

Practicability and Limitations of Enhanced External Counterpulsation as an Additional Treatment for Angina

DIERK WERNER, M.D., JOACHIM KROPP, M.D.,* SEBASTIAN SCHELLONG, M.D.,† CHRIS FRIEDEL, M.D.,† JENS-UWE VOIGT, M.D., JOSEF LUDWIG, M.D., WERNER G. DANIEL, M.D., FESC, FACC, FRANK A. FLACHSKAMPF, M.D., FESC, FACC

Department of Cardiology, Friedrich-Alexander-University Erlangen-Nuremberg, Erlangen; Departments of *Nuclear Medicine and †Internal Medicine, Technical University Dresden, Dresden, Germany

Summary

Background: An increasing number of clinical studies indicates reduction of angina and myocardial ischemia by enhanced external counterpulsation (EECP) therapy. However, given the wide range of contraindications and the long duration of treatment, eligibility and practicality issues have not been addressed systematically.

Hypothesis: Of all candidates for EECP (patients with drug-refractory angina without possibility of revascularization), the majority either have contraindications or have practical problems complying with the time demands that this therapy imposes. In the rest, EECP leads to satisfactory results.

Methods: During 18 months, every consecutive patient with angina despite medical and interventional therapy was evaluated for EECP at one center. Treated patients underwent a bicycle exercise test and perfusion imaging before and after the standard course of 35 h of EECP. In addition, patients were asked about frequency of angina and nitroglycerin usage before and after EECP, and all patients filled out a final questionnaire 1 year after the end of therapy.

Results: Overall, 48 patients were considered candidates for EECP. Of these, 24 were excluded for medical reasons: poor ejection fraction (4), peripheral artery disease (4), anticoagulation (4), and atrial fibrillation (3). Eight further patients declined EECP for lack of time or accommodation. Another 3 of the 16 remaining patients dropped out because of side effects.

In the 13 patients who finished the treatment course, weekly anginal episodes were reduced by 48% ($p < 0.05$), on-demand nitroglycerin puffs were reduced by 51% ($p < 0.05$), work capacity was improved by 22% ($p < 0.05$), and the number of reversible perfusion defects in perfusion scans decreased non-significantly (-28%). However, 4 of 13 treated patients determined 1 year later that the detriment of loss of time exceeded the benefits of EECP.

Conclusion: Similar to previous reports, our study confirms the reduction of angina and improvement of work capacity after EECP. However, using established contraindications, approximately two-thirds of patients considered to be candidates had to be excluded, and one-third of the treated patients regarded EECP therapy retrospectively as too time consuming.

Key words: enhanced external counterpulsation, angina, working capacity, contraindications

Introduction

During the last decade, enhanced external counterpulsation (EECP) became an additional therapeutic option for patients with angina. It works by applying electrocardiogram (ECG)-triggered diastolic pressure to the vascular bed of the lower extremities by means of three air-filled cuffs. This air-driven system was developed by Zheng *et al.*¹ based on experiences with hydraulic devices collected in the 1970s.² The initial clinical experience with EECP came from China; Xu *et al.* reported significant relief of anginal symptoms in 53% of 6,116 patients after a therapeutic course of EECP.³ The first objective assessment of the anti-ischemic effects of EECP was carried out by Lawson *et al.* using thallium scans.⁴ The Multicenter Study (MUST)-EECP trial conducted at seven American university hospitals showed clear benefits of EECP over placebo and training effects.⁵ In a recent study, Masuda *et al.*, using positron emission tomography, measured an increased myocardial blood flow in regions supplied by a stenotic coronary artery after the usual 35-h course of EECP.⁶ Several further studies confirmed the reduction of anginal attacks and on-de-

Address for reprints:

Dierk Werner, M.D.
II. Medical Clinic
Friedrich-Alexander-University
Östliche Stadtmauerstraße 29
91054 Erlangen, Germany
e-mail: Dierk.Werner@nexgo.de

Received: May 3, 2002

Accepted: November 21, 2002

mand nitroglycerin usage as well as an improvement in work capacity after EECP.⁷⁻¹⁰

However, applicability and practicability of EECP treatment in routine patient care have not been well described. Thus, in the present study, over a period of 18 months, EECP was offered to all patients admitted to a large university cardiology division who were suffering from angina despite antianginal medication and without possibility of revascularization.

