☆ CME PAPER ☆

Enhanced External Counterpulsation in the Management of Angina in the Elderly

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Manuscript received May 6, 2002; revised July 23, 2002; accepted September 12, 2002

This study was undertaken to determine whether enhanced external counterpulsation is a safe and effective treatment for angina in octogenarians. In this prospective observational study, demographic and clinical outcome data on patients consecutively enrolled in the International EECP Patient Registry was examined. Of the 3037 patients analyzed, 249 (8%) were ≥80 years old. Octogenarians were more likely to be female and have a history of congestive heart failure (41% vs. 29%; p<0.001). They were less likely to have had previous revascularization. Fewer patients in the octogenarian group (76% vs. 84%; p<0.01) completed a course of treatment. Of those octogenarian patients who completed treatment, 76% reported a reduction in angina and quality of life improved significantly. Adverse events related to treatment were low. At 6-month follow-up, 81% reported maintenance of angina improvement. Thus, enhanced external counterpulsation is a low-risk intervention that offers octogenarians the ability to return to more normal activity and a better quality of life. (AJGC. 2003;12:90–96)

The number of elderly persons is steadily increasing worldwide, especially in developed countries. As life expectancy continues to improve, a corresponding increase in the octogenarian population can be expected. This has a direct impact on the approach to symptomatic coronary artery disease (CAD), which occurs more frequently with advanced age.

One of the most common and challenging dilemmas in treating elderly patients with symptomatic CAD is whether or not to perform coronary revascularization. Pharmacologic opportunities to treat CAD may be limited in the elderly as a result of more frequent adverse drug reactions and compliance issues related to cognitive impairment and/or the cost of medication. There is a consistent curvilinear relationship between advancing age and increasing morbidity and mortality from coronary artery bypass graft surgery[1,2] and percutaneous coronary intervention.[3–6] Patients aged ≥80 years who have CAD are more likely to have a history of myocardial infarction, left main coronary disease, advanced angina, cerebrovascular disease, renal dysfunction, and peripheral vascular disease compared to younger patients.[7] The risk of periprocedural complications during coronary revascularization increases with age, and is largely attributable to the higher incidence of these comorbid conditions. It is unclear whether the acute risks of coronary revascularization are counterbalanced by improved long-term survival or functional outcomes compared to those achieved with medical care.

Enhanced external counterpulsation (EECP) is a noninvasive technique for treating chronic angina in patients who are not candidates for conventional forms of revascularization.

Treatment with EECP is effective in reducing angina with a very low incidence of adverse effects, and thus may be a suitable treatment for use in elderly patients. The aim of this study was to determine the safety, efficacy, and duration of benefit of EECP when applied to elderly patients.

METHODS

The International EECP Patient Registry (IEPR), housed at the Epidemiology Data Center of the University of Pittsburgh Graduate School of Public Health, began in January 1998; to date, more than

5000 patients with chronic angina have been enrolled from over 80 centers in the United States and other countries. The registry aims to collect data on a broad range of patients and therefore entry criteria are simple: that the patient has given informed consent and has had at least 1 hour of EECP treatment for angina.

The registry methodology has been described previously.[8] Data on demographics, medical history, medication, and angina status were collected on consecutive patients prior to and after EECP treatment. No attempt was made to maintain current medication regimens throughout the study, although patients referred for EECP were considered "optimally medically managed." Before treatment and immediately after the last hour, patients were asked to assess their current quality of life, health, and satisfaction with quality of life on five-point Likert scales (1=excellent; 2=very good; 3=good; 4=fair; 5=poor). Patients were interviewed by telephone at 6 months, 12 months, and yearly thereafter to record angina status, cardiac, and other events.

