ENHANCED EXTERNAL COUNTERPULSATION (ECP) FOR TREATMENT OF HEART FAILURE

ISSUE

Blue Shield has received requests for the use of external counterpulsation (ECP) for treatment of heart failure. The Medical Policy Committee on Quality and Technology is asked to review the published data regarding the efficacy and safety of this technology.

CURRENT BLUE SHIELD POLICY

ECP for the treatment of stable angina pectoris was reviewed by the Medical Policy Committee on Quality and Technology in October 1998 and again in 1999 and found the technology did not to meet the TA criteria. This is the first review of ECP for treatment of heart failure. In July 1999 CardioMedics Inc. (Irvine, CA) requested that CMS alter the language of the instruction so that coverage of this treatment would not exclude manufacturers other than Vasomedical (Westbury, NY). CMS accepted CardioMedics Inc. formal request. EECP is now referred to as ECP.

BACKGROUND

Heart failure (HF) is a significant cause of morbidity and mortality in the United States. Nearly 5 million persons have been diagnosed with HF and it is responsible for approximately 15 million office visits, 6.5 million hospital days and nearly 300,000 deaths annually. Total inpatient and outpatient costs for the treatment of heart failure represent almost 6% of the entire annual health care budget, with approximately $500 million dollars spent annually on drugs (ACC/AHA Guidelines 2001)

The majority of patients with heart failure have symptoms due to an impairment of left ventricular function. Coronary artery disease is the cause of depressed left ventricular ejection fraction in about two-thirds of patients. Systolic function of the heart is governed by the contractile state of the myocardium, the preload of the ventricle, the afterload applied to the ventricles and the heart rate. Cardiac function may be compromised as a result of alterations in any of these determinants, but most commonly is due to depression of myocardial contractility. (CMDT chapter 10)
BACKGROUND, continued

Heart failure is a progressive disorder manifested by a process referred to as cardiac remodeling. There is increasing evidence that this process is mediated by neurohormonal factors that lead to sodium retention, peripheral vasoconstriction, and perhaps direct toxic effects on cardiac cells.

Heart failure is a clinical syndrome characterized by specific symptoms and signs. Patients with predominant left heart failure have symptoms of low cardiac output and elevated pulmonary venous pressure (and usually present with decreased exercise tolerance (dyspnea and/or fatigue). Signs of fluid retention predominate in right heart failure with the patient exhibiting edema, hepatic congestion and occasionally ascites. The most useful test in the evaluation of patients with HF is the two-dimensional echocardiogram; patients with an ejection fraction less than 40% are generally considered to have systolic dysfunction.

Conventional pharmacologic therapy for HF generally consists of four types of medications: a diuretic, an ACE inhibitor, a beta-adrenergic blocker, and (often) digitalis. The evidence supporting the use of these drugs in the treatment of HF is strong. For example, diuretics have been shown to improve cardiac function symptoms and exercise tolerance (Brater 1998); while ACE inhibitors and beta-blockers not only improve symptoms and function but also have been shown to reduce mortality. Patients with predominant diastolic dysfunction require different treatment strategies than do patients with predominant systolic dysfunction.

External counterpulsation (ECP)

The current ECP technique was introduced in the early 1980s by Geeing and colleagues in China (Geeing ZS; Li TM; Kambie H; Chen GH; Yu LQ; Cai SR; Zhan CY; Chen YC; Wo SX; Chen GW; Ma H; Chen PJ; Hunage BJ; Nose Y. 1983.)

ECP is an external circulatory-assist device that consists of an air pressure generator connected to three sets of pneumatic cuffs. A noninvasive technique, ECP employs the serial inflation of the three sets of cuffs that wrap around the patient’s calves, thighs and buttocks.
BACKGROUND, continued

Inflation and deflation of the cuffs is timed to synchronize with the patient’s ECG and the waveform of the arterial pressure is monitored non-invasively. ECP provides augmentation of diastolic blood flow and coronary blood flow in a fashion similar to the intra-aortic balloon pump. ECP is an outpatient procedure. Treatment is typically given in 35 one-hour sessions over seven weeks.

The overall hemodynamic effect of counterpulsation is to provide diastolic pressure augmentation and thereby to increase coronary blood flow, to unload the systolic cardiac workload and thereby to decrease myocardial oxygen demand, and to increase venous return and thereby to increase cardiac output (Kashmi et al 2002; Arora et al 2001). When counterpulsation is applied repeatedly over a course of several weeks, persistent augmentation of diastolic flow is thought to stimulate the development of collateral circulation to ischemic areas, with consequent improvement in angina symptoms and signs of ischemia (Michaels et al 2000; Arora et al 1999). In heart failure, ECP is thought to be beneficial by increasing cardiac output, reducing systemic vascular resistance, improving renal perfusion and by having a beneficial impact on the neurohormonal factors that contribute to heart failure (Strobeck 2002; Arora et al 2002).

