic and idiopathic patients. Functional status improved by 1 NYHA classification at 6 months in 52% of patients, while 34% of patients maintained their functional status. 35% of patients reported improvement in quality of life at 6 months.

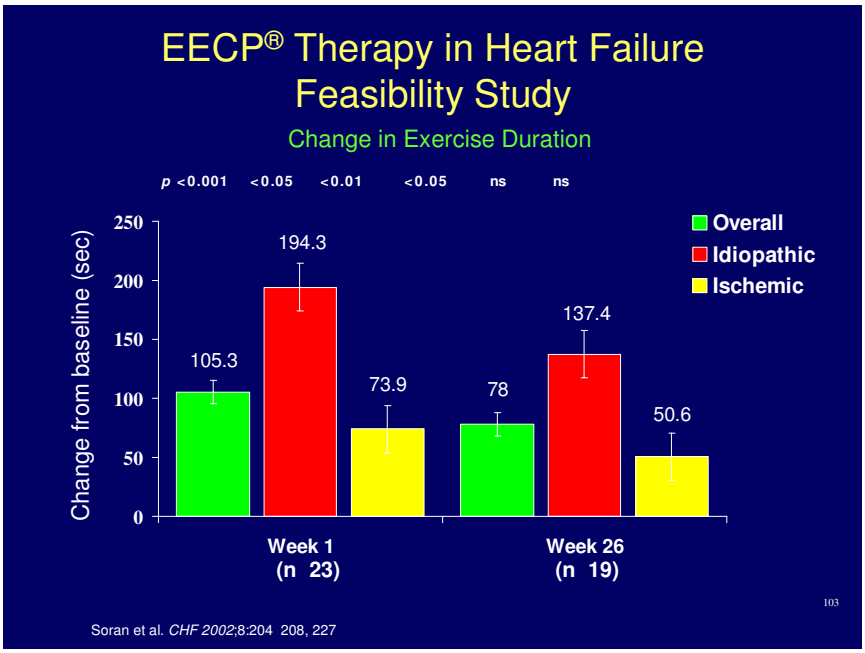


Figure 23. Feasibility Study Results: Exercise Duration

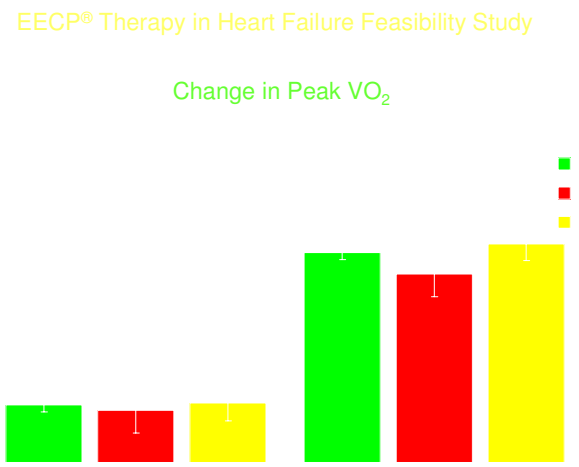


Figure 24. Feasibility Study Results: Peak VO_2

These results along with the IEPR results prompted initiation of the Prospective Evaluation of EECP in Congestive Heart Failure (PEECH) trial.

Prospective Evaluation of EECP in Congestive Heart Failure (PEECH) Trial[42]

The effects of EECP® therapy on exercise performance, symptom status and quality of life in patients with ischemic and non-ischemic cardiomyopathy were evaluated in a prospective, randomized, multicenter study conducted in 187 patients with Class II/III NYHA stable congestive heart failure and an ejection fraction ≤ 35%. Patients were randomized in a 1:1 fashion to EECP® therapy plus protocol-mandated optimal pharmacologic therapy (OPT) as recommended by the ACC/AHA guidelines for CHF, or to OPT alone. Optimal pharmacologic therapy included an ACE inhibitor or ARB for at least 1 month prior to enrollment and beta-blocker therapy for at least 3 months prior to enrollment. Patients had to be able to exercise for 3 minutes or more, limited by shortness of breath or fatigue, thereby limited only by symptoms of heart failure (not angina).

