EECP therapy continues to demonstrate potential as a treatment for chronic angina

Marilyn Lang, RN, ART

The medical device market for interventional cardiology and cardiac surgery is sizzling. From "smart" pacemakers to titanium-tough stents, flexible, plaque-seeking catheters, compact ventricular assist devices, laser procedures, angiogenesis, and robotic-assisted coronary artery bypass surgery, the gamut of choices for invasive treatment of coronary heart disease (CHD) is rapidly multiplying. One consequence of the proliferation of devices and procedures is that more patients are undergoing multiple interventional and surgical revascularization procedures to obliterate new and recurring arterial clogs.

Amid all the biotech hoopla, a not-so-glamorous, noninvasive procedure—enhanced external counterpulsation (EECP)—is quietly emerging as a clinically efficacious and cost-effective treatment for patients with symptomatic ischemic heart disease for whom "one more invasive procedure" isn't logistically feasible or psychologically desirable.

According to the American Heart Association's 1999 Heart & Stroke Statistical Update, approximately 6.5 million individuals in the U.S. with CHD have angina. About 2% of them have refractory or chronic angina—two types of advanced CHD that often aren't well controlled with maximum medical therapy or aren't amenable to invasive revascularization. And as the population ages and more individuals survive acute coronary events, the number of people with end-stage disease is expected to grow.

BASIC CARDIAC PHYSIOLOGY APPLIES

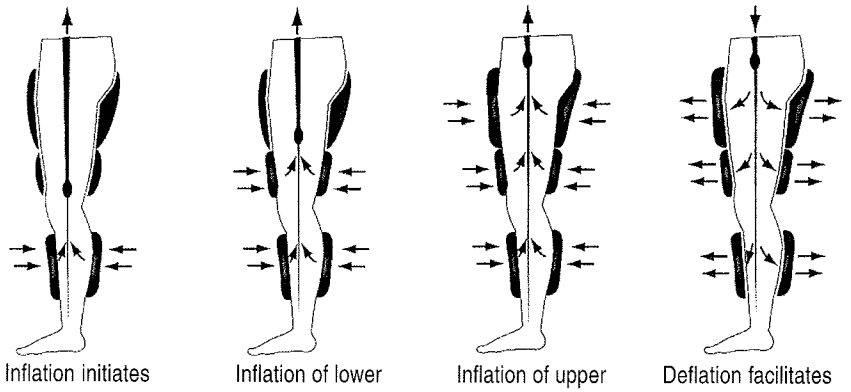
EECP therapy produces hemodynamic effects similar to those achieved with an intra-aortic balloon pump. The concept of external counterpulsation was first introduced in the U.S. in the mid-60s, but clinical studies on EECP weren't undertaken until the late 1980s, after researchers in China refined the original pump design and developed the current system of sequential counterpulsation.

The EECP system consists of an air compressor, a console, treatment table, and three pneumatic cuffs that are similar in design to a mast suit. The cuffs are applied to the patient's calves, lower thighs, upper thighs, and buttocks, and attached to the compressor, which sequentially inflates them up to 300 mm of pressure in sync with the patient's cardiac cycle. In early diastole, pressure is applied distally to proximally to the lower extremities and at end diastole the pressure is released from all the cuffs simultaneously (see Figure 1). The effects produced with the intermittent compression are increased diastolic pressure and retrograde aortic flow; increased venous return; and systolic unloading which results in increased cardiac output and coronary perfusion.

A PAIN-"LESS" PROCEDURE

Early adopters of EECP are completely convinced of the efficacy and safety of this pain limiting procedure. "The most therapeutic dose of EECP hasn't been established as yet," says John E. Strobeck, MD, director of the Heart Lung Center, Hawthorne, NJ. "But 85% of the patients in our clinic who complete 35 hour sessions over 7 weeks get good results, and there is some early evidence that with a longer course of treatment (50 to 60 hours) the success rate is 98%."