TA Criterion 1

In June 2002 EECP® Therapy System (Vasomedical Inc. Westbury, NY) and CardiAssist™ ECP System (CardioMedics Inc. Irvine, CA) received 510K FDA clearance as a non-invasive external counterpulsation device intended for the use in the treatment of patients with congestive heart failure, stable or unstable angina pectoris, acute myocardial infarction, or cardiogenic shock.

TA criterion 1 is met.
TA Criterion 2: The scientific evidence must permit conclusions concerning the effectiveness of the technology regarding health outcomes.

No randomized trials have been published comparing outcomes of ECP for treatment of heart failure with standard therapy. The one published peer reviewed paper on ECP and HF was an open, nonrandomized feasibility trial. (Soran et al 2002) Published abstracts include a study of 8 patients with NYHA Class II or III HF and ejection fraction < 40% (Gorcscan et al 2000) a study of 40 patients with NYHA Class II HF. (Soran et al. 1999) and an abstract that compared use of ECP in 24 patients with ischemic cardiomyopathy with and without severely impaired LV ejection fraction (Vilkas et al 2002). In all of these studies, patients received 35 1-hour ECP sessions administered once a day, 5 days a week for 7 weeks.

The primary outcome in the study by Soran et al was safety as reflected by adverse events and laboratory parameters. Safety of ECP in patients with HF has been of concern since ECP increases venous return and therefore has the potential to worsen HF or precipitate pulmonary edema in patients with severely decreased ejection fraction (Lawson 2001).

Secondary outcomes in this study included change in exercise capacity and quality of life endpoints. Quality of life and overall perception of health has been an important outcome in some studies of ECP and angina (Springer et al 2001). In addition to improved exercise duration and quality of life measures, outcomes discussed in the abstracts include preload-adjust maximal power or “PAMP (a measure of LV performance) heart rate and measures of cardiovascular function such as strove volume, cardiac output, cardiac index and systemic vascular resistance. Important clinical outcomes for HF such as rates of hospitalization, morbidity and mortality have not been examined for ECP.

Overall, the published evidence is insufficient for drawing firm conclusions regarding the efficacy of ECP in the treatment of heart failure.

TA criterion 2 is not met.

Levels of Evidence: 3, 5
TA Criterion 3: The technology must improve the net health outcomes.

Patient Benefits

Nonrandomized Trials

Soran et al (2002) published the results of a multicenter, open, prospective, nonrandomized (single-group) feasibility trial at three centers to assess the feasibility of using ECP to treat patients with heart failure. A total of 32 patients were enrolled, 11 with idiopathic dilated cardiomyopathy and 21 with ischemic cardiomyopathy. The mean age of the patients was 56; 18.8% were female, the mean LVEF was 23% (18.7% in the idiopathic group) and overall 40.6% had angina. There were a number of exclusion criteria including unstable angina, edema above the ankle, serum creatinine > 2mg/dL, AICD or pacemaker, advanced COPD, and a history of DVT. Heart failure treatment was optimized and stable prior to treatment.

Each patient received 35 1-hour ECP sessions administered once a day, 5 days a week on average for 7 weeks. Patients were assessed at 1 week, 3 months and 6 months after the end of the treatment period. At the one-week follow-up, 23 patients completed the protocol; at 6 months 19 patients completed the protocol and were evaluated. At one week and at 6 months, there was a significant increase in peak oxygen uptake and in exercise duration over baseline. Quality of life was assessed at 1 week and 6 months with the Minnesota Living with Heart Failure Questionnaire (MLHFQ) scores. They found that at one week patients had a significant increase in MLHFQ scores over baseline in both the physical and emotional dimensions; by 6 months only the change in emotional dimension remained significant.

A total of 46 adverse events were reported for 23 patients; 14 events involving 8 patients led to hospitalization. Almost all adverse events occurred during the treatment period. Authors grouped adverse events into those they felt were related to ECP and those they concluded were not related (though it is not clear how this decision was made). In the "related" category were arrhythmia (requiring withdrawal from the study), bradycardia, shin tenderness, skin abrasion, back pain, muscle pain and swelling under the knee. Adverse events thought not to be related to ECP included palpitations, atrial fibrillation, angina and worsening HF and pulmonary embolus.
TA Criterion 3 (Patient Benefits: Nonrandomized Trials), continued

The authors conclude that ECP appears safe when used as an adjunct therapy for heart failure and that the results "suggest" that ECP can improve exercise capacity, quality of life and functional status. They conclude that “the results of this feasibility study warrant the initiation of a randomized controlled study to ascertain the efficacy of ECP as an adjunctive therapy in the management of patients with chronic stable heart failure.”

Pending Trials

A single-blind large multicenter trial of ECP in heart failure, the Prospective Evaluation of ECP in CHF trial (PEECH trial) is currently in process. It will compare how well ECP augments standard care to standard care without ECP, in the treatment of stable patients with HF.