The PEECH trial had pre specified parameters including:

- Exercise duration using a standardized exercise tolerance test (ETT) on a treadmill (modified Naughton protocol), or
- Peak VO_2 at 6 months

The co-primary endpoints were the percentage of patients with at least a 60-second increase in exercise duration from baseline to 6 months or the percentage of patients with at least a 1.25ml/min/kg increase in Peak VO_2 from baseline to 6 months.

The PEECH trial was powered in order to evaluate the statistical significance of predefined, clinically relevant parameters, with thresholds for success established high enough to minimize any potential for placebo effect. Elements of the study design included:

- Randomization
- Use of objective primary endpoints
- Blinding of clinical evaluators
- Independence and blinding of core laboratory evaluators
- Rigorous selection criteria for subjections
- Optimization of guideline mandated medical therapy

A sample size of 180 subjects was needed to show whether EECP® therapy was effective, using 90% power, if the difference between groups:

- For either primary endpoint was significant with a p-value ≤ 0.025, or
- For both primary endpoints with a p-value ≤ 0.05

Patients were not blinded to treatment allocation however each of the 29 study sites had 2 investigating teams, 1 blinded and 1 open:

- Blinded investigators only performed subject evaluations
- Open investigators supervised or performed subject treatment visits and daily interactions.

Secondary endpoints considered included changes in exercise time and Peak VO_2, NYHA functional classification, quality of life, adverse experiences and predefined clinical outcomes.

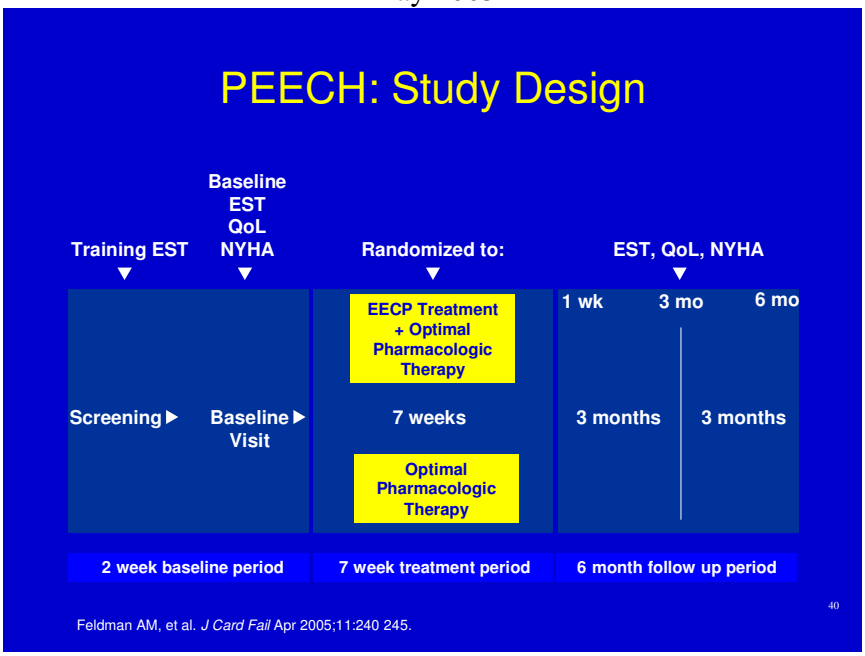


Figure 25. PEECH: Study Design

Initially, patients were screened to assess baseline exercise stress testing capability, NYHA functional status and quality of life using both the Minnesota Living with Heart Failure Questionnaire and SF-36. A training cardiopulmonary exercise stress test (EST) was performed at the first visit, and a second EST performed at the 2nd visit was used to establish baseline values. Once the 2-week baseline period was completed, patients were then randomized to one of the two treatment arms. After 35 one-hour treatment sessions with EECP® therapy or 7 weeks of OPT, a six-month follow-up period ensued with testing at 1 week, 3 months and 6 months post-completion of therapy. Patients on optimal medical therapy only were seen at the same time intervals starting 8 weeks after randomization. Analysis was by intention to treat with the last observation carried forward (Figures 25 and 26).