The EECP sequence (Figure 1)



Inflation initiates retrograde pulse wave **STEP 1**

Inflation of lower thigh cuffs 50 ms later **STEP 2**

Inflation of upper thigh cuffs 50 ms later **STEP 3**

Deflation facilitates cardiac unloading **STEP 4**

Source: Vaso Medical, Inc., Westbury, NY. Used with permission

Strobeck first began to use EECP in his interventional cardiology practice in 1996. "EECP is an absolutely safe treatment for properly selected patients," he says. " The treatment dropout rate is low, the adverse effects aren't limiting, and there are very few absolute contraindications."

The measure of success of EECP therapy is that patients experience less anginal pain, they use fewer nitrates, their time to exercise-induced ischemia is extended, and they report sustained improvements in their quality of life. These end-points have been demonstrated to some extent in several trials that enrolled patients with preserved left ventricular function, including the MUST-EECP (*The Multicenter Study of Enhanced External Counterpulsation: Effect of* EECP *on Exercise Induced Myocardial Ischemia and Anginal Episodes*) trial.

"The single most important finding of the MUST-EECP trial is that the time to ST-segment depression (≥ 1-mm) on exercise testing was significantly longer in the active treatment cohort," says Rohit R. Arora, MD, director of critical cardiac care services, Columbia-Presbyterian Medical Center, New York, NY, and the trial's principle investigator. "In the absence of angiographic evidence, this endpoint demonstrates the effectiveness of EECP therapy to improve myocardial perfusion."

Patients in the active treatment cohort who completed more than 34 sessions also had significantly fewer angina episodes, but a trend toward a decreased use of nitrates wasn't significant. This may have been confounded by the fact that on-demand and prophylactic use were not assessed independently.

The incidence of both clinical- and device-related adverse events was significantly higher in the active cohort (33 vs. 15; $p < 0.005$, and 37 vs.10; $p < 0.001$, respectively). Musculoskeletal pain in the legs and back was the most frequent device-related event (22.7%). Strobeck and Arora report that the number of patients who experience musculoskeletal pain is much lower in clinical practice—less than 5% as evidenced by outcomes data tracked by the International Enhanced Counterpulsation Registry (see page 7).

The effects of EECP appear to be durable as well. Twelve months after the completion of therapy, the patients in the active treatment cohort self-reported greater improvements in the level of bodily pain as measured by the SF-36. Additionally, patients reported greater improvements in health and function on the Quality of Life Index Cardiac Version III.

CLINICAL AND OPERATIONAL ISSUES

The HFCA-approved indications for use of EECP are for the treatment of refractory and chronic angina that isn't well-controlled by, or amenable to, other therapeutic modalities assuming an acceptable degree of risk. The MUST-EECP trial applied rigorous exclusion criteria to its patient selection, but its scope of use is "Much broader in actual clinical practice," says Arora.

***"Patients with certain diffuse lesion patterns and anatomic vessel abnormalities aren't optimally suited for* EECP."**

Patients aren't good candidates for EECP if they have left main artery disease, significant aortic insufficiency, an abdominal aortic aneurysm, severe peripheral vascular disease, lower extremity edema, or frequent atrial arrhythmia, have a history of deep vein thrombosis, or are pregnant. "Proper patient selection is important," says Strobeck. "This procedure can't be done on every patient with angina and it should only be done within a cardiology program."

He adds, "Patients with certain diffuse lesion patterns or difficult anatomic vessel abnormalities —such as a kinked bypass graft—also aren't optimally suited for EECP, and should be referred for surgery or undergo PCI."

At the Heart Lung Center, the initial patient screening process includes the following:

- Confirmation that the pain is cardiac in origin. Stress testing and occasionally angiography are performed, as needed, to establish a definitive diagnosis.
- A complete history and physical exam are done to rule out the presence of conditions that are contraindications to treatment.
- A thorough assessment of the vasculature of the legs and abdomen is done. Occlusions

DATA SUGGEST EECP BENEFICIAL FOR PATIENTS WITH LEFT VENTRICULAR DYSFUNCTION

Until recently, the safety and effectiveness of enhanced external counterpulsation (EECP) therapy for the treatment of refractory and chronic angina has been demonstrated primarily among patients with preserved left ventricular function (PLVF). New data from the multicenter International Enhanced Counterpulsation Registry (IEPR), which were recently presented at the Heart Failure Society Annual Meeting, suggest that individuals with left ventricular dysfunction (LVD) also benefit from EECP.