Methods

Inclusion and Exclusion Criteria

To assess EECP under clinical everyday conditions, we screened approximately 3,000 patients admitted to our hospital for coronary angiography over a period of 18 months. Patients with angina despite treatment with at least two antianginal drugs and no possibility of revascularization by coronary intervention or bypass surgery were considered further for EECP.

We applied the exclusion criteria of the MUST-EECP trial:⁵ ejection fraction <30% measured angiographically, significant aortic valve disease, aortic aneurysm, symptomatic peripheral vessel disease, implanted pacemaker or defibrillator, history of deep vein thrombosis, varicosities, atrial fibrillation, or anticoagulation with an International Normalized Ratio (INR) >2. In addition to coronary angiography, every patient underwent clinical examination, echocardiography, and duplex sonography of the veins of the lower extremity and the abdominal aorta.

Study Protocol

Patients included in the study were treated with EECP (Vasomedical, Inc., Westbury, N.Y., USA) for 35 h, 1 or 2 h daily, over a period of 4 to 7 weeks. This therapeutic regime was used in all previous studies based on an initial study by Zheng *et al.* in which a definitive improvement of exercise tolerance was demonstrated in the majority of patients after three courses of 12 h of EECP, 1 h daily.¹ Before starting EECP therapy, every patient underwent an initial test run of EECP. During this test, diastolic blood pressure augmentation by EECP was assessed by the systolic/diastolic pulse ratio measured by finger plethysmography. The time delay between the R wave of the ECG and the onset of counterpulsation pressure was adjusted to maximize diastolic pressure augmentation.^{1,11}

Patients were asked in a questionnaire to indicate the frequency of anginal attacks and nitroglycerin usage during the week before and after the course of EECP. One year after the EECP course, all patients filled out a further questionnaire asking whether they would again participate in the study and to state the reason in case of refusal. The medication of the patients was not changed during the entire study. A symptom-limited bicycle exercise test was carried out before and after therapy, starting with a work capacity of 50 W and increasing every 2 min by 25 W. In addition, before and after the EECP course, every patient underwent bicycle stress perfusion imag-

ing by technetium-99m (^{99m}Tc)-MIBI single-photon emission computed tomography (SPECT), dividing the left ventricle into 33 segments. At rest, segments with <50% of maximal segmental uptake were considered to be fixed perfusion defects. Segments with >75% of maximal uptake at rest and <75% of maximal uptake during exercise were considered to indicate reversible perfusion defects. The difference between values at rest and during exercise had to be at least 10%. The study protocol was approved by the institutional Ethics Committee. Informed consent was obtained from all study participants according to the declaration of Helsinki.

Statistics

Baseline values were compared with values after the 35 h of EECP by a paired nonparametric test (Mann-Whitney-U-test). The level of significance was set at $p < 0.05$.

Results

Included and Excluded Patients

During the 18-month screening period, 48 patients had angina (Canadian Cardiovascular Society Class I-III) despite medical therapy and no possibility of revascularization, or refused invasive revascularization. These patients were further assessed for EECP. Four patients were excluded for ejection fraction <30%, four patients for severe peripheral artery disease, four patients for anticoagulation with an INR of >2.0, three patients for atrial fibrillation, and one patient, respectively, for each of the following conditions: aortic regurgitation, recent deep vein thrombosis, history of severe lung embolism, severe varicosities, abdominal aortic aneurysm, and atrophy of skeletal muscles after poliomyelitis. Eight patients declined to take part in the study: six for lack of time and two for accommodation. Three further patients were excluded for reasons related to the EECP procedure: in two patients, the systolic-diastolic ratio in the finger plethysmography was <0.8, indicating that diastolic augmentation was insufficient, and one patient had permanent DDD pacing that prevented correct triggering by the EECP machine. Figure 1 demonstrates the ratio of included and excluded patients considered for EECP.

Of the remaining 16 patients, two stopped therapy after 3 and 15 h, respectively, of EECP because of recurrent pain in the legs during the course; one slender patient suffered from skin abrasion by the buttock belt which could not be overcome by paddings between the belt and the skin. This patient dropped out of the study after 12 h of therapy.