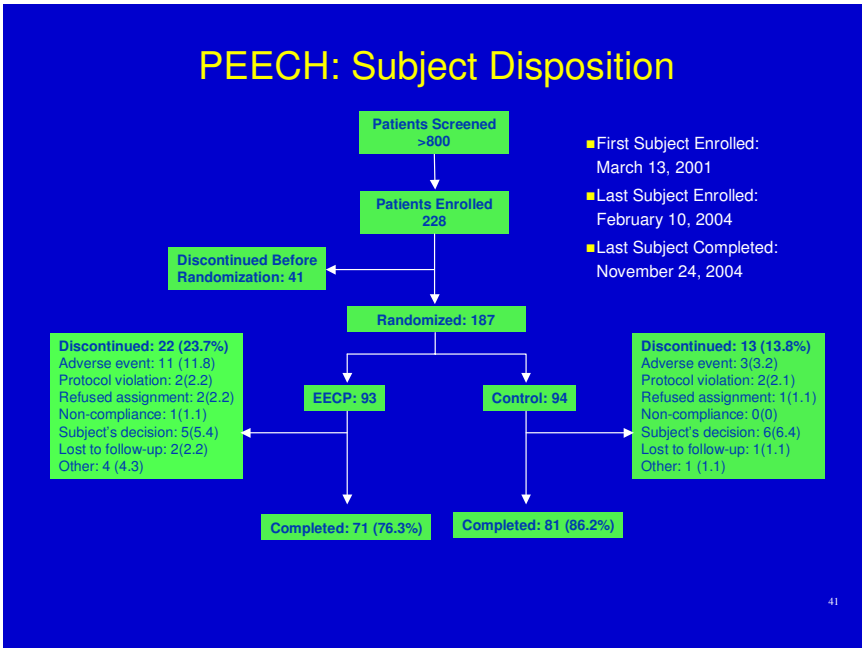


Figure 26. PEECH Study: Subject Disposition

There were no statistical differences in the demographics of the patients randomized to the treatment arms for this trial.

Gender, age, sex, ischemic etiology, and mean EF as well as OPT were similar. Approximately 2/3 of patients were NYHA Class II CHF compared to 1/3 Class III NYHA CHF (Figure 27).

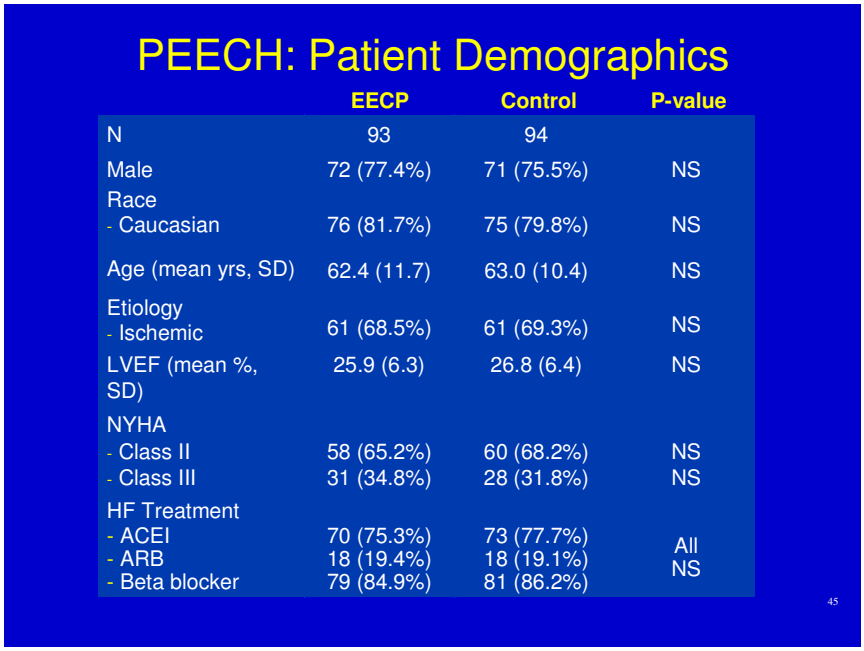


Figure 27. PEECH Study: Patient Demographics

The PEECH trial demonstrated positive results for the use of EECP® therapy as an adjunctive therapy for the treatment of patients with NYHA Class II/III heart failure with EF≤ 35% by meeting the predefined requirements for significance of the co-primary endpoint for exercise duration. By the primary intent to treat analysis, 35% of the EECP® therapy and 25% of the control group increased exercise time by at least 60 seconds (p=0.016) at 6 months (Figure 28) There was no difference observed in the proportion of patients achieving an increase in Peak VO_2 >1.25mL/kg at 6-months.