The EECP device consists of three paired pneumatic cuffs that are applied to the lower extremities. The cuffs are sequentially inflated (applying 250–300 mm Hg of external pressure) during diastole, returning blood in the lower extremities to the central circulation, producing aortic diastolic augmentation, and increasing venous return and cardiac output. The cuffs are deflated in systole, reducing peripheral resistance to flow and providing left ventricular unloading. Daily 1- to 2-hour treatment sessions are typically administered on an outpatient basis for a total treatment course of 35 hours. All treatment was carried out using the model MC_2, EECP system (Vasomedical, Inc., Westbury, NY).

Results are presented as percentages or means (±SD). Chi-squared or Fisher's exact test were used to compare categorical data, and the Wilcoxon rank-sum test was used for continuous variables. A p value of <0.05 was considered significant for comparison of groups. Events occurring up to 9 months from the start of EECP therapy have been analyzed. Calculations were performed using the SAS (SAS Institute, Cary, NC) statistical package. The study was granted ethical approval and all patients gave informed consent.

RESULTS

Of 3037 patients analyzed, 249 (8%) were ≥80 years. Characteristics of the study population are presented in Table I. The elderly population was more likely to be female and had a longer history of CAD (mean, 12±9 years vs. 10±8 years; $p<0.05$). Family history of CAD, diabetes mellitus, hypertension, hyperlipidemia, smoking, and previous myocardial infarction were reported less often in the elderly population. Similarly, the elderly were significantly less likely to have had a previous revascularization procedure (74% vs. 86%; $p<0.001$). There was slightly more non-cardiac vascular disease in the elderly group. Angina was somewhat more severe in the elderly by Canadian Cardiovascular Society angina classification, although all patients were highly symptomatic. The frequency of angina episodes was slightly less in the older group (8 angina episodes/week vs. 10 episodes/week; $p<0.05$). Elderly patients were significantly more likely to have a history of heart failure, even though mean left ventricular ejection fraction was similar in both groups. Multivessel disease was present in 78% of all patients and the majority of all patients were considered unsuitable for further revascularization.

Beta blockers (57% in the elderly vs. 64% in younger patients; $p<0.05$), calcium channel blockers (41% vs. 48%; $p<0.05$), and lipid-lowering agents (46% vs. 71%; $p<0.001$) were prescribed less often in the elderly group. There were no significant differences in the proportion of patients taking aspirin (69% vs. 71%; p=NS), angiotensin-converting enzyme inhibitors (33% vs. 37%; p=NS), and angiotensin receptor blockers (10% vs. 11%; p=NS). Nitrates were prescribed more often in the elderly group (81% vs. 73%; $p<0.01$).

Post-EECP treatment outcomes are shown in Table II. Fewer elderly patients were able to complete a course of treatment. The rates of major adverse cardiac events (e.g., death, myocardial infarction, percutaneous coronary intervention, coronary artery bypass graft) during treatment were very low in both groups. Failure to complete a course of treatment in the elderly population was frequently due to an intervening non-cardiac medical event or patient choice. There was a trend toward more congestive heart failure exacerbation, skin problems, and other events occurring during treatment in the elderly group. Of those elderly patients who were able to complete a course of treatment, most achieved a significant reduction in angina. Canadian Cardiovascular Society angina class was decreased by greater than or equal to one class in 76% of the elderly group compared to 82% in younger patients ($p<0.05$), and weekly angina episodes and nitroglycerin use were decreased by six episodes in the elderly compared to seven episodes in younger patients (p=NS) (Figure 1). While angina reduction in the elderly occurred slightly less often than in the younger population, the benefit was sustained in 81% of patients in both groups at 6 months

Table I. Patient Characteristics

	Age <80 Years (N=2788)	Age ≥80 Years (N =249)	*P* Value
Mean age (years)	64.8±9.5	84.4±4.0	
Female	24%	30%	0.05
Prior MI	66%	59%	0.05
Prior PCI	64%	48%	0.001
Prior CABG	68%	58%	0.001
Non-cardiac vascular disease	28%	34%	0.05
CAD risk factors			
Hypertension	70%	61%	0.01
Diabetes	44%	30%	0.001
Smoking			0.001
Present	7.6%	1.2%	
Past	65%	56%	
Never	28%	43%	
Family history of CAD	77%	66%	0.001
Hyperlipidemia	80%	59%	0.001
History of CHF	29%	41%	0.001
Mean LVEF	46%±14%	46%±15%	NS
LVEF <35%	18%	20%	NS
Candidate for neither PCI/CABG	79%	81%	NS