Patient Characteristics

The remaining 13 patients (10 men, 3 women, mean age 60.5 ± 8.5 years) completed the therapeutic course. Of these, 10 had a history of myocardial infarction. Mean ejection fraction was $55.5 \pm 12.0\%$. On coronary angiography, four patients had single-, five had double-, and four had triple-vessel

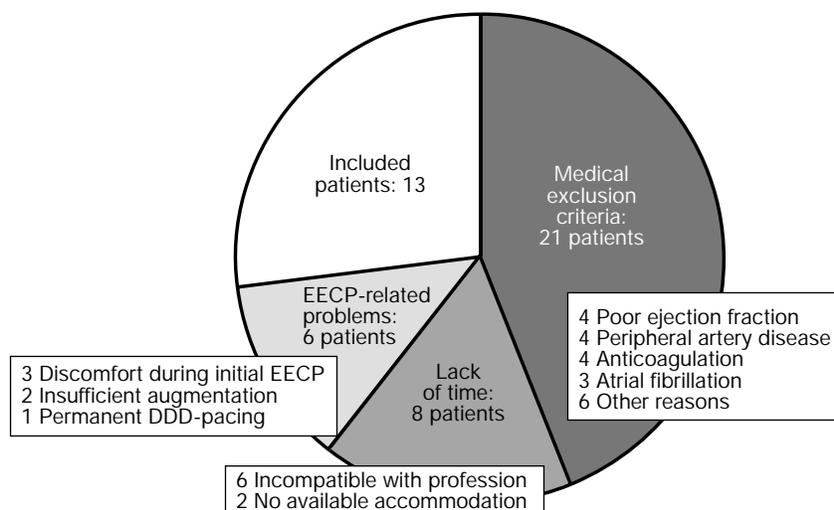


FIG. 1 Included and excluded patients with reasons for exclusion from enhanced external counterpulsation (EECP). The total represents the 48 patients meeting the general inclusion criteria for EECP therapy (angina despite medical therapy and patient not eligible for revascularization).

disease. Two patients had a history of coronary artery bypass graft (CABG) surgery and four patients of coronary interventions (PTCA). One patient refused CABG or PTCA. Baseline antianginal medication consisted of 2.4 ± 0.8 drugs (10 nitrates, 8 molsidomine, 7 beta blocker, 4 calcium-channel antagonists). This drug therapy was not changed during the entire study.

Clinical and Scintigraphic Effects of Enhanced External Counterpulsation

Patients reported an average decrease in weekly anginal episodes from 6.4 ± 5.4 to 3.3 ± 4.2 ($p < 0.05$) and a decrease in weekly use of sublingual nitroglycerin from 5.5 ± 5.3 to 2.7 ± 3.9 puffs ($p < 0.05$) immediately after therapy (Table I). Symptom-limited exercise testing showed improved work capacity from 117.3 ± 34.4 to 137.8 ± 17.5 W ($p < 0.05$), corresponding to an increase in exercise time from 7.4 ± 2.8 to 9.0 ± 1.4 min. At the end of exercise, blood pressure was not different before and after EECP (178 ± 31 vs. 181 ± 29 mmHg); however, maximum heart rate was significantly higher during the second exercise testing (125 ± 18 vs. 137 ± 17 beats/min, $p < 0.05$). In five patients, ST-segment depression occurred during exercise. There was no significant change in maximal ST-segment depression before and after EECP (0.19 ± 0.10 vs. 0.15 ± 0.07 mV, NS).

In the nuclear perfusion study, global uptake increased by $4.2 \pm 7.5\%$ at rest and by $1.8 \pm 4.9\%$ during exercise (NS). The total number of segments with reversible perfusion defects during exercise decreased from 64 to 46 (NS).

Subjective Assessment of Therapy by Patients

Final subjective assessment of the therapy was obtained 1 year after finishing therapy. No patient died or was lost to fol-

low-up. Six patients (46%) were satisfied with the clinical improvement. Seven patients (54%) indicated that they would not undergo EECP therapy again. Three of the latter had no sufficient subjective improvement of anginal symptoms; the four others thought the symptomatic benefit did not justify the time needed for therapy.