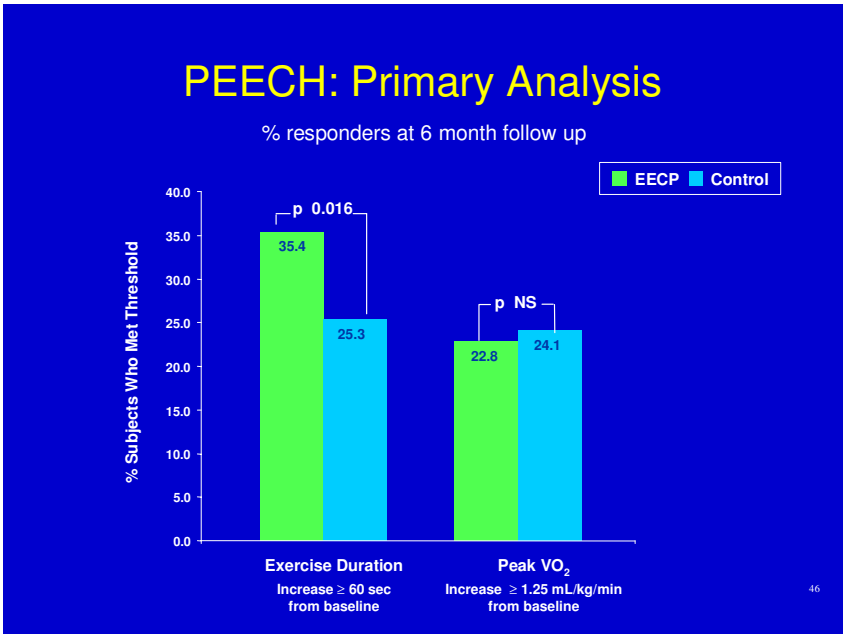


Figure 28. PEECH Results: Primary Endpoints

The secondary endpoint of absolute change in exercise time was also improved as EECP® therapy significantly improved exercise capacity at 1 week, 3 months and 6 months. Exercise time increased by 24.7 seconds in the active treatment group and decreased by 9.9 seconds in the control group (p=0.013) at 6 months (Figure 29).

EECP® therapy also significantly improved functional status (NYHA class) and quality of life as compared to those patients receiving OPT alone (Figures 30 and 31).

Peak VO_2 showed small positive changes in the EECP® therapy group at 1 week and 3 months, as compared to the control group which only showed worsening of the Peak VO_2 (Figure 32).