MI=myocardial infarction; PCI=percutaneous coronary intervention; CABG=coronary artery bypass graft surgery; CAD=coronary artery disease; CHF=congestive heart failure; LVEF=left ventricular ejection fraction; NS=not significant

Table II. Post-Enhanced External Counterpulsation Treatment

	Age <80 Years (N =2788)	Age ≥80 Years (N =249)	*P* Value
Hours of treatment (mean)	34±10	32±12	0.05
Completed as prescribed	84%	76%	0.01
Stopped due to clinical event	9%	11%	NS
Patient discontinued	7%	11%	0.05
Events during treatment			
Skin breakdown	1.1	2.4	NS
CHF	1.7	3.2	NS
Other event	10	16	NS
Six-month follow-up	(n=2008)	(n=183)	
MACE			
Death	3	6	0.05
MI	2.7	3.8	NS
PCI	3.1	1.1	NS
CABG	1.3	1.1	NS
Cardiac hospitalization	12	6	0.05

NS=not significant; CHF=congestive heart failure; MACE=major adverse cardiac event (death, myocardial infarction [MI], percutaneous coronary intervention [PCI], coronary artery bypass graft surgery [CABG])

(Figure 2). Neither age group recorded many changes in medication use from pre- to post-EECP, although actual doses were not recorded. Beta blocker use was unchanged in 91% of the younger group vs. 94% of the elderly group; angiotensin-converting enzyme inhibitors in 93% vs. 92%; calcium channel blockers in 92% vs. 91%; and angiotensin receptor blockers in 95% vs. 96%, respectively (all p=NS). There was significant improvement reported post-EECP in patient-assessed quality of life ($p<0.001$), health ($p<0.001$), and satisfaction ($p<0.001$), as shown in Figure 3. During the 6-month follow-up period, the rate of cardiac hospitalization was lower in the elderly than in the younger group. Also, during the 6-month follow-up period, the rates of major adverse cardiac events were comparable; however, the mortality rate (not age adjusted) in the elderly group was slightly higher than in the younger group.

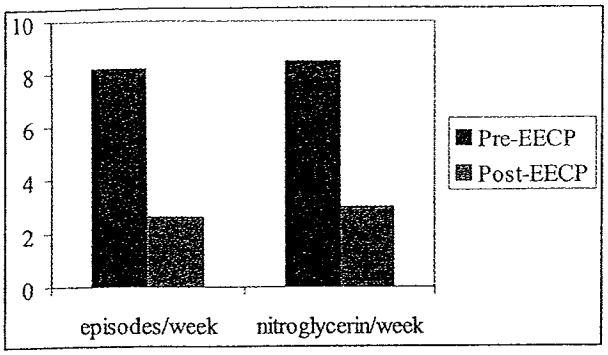

Figure 1. Angina frequency and nitroglycerin use pre- and post-enhanced external counterpulsation (EECP) in patients ≥80 years

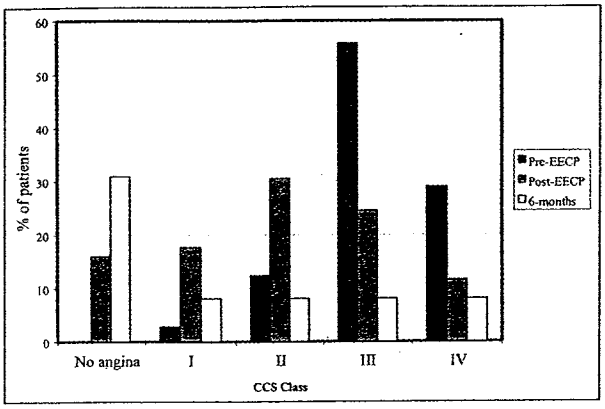

Figure 2. Canadian Cardiovascular Society (CCS) angina class in patients ≥80 years pre- and post-enhanced external counterpulsation (EECP)