Discussion

Enhanced external counterpulsation is increasingly used as an additional treatment option for otherwise not sufficient-

TABLE I Results of 35 h enhanced external counterpulsation therapy in 13 patients with stable angina

Parameter	Before EECP	After EECP
Weekly anginal episodes	6.4 ± 5.4	3.3 ± 4.2^a
Weekly use of on-demand NTG (puffs)	5.5 ± 5.3	2.7 ± 3.9^a
Maximal work capacity (in W)	117.3 ± 34.4	137.8 ± 17.5^a
ST-depression during exercise (mV, 5 patients)	0.19 ± 0.10	0.15 ± 0.07
Blood pressure, end of exercise (mmHg)	178 ± 31	181 ± 29
Heart frequency, end of exercise (beats/min)	125 ± 18	137 ± 17^a
Exercise thallium perfusion imaging		
Number of fixed perfusion defects	58	53
Number of reversible perfusion defects	64	46

^a $p < 0.05$.

Abbreviations: EECP = enhanced external counterpulsation, NTG = nitroglycerin.

ly treatable angina. It is postulated that the mechanism of action is the opening of myocardial collaterals by increased transmural pressure gradients.^{12,13} This concept is supported by animal studies showing increased capillary density after EECP¹⁴ and measurement of myocardial blood flow in patients.⁶ Furthermore, improved exercise tolerance after EECP seems to involve both peripheral and cardiac effects.¹⁵ Randomized and nonrandomized studies have confirmed the anti-ischemic potential of this therapy.^{1, 7, 9} In the present study, we evaluated EECP for its practicality under clinical routine conditions.

Included and Excluded Patients

Enhanced external counterpulsation is considered to be a well-tolerated, noninvasive therapy without major side effects. In several studies, we have treated a total of 176 patients and volunteers for clinical therapy or hemodynamic studies for a period of 1,232 h and observed only smaller side effects such as skin abrasion (n = 2), hematoma of the legs (n = 2), severe pain in the legs (n = 2), or reproducibly premature atrial beats during EECP (n = 1).¹⁶

However, EECP has a considerable number of generally accepted exclusion criteria. In the present study, 32 of an initial cohort of 48 or two-thirds of eligible patients were excluded. The most frequent exclusion criteria were severe peripheral artery disease, low ejection fraction, and anticoagulation. Peripheral artery disease causes less effective EECP, and EECP may also further reduce the perfusion of the legs by increasing blood return to the body. Cai *et al.* demonstrated that EECP causes reduced blood flow in the lower extremities when cuff inflation was sustained for longer than 50 to 60% of the cardiac cycle.¹⁷ Patients with low ejection fraction were formerly considered to be at risk for pulmonary congestion because of the increased venous return during EECP.¹⁸ Meanwhile, data of the International EECP registry at the University of Pittsburgh demonstrated that EECP can safely be carried out in patients with low ejection fraction; however, the rate of dropouts and the rate of development of manifest heart failure during therapy was higher in these patients.¹⁹ On the other hand, there are data suggesting that EECP may improve left ventricular function in patients with heart failure.²⁰

Furthermore, EECP may cause minor muscle damage. We have demonstrated that 1 h of EECP doubles the serum levels of creatine kinase and myoglobin measured 4 h after therapy.¹⁶ Thus, therapeutic anticoagulation may be associated with a higher risk of hematoma caused by EECP. Atrial fibrillation and pacemakers with double-chamber stimulation cause problems in triggering diastolic augmentation. Also, the changing power of diastolic augmentation during the irregular rhythm of atrial fibrillation is uncomfortable for the patients. Since external (as well as intra-aortic) counterpulsation leads to intermittent widening of the abdominal aorta,^{21,22} aortic aneurysm is regarded a contraindication.

We excluded two patients with insufficient diastolic augmentation of < 0.8 of peak systolic pressure area. Zheng *et al.*¹ compared the degree of diastolic augmentation in three stud-

ies reporting clinical success by external counterpulsation with three studies that found no benefit from external counterpulsation. The most important difference between these studies was the degree of diastolic augmentation. Supporting this finding, a recent study by Michaels *et al.*²³ compared the degree of reduction of angina with the degree of diastolic augmentation assessed by finger plethysmography in 1,004 patients enrolled in the International EECP Patient Registry at the University of Pittsburgh. There was a trend toward greater reduction of angina in patients with a diastolic to systolic pressure area of < 1.5. Some of the former contraindications may prove unwarranted with increasing experience with this procedure. Nevertheless, the exclusion of two-thirds of consecutively screened patients in our study indicates that the routine applicability of EECP is limited.²⁴

Clinical Results

Patients in our study reported a reduction of anginal attacks by 48%, and the usage of on-demand nitrates was reduced by 51%. In the MUST-EECP trial, anginal symptoms were reduced by 28% and the usage of nitrates by 60%. Similar to all other studies, we found an increase in maximal work capacity by EECP therapy. Table II shows the changes in exercise capacity after EECP from all published studies. The increase of exercise duration ranged between 10 and 25% in the different studies.