Created in January 1998 and maintained by the Department of Epidemiology at the University of Pittsburgh Graduate School of Public Health, the IEPR is used to track short- and long-term outcomes related to anginal episodes, medication use, and improvements in angina classification. To date, some 60 treatment centers have enrolled approximately 1,500 patients in the registry. Data are collected before and after treatment, at six months after completion of treatment, and annually for three years.

An analysis of data on 705 patients newly enrolled in the IEPR—169 with LVD and 536 patients with PLVF—shows that patients with LVD appear to demonstrate improvements similar to those seen in patients with PLVF (see Figure 2). Significant differences in the groups' baseline characteristics were that patients in

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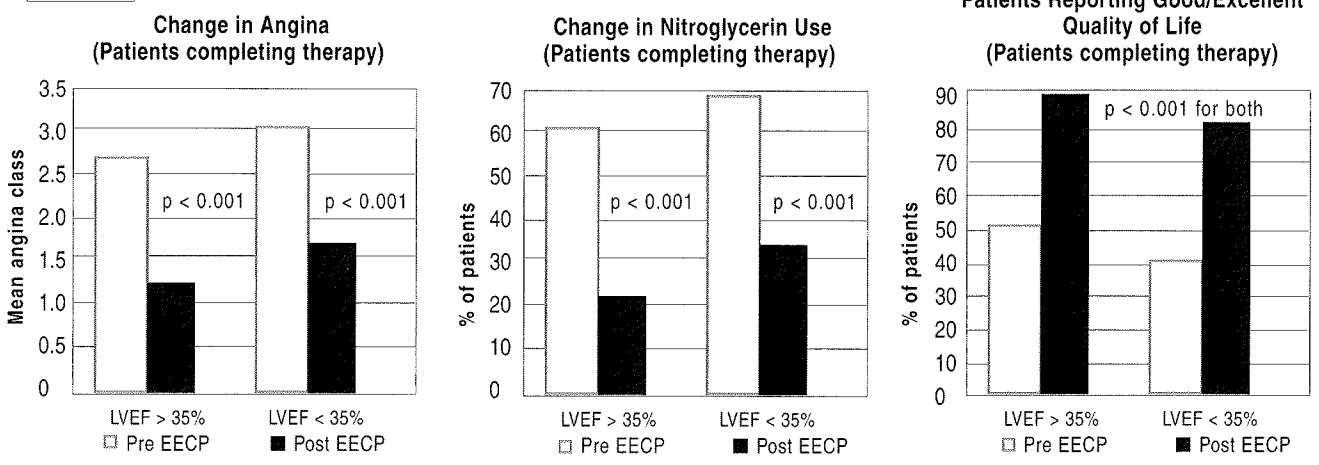
Figure 2

	PLVF (n = 536) EF > 35%	LVD (n = 169) EF < 35%
Mean age	66	67
Male (%)	74	79
Prior CABG (%)	57	70*
Prior MI (%)	62	84*
CHF (%)	19	60*
Diabetes (%)	39	35
Yrs since CAD dx	8	12*
Angina Class III/IV	66	86*
Multivessel disease	76	89*
Candidate for PTCA	23	14**
Candidate for CABG	30	16*

	PLVF (n = 536)	LVD (n = 169)
Hours of treatment	34.3	34.9
Completed therapy (%)	83	84
Diastolic Augmentation:		
Ratio at start tx	0.85	0.99*
Ratio at end of tx	1.12	1.32*
Adverse events:		
CHF (%)	1.5	6.5
Unstable angina (%)	2.2	3.0
MI (%)	0.6	0
CABG/PTCA (%)	1.0	0
Skin irritation (%)	1.5	0
Muscle pain (%)	1.1	2.4

* $p < 0.001$; ** $p < 0.05$ **Key:** PLVF (Preserved left ventricular function); LVD (Left ventricular dysfunction)) EF (Ejection fraction)

Figure 3



Source: The International Enhanced Counterpulsation Registry. Reprinted with permission.

in the legs or iliac-femoral artery limit the effectiveness of EECP.