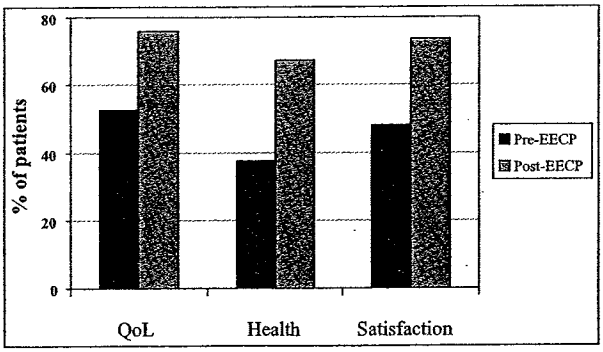

Figure 3. Enhanced external counterpulsation (EECP) patients ≥80 years reporting "good," "very good," or "excellent" quality of life (QoL)

DISCUSSION

During the past decade, there have been an increasing number of patients with anginal symptoms who are not suitable candidates for revascularization procedures. It is this group of patients who appear to benefit most from EECP. This study provides data from a prospective observational study that demonstrates how elderly angina patients respond to treatment with EECP. These data expand upon earlier reports that EECP is safe and effective in treating angina pectoris in octogenarians.

Normal aging of the cardiovascular system produces important changes in hemodynamics. The effects of aging alter the normal myocardial response during relaxation and impede diastolic function. Often, the aged heart has difficulty maintaining output against a high afterload in the face of impaired contractility and a blunted chronotropic response. End-diastolic volumes increase to maintain stroke output, but this increases left ventricular wall tension and myocardial oxygen demand. The cardiovascular hemodynamic effects of EECP have been previously reviewed.[9,10] The benefits of intra-aortic balloon counterpulsation (IABP) have been well described and are well recognized. A known effect of IABP is augmentation of diastolic coronary artery flow. Studies have shown that both IABP and EECP provide a comparable increase in coronary flow.[11,12] However, in contrast to IABP, EECP can provide a chronic antianginal response. By sequentially compressing the lower extremity venous beds, EECP increases venous return, which has been shown to increase cardiac filling pressures and cardiac output. Cuff deflation just prior to the onset of systole results in reduced peripheral resistance to flow and provides systolic unloading.[12]

Although the exact mechanism by which EECP improves symptoms in patients with chronic angina remains undefined, recent studies suggest that EECP might increase recruitment and/or development of collateral circulation. Shear stress is a potent activator of pathways involving angiogenesis and essential autoregulatory mechanisms at the level of the endothelium. Several angiogenesis factors are necessary for the development of functional collateral circulation. Recent studies have shown that EECP promotes the release of angiogenesis factors such as hepatocyte growth factor, fibroblast growth factor, and vascular endothelial growth factor.[13]

Studies using radionuclide stress testing have documented improved myocardial perfusion, exercise tolerance, and decreased angina following EECP treatment in about 80% of patients, with the benefit sustained in a majority of treated patients over a 3-year follow-up period.[14–16] These effects are sustained after treatment and may be responsible for some observed post-treatment changes, including a peripheral conditioning effect resembling that of exercise as well as improved coronary vasomotor tone and function and cardiac perfusion. All of these mechanisms may contribute to the persistent clinical benefits demonstrated for up to 5 years after treatment.[17]

CONCLUSION

EECP provides a low-risk intervention that can assist the clinician in treating elderly patients ≥80 years of age with symptomatic CAD. Episodes of angina and nitroglycerin use were decreased, while quality of life improved in many patients. Angina relief was sustained at 6-month follow-up in a population where the majority of patients are not candidates for coronary revascularization.