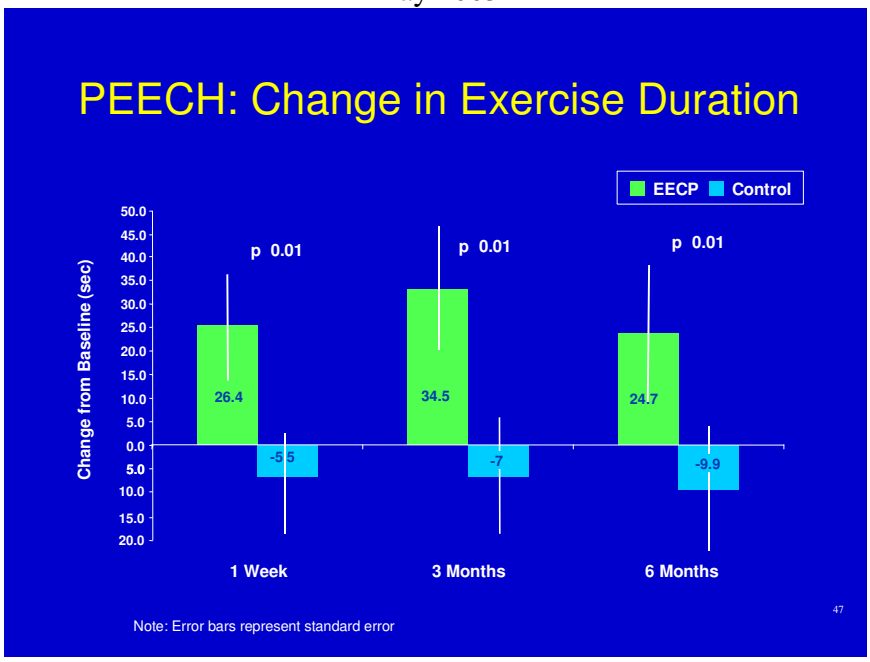


Figure 29. PEECH Results: Change in Exercise Duration

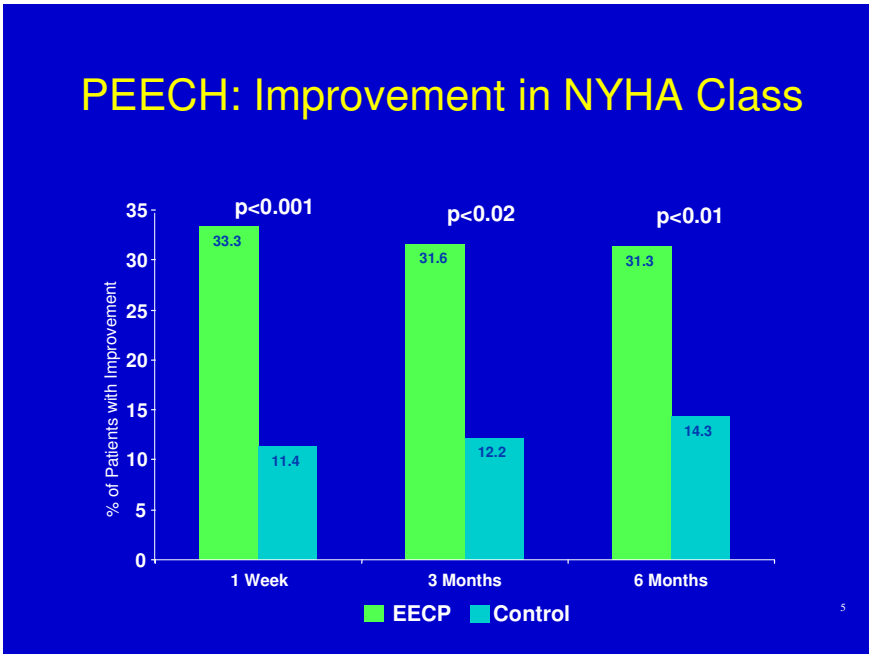


Figure 30. PEECH Results: Improvement in NYHA Class

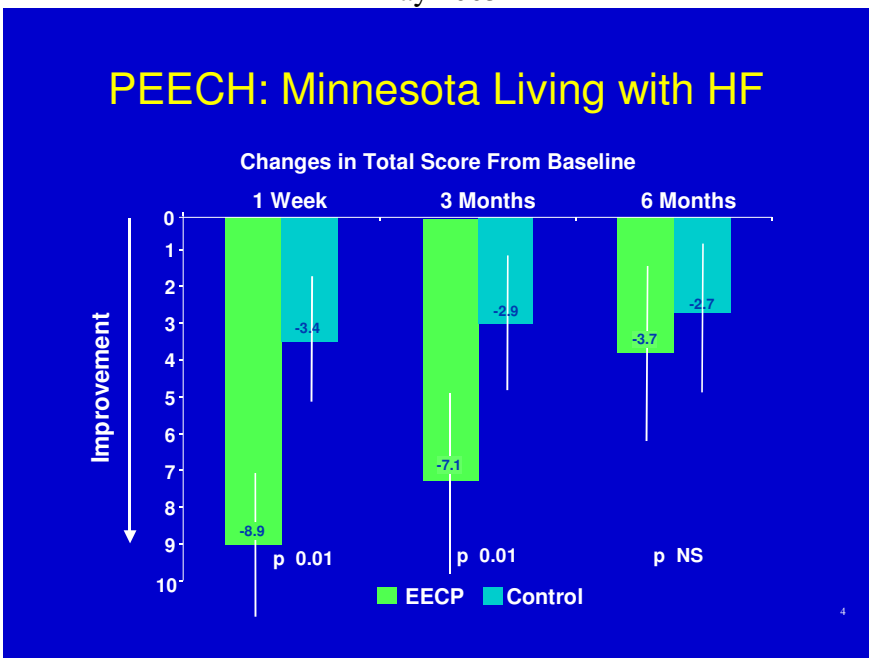


Figure 31. PEECH Results: Improvement in Quality of Life Scores

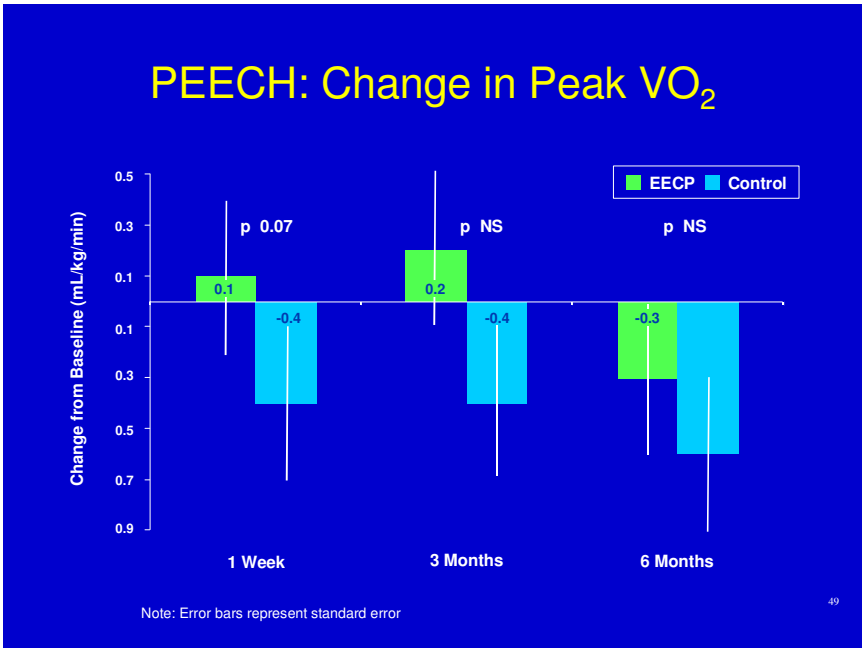


Figure 32. PEECH Results: Change in Peak VO_2

An *ad hoc* analysis performed specifically for this application showed that within the greater than 65 year old subgroup, EECP® therapy demonstrated statistically significant improvements at 6-months following completion of treatment in both primary endpoints of exercise duration (p=0.008) and Peak VO_2 (p=0.017) when compared to OPT alone (Appendix E. Figures 33-35).

Ad hoc analysis of results according to baseline NYHA status showed a statistically significant result favoring those receiving EECP® therapy in the proportion of NYHA Class II patients achieving an increase in Peak VO_2 at one week (p=0.013) and a trend at one week in the proportion of Class II patients achieving an increase in exercise duration (p=0.062). Differences were not statistically significant at any other time points for Class II and at no time points for Class III patients.

Analysis of these subgroups was not predefined and the study not powered to determine statistical significance within this subgroup.

(*N.B.* All other analyses presented in this application were predefined according to the PEECH trial protocol.)

A subgroup analysis of the ischemic compared to the non-ischemic patients with heart failure seemed to show a greater benefit in the ischemic population, but, here too, the small sample size of non-ischemic patients makes it inappropriate to draw any meaningful conclusions (Appendix E. Figure 36). The subgroup analysis by etiology was predefined but not powered to determine statistical significance.

Adverse Events
Adverse events were monitored and reported as required by the study protocol. There were no statistical differences between groups for adverse events or serious adverse events. Twenty-seven patients (30%) of the EECP® therapy group and 23 patients (26%) of the OPT group required hospitalization during the course of treatment. There were no deaths in the EECP® treated group and two noted in the OPT group (Appendix F.).