Patient Risks

Since ECP increases venous return and preload during treatment, there has been concern that it may cause pulmonary congestion and an exacerbation of HF, especially in patients with severe left ventricular dysfunction. One recent study (Lawson et al 2001) examined the benefit and safety of ECP in treating patients with coronary artery disease and a history of HF. They analyzed a subset of the ECP Patient Registry with HF (mean LVEF 39%) and compared them with a cohort of patients without HF and found that improvement in angina was similar in both groups but that the HF group had a significantly greater likelihood of an adverse cardiac event (e.g. 5.5% experienced a worsening of their HF). The authors conclude, however, that there did not appear to be an excess of major adverse cardiac events given this high-risk group of patients, but that a randomized trial was needed to address these concerns.

TA criterion 3 is not met.
TA Criterion 4: The technology must be as beneficial as any established alternatives.

Alternatives to ECP for treatment of patients with heart failure primarily consist of different classes of drugs as discussed earlier under Background. Most of these drugs have been subjected to multiple large clinical trials that have demonstrated significant clinical benefit. For example, ACE inhibitors, beta-blockers and aldosterone antagonists have all been shown to reduce the risk of death and hospitalization in HF patients. In addition, ACE inhibitors, beta-blockers and digitalis have been shown to reduce symptoms and improve quality of life for these patients. Since ECP is not meant to supplant these drugs but instead serve as an adjunctive treatment for patients with compensated HF on appropriate medications it is not entirely accurate to describe it as an alternative treatment.

However, given the current data, it is impossible to conclude that ECP provides significant long term benefit to patients with HF who are already well compensated on established medical therapy.

TA criterion 4 is not met.

TA Criterion 5: The improvement must be attainable outside the investigational settings.

The published data are not sufficient to conclude that the efficacy and safety of ECP for the treatment of heart failure procedure have been established in the investigational setting, let alone under conditions of unusual medical practice.

TA criterion 5 is not met.

RECOMMENDATIONS OF OTHERS

Blue Cross Blue Shield Association

The Blue Cross Blue Shield Association has not yet reviewed ECP for the treatment of heart failure.

ACC/AHA Practice Guidelines 2001

“Until more data are available, this approach cannot be recommend for the management of patients with symptomatic left ventricular systolic dysfunction.”
Centers for Medicare and Medicaid (CMS)

CMS has not yet reviewed ECP for the treatment of heart failure.

CONCLUSION

There is only one published study that examines ECP as a treatment for patients with heart failure (Soran 2002). This was a feasibility study with the primary end-point being safety of ECP as reflected by adverse events. In this study, there were a total of 844 treatment sessions performed and 46 adverse events reported in 23 patients, 14 of which led to hospitalization for 8 patients. Significant improvements were seen in exercise capacity (peak oxygen uptake and exercise duration) and in quality of life assessments. From this study alone, it is difficult to draw firm conclusions about the safety of ECP for the treatment of HF. As the authors themselves caution, the size of population was small and comparisons were not made with a control group.

The established treatments for heart failure include diuretics, ACE inhibitors, beta-blockers and other drugs that have been subjected to multiple large clinical trials that have demonstrated significant clinical benefit. ECP has been proposed as an adjunctive treatment to these proven therapies but the safety and efficacy data are lacking in current studies.

A multicenter trial (the PEECH trial) is currently in process that should help answer some of the questions about the safety and efficacy of ECP in patients with heart failure. Until the results of this study are analyzed and published, it is not possible to endorse its use in patients with heart failure outside of the investigational setting.

TA criteria 2-5 are not met

RECOMMENDATION

It is recommended that the use of enhanced counterpulsation (ECP) for treatment of heart failure does not meet Blue Shield TA Criteria.

Committee approval as recommended.

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REFERENCES


Geeing ZS; Li TM; Kambie H; Chen GH; Yu LQ; Cai SR; Zhan CY; Chen YC; Wo SX; Chen GW; Ma H; Chen PJ; Hunage BJ; Nose Y. Sequential external counterpulsation (SECP) in China. Trans Am Soc Artif Organs, 1983, 29:599-603


Hunt SA; Baker DW; Chin MH; Cinquegrani MP; Feldman AM; Francis GS; Ganiats TG; Goldstein S; Gregoratos G; Jessup ML; Noble RJ; Packer M, Silver MA; Stevenson LW. ACC/AHA guidelines for the evaluation and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1995 Guidelines for the Evaluation and Management of Heart Failure). 2001. American College of Cardiology Web site. Available at: http://www.acc.org/clinical/guidelines/failure/hf_index.htm


Michaels AD; Kennard ED; Kelsey SE, Houbkov R; Soran O; Spence S; Chou TM. Does Higher Diastolic Augmentation Predict Clinical Benefit from Enhanced External Counterpulsation? Clin Cardiology 2001 Jun; 24(6):453-8

Soran O. et al. Abstract presented at the Heart Failure Society Annual Meeting, September 1999

REFERENCES, Continued


Tierney Jr. LM; McPhee SJ; Papadakis MA. Current Medical Diagnosis and Treatment (McGraw-Hill) Chapter 10.

Vilkas et al; 2002 An abstract that compared use of EECP in 24 patients with ischemic cardiomyopathy with and without severely impaired LV ejection fraction. In all of these studies, patients received 35 1-hour EECP sessions administered once a day, 5 days a week for 7 weeks.