Acknowledgment: Vasomedical Inc., Westbury, NY, sponsors the International Enhanced External Counterpulsation Patient Registry (IEPR).

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CME Questions

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INSTRUCTIONS FOR COMPLETING THIS FORM

Read the selected paper and answer *all* the questions that follow. After each question there is a series of possibly correct answers. Please select the one best answer for each and place your selection on the answer grid. **YOU MUST ALSO COMPLETE THE CME EVALUATION SECTION** and return the form within 6 months of the paper's publication to receive credit. Letters of credit will be mailed to participants biannually.

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OBJECTIVE AND TARGET AUDIENCE

All physicians who care for geriatric patients are eligible to receive credit. At the conclusion of this activity, participants should be able to: 1) summarize the important points discussed in the paper reviewed; 2) identify patients to whom the paper is relevant; 3) modify management practices as new information is learned; and 4) identify deficiencies in their knowledge base.

QUESTIONS: PLEASE SELECT THE ONE BEST ANSWER FOR EACH AND PLACE YOUR SELECTION ON THE ANSWER GRID.

1. With regard to elderly patients, which one of the following statements is false?
   A_____Pharmacologic opportunities to treat coronary artery disease may be limited in the elderly due to more frequent adverse drug reactions and compliance issues related to cognitive impairment.
   B_____There is a curvilinear relationship between advancing age and increasing morbidity and mortality from coronary artery bypass graft surgery and percutaneous coronary intervention.
   C_____Patients aged >80 years who have coronary artery disease are less likely to have a history of myocardial infarction, left main disease, advanced angina, cerebrovascular disease, and other organ impairment compared with younger patients.
   D_____The risk of periprocedural complications during coronary revascularization increases with age, and this is largely attributable to the higher incidence of these comorbid conditions.

2. Which one of the following statements is false regarding the function or use of enhanced external counter pulsation (EECP) devices?
   A_____The cuffs are sequentially inflated during diastole, and deflated in systole.
   B_____Inflation during diastole produces aortic diastolic augmentation, increasing venous return and cardiac output.
   C_____Deflation in systole acts to reduce peripheral vascular resistance to flow and provides left ventricular unloading.
   D_____Daily 6-hour treatment sessions are typically administered for a total of 60 hours.

3. With regard to the study discussed in the review, which of the following statements is true?
   A_____The elderly population, when compared to the younger population, was more likely to be male, and have a shorter history of coronary artery disease.
   B_____Fewer younger patients were able to complete a course of treatment with EECP.
   C_____Improvement in angina symptoms, as measured by reduction in the Canadian Cardiovascular Society angina class, occurred more frequently in the elderly group compared with the younger group.
   D_____There was significant improvement in post-EECP patient-assessed quality of life in both the younger and older groups.

4. With regard to EECP, which of the following statements is false?
   A_____Studies using radionuclide stress testing have documented improved myocardial perfusion, exercise tolerance, and decreased angina following EECP treatment in about 80% of patients.
   B_____Studies have shown that both intra-aortic balloon pump placement and EECP provide a comparable increase in coronary flow.
   C_____EECP may improve symptoms in patients with chronic angina through increased recruitment and/or development of collateral circulation.
   D_____Despite significant early improvement documented in the literature, EECP has not been shown to be beneficial in reducing angina over 3 years of follow-up.

CME Answers

Answer the questions from the previous page by selecting the best choice of A, B, C, D, or E

Questions: 1.__ 2.__ 3.__ 4.__

CME Evaluation

	Agree				Disagree
1. My knowledge was enhanced by this activity.	1.__	2.__	3.__	4.__	5.__
2. The activity helped to clarify issues specific to geriatric patients.	1.__	2.__	3.__	4.__	5.__
3. The information obtained from this exercise will have an impact on my care of patients.	1.__	2.__	3.__	4.__	5.__
4. The format of the exercise was useful.	1.__	2.__	3.__	4.__	5.__

5. Suggestions for future topics:

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