According to Strobeck, virtually every patient who completes a course of treatment experiences a lessening of angina symptoms regardless of whether he/she was previously experiencing an intermittent exertional angina or a more severe debilitating angina pattern. "Some patients get a vigorous response after just a single course, while others will need to have it repeated to get measurable results," he says.

As therapy progresses and patients become pain-free, they are encouraged to increase their activity through a walking program, or some other form of mild-to-moderate aerobic exercise. Typcially, patients will require less in the way of nitrates, but no other significant modifications are made in their pre-therapy medication regimen.

"Drugs such as the nitrates and calcium channel blockers maintain and improve endothelial function," says Strobeck. "So it isn't advantageous to discontinue them, particularly since the delivery of the drugs' beneficial effects is improved due to better coronary perfusion."

THE ECONOMICS OF EECP THERAPY

EECP therapy is a covered benefit for Medicare beneficiaries, although states are providing varying levels of reimbursement for it. "The cost for a seven-week program is $7,500," says Arora. "That's substantially less than the inhospital costs for surgery, and similar to inpatient and outpatient costs associated with PCI."

Vaso Medical, Inc.,Westbury, NY, distributes the EECP systems. The purchase price (including the entire system, replacement parts, disposable leggings for patients to wear during therapy, staff training, 24-hour clinical support, and patient education and marketing materials) is about $200,000. Monthly leases are also available.

At a minimum, an 8x10 space is needed to comfortably accommodate the equipment. One nurse or a trained tech can manage three therapy tables and treat up to 15 patients per day (1.5 hours per patient including set up and clean-up). Pulse oximetry equipment is used in the research setting but it isn't required in clinical practice.

For more information, call Tony Peacock, Vaso Medical's vice president marketing and clinical affairs, at 800/455-3327, Ext. 120, or visit http://www.eecp.com

EECP APPEARS TO BE BENEFICIAL FOR PATIENTS WITH LVD

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the LVD cohort were more likely to have multivessel disease, previous CABG, AMI, and CHF (see Fig. 3).

"The physiology associated with EECP therapy would predict that patients with CAD-related LVD would derive the same benefit as those with PLVF," says John Strobeck, MD. "Its role in patients with LVD caused by cardiomyopathy is less clear."

Partial results from another very small study of 40 patients showed that among patients with NYHA Class II heart failure who were on optimal medical therapy, improvements in exercise duration, improved NYHA class, and quality of life were noted after seven weeks of EECP therapy as compared with baseline (See Fig. 4).

PRELIMINARY DATA ON 6 PATIENTS **(Figure 4)**

Mean age	61.3 ± 11.2	
Hours of treatment	35 over 7 weeks	
Completed therapy (%)	84% (1 drop-out after 21 sessions due to back pain)	
	Pre EECP	**Post EECP**
NYHA Class II	5	1
NYHA Class I	0	4
VO2 max (ml/kg/min)	13.63 ± 1.54 (p = 0.004)	15.89 ± 2.14
Exercise duration (in seconds)	592.5 ± 96.26 (p = 0.008)	756 ± 132
Quality of life (Minnesota Living with Heart Failure Questionnaire)	36.3 ± 10.2	22.3 ± 6.0

Source: "Efficacy and safety of enhanced external counterpulsation in mild to moderate heart failure: A preliminary report," Ozlem Z. Soran, MD, et al., Abstract presented at the Heart Failure Society Annual Meeting, September 1999.

References:

1. "The Multicenter Study of Enhanced External Counterpulsation (MUST-EECP): Effect of EECP on exercise induced myocardial ischemia and anginal episodes," Rohit R. Arora, MD, et al., Journal of the American College of Cardiology, vol., 33, #7, June 1999, pp. 1833-1840.

2. "Results of the Multicenter Study of Enhanced External Counterpulsation (MUST-EECP) outcomes study: Quality of life benefits sustained twelve months after treatment," Rohit Arora, MD, et al., Oral Abstract presented at the 48th Scientific Session of the American College of Cardiology, March 1999.