During the treatment period, 7 subjects in the EECP® treated group had serious adverse events including 1 with worsening heart failure and 1 with pulmonary embolism. In the OPT group, 8 patients were reported to have serious adverse events.

Adverse events that occurred in relation to the application of EECP and resulted in discontinuation included sciatica (1), leg pain (1), and arrhythmia which interfered with the device thus creating discomfort and treatment inefficiency (2). Additionally, there was one EECP subject who dropped out due to compliance problems.

Also, a decrease in oxygen saturation was observed by pulse Oximetry in 11 (12.4%) subjects in 30 (11%) of 2,859 EECP® therapy sessions administered during the trial.

Except for one case of oxygen desaturation followed by a worsening of heart failure after the treatment session, all other episodes were reversed by a protocol-mandated brief interruption of the treatment session and improved breathing.

During follow-up, 21 subjects in the EECP® group and 23 in the OPT group reported serious adverse events, 1 in the EECP® group reporting deep vein thrombosis (DVT) and 1 in the control group reporting worsening heart failure.

Summary of PEECH Results

The addition of a standard regimen of EECP® therapy to optimal pharmacologic therapy improved exercise time for at least 6 months following completion of therapy in patients with NYHA class II/III heart failure with an EF≤35%. The prospectively defined co-primary endpoint for exercise duration was met with significantly more patients in the EECP® therapy group increasing exercise duration by greater than 60 seconds compared to the control group having OPT alone. In the subgroup of patients >65 years of age, analysis showed statistically significant increases in exercise duration at 3 and 6 months.

Despite the increases noted in exercise duration, EECP® therapy did not effect a significant improvement in the proportion of patients achieving the predefined threshold increase (≥1.25mL/kg/min) in Peak VO_2 at 6 months overall. Small increases in Peak VO_2 that did not reach statistical significance were seen at 1 week and 3 months in the EECP® therapy group, while changes in the control group decreased at all time points. However, a significantly greater proportion of patients≥65 years of age undergoing EECP® therapy did achieve the predefined threshold and also achieved a significant improvement in Peak VO_2 at 3 and 6 months following completion of therapy compared to patients in the control group.

Secondary endpoints for functional status (NYHA classification), exercise capacity and quality of life were improved significantly compared to OPT alone and were consistent with the improvement in exercise duration.

EECP® therapy was well tolerated in this group of patients and the PEECH trial results demonstrate that EECP® therapy can be a beneficial adjunctive therapy in patients with NYHA class II/III heart failure receiving optimal pharmacologic therapy. Additionally, registry data demonstrated sustained improvements at 1-2 years in symptoms, functional status and quality of life for patients with angina and stable CHF.

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Discussion

Given the goals of heart failure treatment are to prolong life and improve/maintain the quality of life by improving symptoms, the randomized, controlled PEECH study along with the results from the IEPR demonstrate that EECP® therapy improves exercise capacity, functional status, symptoms and quality of life for patients with NYHA class II/III stable heart failure with an EF ≤ 35% who are on optimal medical therapy. Based on these results, we are requesting consideration of revision to coverage language as noted on the following pages.

May 2005

Current & Proposed Coverage Language

Current Description of ECP in the Medical Coverage Database of the Centers for Medicare & Medicaid Services (CMS), Section 20.20 (formerly 35-74)

***External counterpulsation (ECP)**, commonly referred to as enhanced external counterpulsation, is a non-invasive outpatient treatment for coronary artery disease refractory to medical and/or surgical therapy.*

Indications and Limitations of Coverage

Although ECP devices are cleared by the Food and Drug Administration (FDA) for use in treating a variety of cardiac conditions, including stable or unstable angina pectoris, acute myocardial infarction and cardiogenic shock, (patients with congestive heart failure were added to the list by the FDA on June 14, 2002), the use of this device to treat cardiac conditions other than stable angina pectoris is not covered, since only that use has developed sufficient evidence to demonstrate its medical effectiveness. Non-coverage of hydraulic versions of these types of devices remains in force.

Coverage is provided for the use of ECP for patients who have been diagnosed with disabling angina (Class III or Class IV, Canadian Cardiovascular Society Classification or equivalent classification) who, in the opinion of a cardiologist or cardio thoracic surgeon, are not readily amenable to surgical intervention, such as PTCA or cardiac bypass because: (1) their condition is inoperable, or at high risk of operative complications or post-operative failure; (2) their coronary anatomy is not readily amenable to such procedures; or (3) they have co-morbid states which create excessive risk.

A full course of therapy usually consists of 35 one-hour treatments, which may be offered once or twice daily, usually 5 days per week. The patient is placed on a treatment table where their lower trunk and lower extremities are wrapped in a series of three compressive air cuffs, which inflate and deflate in synchronization with the patient's cardiac cycle.

During diastole the three sets of air cuffs are inflated sequentially (distal to proximal) compressing the vascular beds within the muscles of the calves, lower thighs and upper thighs. This action results in an increase in diastolic pressure, generation of retrograde arterial blood flow and an increase in venous return. The cuffs are deflated simultaneously just prior to systole, which produces a rapid drop in vascular impedance, a decrease in ventricular workload and an increase in cardiac output.

The augmented diastolic pressure and retrograde aortic flow appear to improve myocardial perfusion, while systolic unloading appears to reduce cardiac workload and oxygen requirements. The increased venous return coupled with enhanced systolic flow appears to increase cardiac output. As a result of treatment, most patients experience increased time until the onset of ischemia, increased exercise tolerance, and a reduction in the number and severity of anginal episodes. Evidence was presented that this effect lasted well beyond the immediate post-treatment phase, with patients symptom-free for several months to two years.

The procedure must be done under direct supervision of a physician.

Proposed Coverage Language

External counterpulsation (ECP), commonly referred to as enhanced external counterpulsation, is a non-invasive outpatient treatment for patients with ***cardiovascular disease not readily amenable to medical therapy or revascularization.***

Indications and Limitations of Coverage

Although ECP devices are cleared by the Food and Drug Administration (FDA) for use in treating a variety of cardiac conditions, including stable or unstable angina pectoris, ***congestive heart failure, acute myocardial infarction and cardiogenic shock. The use of this device to treat cardiac conditions other than stable angina pectoris and stable congestive heart failure is not covered.*** Non-coverage of hydraulic versions of these types of devices remains in force.

*Coverage is provided for the use of ECP for patients who have been diagnosed with angina (**Class II**, III or IV, Canadian Cardiovascular Society Classification or equivalent classification), who **are not readily amenable to revascularization, AND***

for patients who have been diagnosed with stable congestive heart failure (NYHA class II-III), with EF ≤35%, on optimal pharmacologic therapy.

Site of Service
Medicare has identified this service as outpatient only for hospitals and physician office services.

Coding and Payment

Diagnosis code(s):

Angina	413.0	Angina Decubitus
	413.9	Angina Pectoris NEC/NOS
	414.0X	Coronary Atherosclerosis Unspecified Vessel/Graft
	414.8	Chronic Ischemic Heart Disease NEC
	414.9	Chronic Ischemic Heart Disease NOS
Cardiomyopathy	425	Cardiomyopathy
Heart Failure	428.0	Congestive Heart Failure NOS
	428.1	Left Heart Failure
	428.22	Chronic Systolic Heart Failure
	428.42	Chronic Systolic/Diastolic Heart Failure
	428.9	Heart Failure NOS

Procedure code(s):

CPT/HCPCS	G0166 ECP, External Counterpulsation, per treatment
APC Assignment	0678 ECP, External Counterpulsation, per treatment

Appendix

A. 510(k) Documentation

B. Clinical Data Tables for:

1. MUST – EECP Sub Group Analysis for Class II (Confidential)
2. IEPR 2 year Outcomes Sub Group Analysis for Class II (Confidential)

C. Cost Utility Analysis (Confidential)

D. Prospective Evaluation of EECP in Congestive Heart Failure: The PEECH Trial. Presented at the American College of Cardiology 2005 Scientific Session, March 6-9, 2005; Orlando, Florida. Late Breaking Clinical Trials, 05-LBCT-31970-ACC.

E. PEECH Results – Sub Group Analyses (Confidential)

F. PEECH Results – Adverse Events (Confidential)

G. Select Peer-Reviewed Publications

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