Lawson *et al.* investigated whether the increase in work capacity is cardiac in origin or a peripheral training effect. They compared the increase in exercise duration after EECP with changes in myocardial perfusion assessed by radionuclide imaging. Responders to EECP showed increased work capacity with unchanged maximal product of heart rate and blood pressure after EECP therapy. Nonresponders showed no significant improvement of maximal work capacity; however, the double product was significantly decreased after therapy, indicating lower peripheral resistance. Hence, improved exer-

TABLE II Summary of published increases in exercise tolerance in patients with coronary artery disease after enhanced external counterpulsation

Study (exercise test)	Increase of exercise duration in s (%)
Lawson <i>et al.</i> 1992 (treadmill)	488 ± 43 vs. 583 ± 46 (19.4)
Karim <i>et al.</i> 1995 (treadmill)	413 ± 13 vs. 482 ± 25 (16.7)
Lawson <i>et al.</i> 1996 (treadmill)	430 ± 32 vs. 530 ± 30 (23.2)
MUST-EECP (verum group)	
1999 (treadmill)	426 ± 20 vs. 470 ± 20 (10.3)
MUST-EECP (sham group)	
1999 (treadmill)	432 ± 22 vs. 464 ± 22 (7.4)
Brown <i>et al.</i> 2000 (treadmill)	404 ± 140 vs. 488 ± 147 (20.7)
Urano <i>et al.</i> 2001 (bicycle)	334 ± 90 vs. 416 ± 101 (24.6)
Present study (bicycle)	443 ± 165 vs. 541 ± 84 (22.1)

Abbreviation: MUST-EECP = Multicenter Study of Enhanced External Counterpulsation.

cise tolerance after EECP seems to involve both a peripheral and a cardiac effect.¹⁵ Similarly, a recent investigation showed that the maximal product of heart rate and blood pressure for the same peak work load was significantly lower in patients after therapy.²⁵

Similar to other studies, we found improvement in myocardial perfusion by ^{99m}Tc-MIBI-SPECT after therapy. The absolute number of segments indicating myocardial ischemia decreased from 64 to 46 (−28%); however, this finding failed to reach statistical significance. In a similar study, a significant decrease of reversible perfusion defects from 54 to 32 (−41%, $p < 0.01$) was found in a group of 12 patients using a 13-segment model for the thallium scans.⁹ Another study even reported complete resolution of ischemic defects by thallium scan in 12 of 18 patients and a reduction of ischemia in 2 of 18 patients.⁴ Masuda *et al.*, using positron emission tomography, found a significant increase of myocardial blood flow from 0.71 to 0.87 ml/min/g at rest and from 1.39 to 1.73 ml/min/g after dipyridamole in myocardial segments supplied by a stenotic artery in 12 patients before and after EECP.⁶ The lack of statistical significance in the perfusion improvement in our study may be due to less severe baseline ischemia in our patients, in line with their mild to moderate anginal symptoms.

All patients assessed the therapy subjectively after 1 year. Half of the patients were satisfied with the therapy after this period. Furthermore, 1 year follow-up of the patients involved in the placebo-controlled MUST-EECP trial showed a significant difference in health-related quality of life assessment between the treatment and sham groups.²⁶ However, approximately one-third of our patients estimated that the detriment of the loss of time exceeded the benefits of EECP. Furthermore, 12% of the initially included patients could not accommodate the time expense for EECP therapy into their professional lives. These data show that the 4- to 7-week duration of standard EECP therapy substantially limits the applicability of this procedure.

Conclusions

Confirming previous reports, our study showed reduction in anginal symptoms, decrease in nitroglycerin use, and improvement in work capacity after a 35-h course of EECP therapy. Using established inclusion and exclusion criteria, however, we found that the fraction of patients actually eligible for this therapy is surprisingly small and is further diminished by practicality issues such as time consumption.

References

1. Zheng ZS, Li T, Kambic H, Chen G, Yu L, Cai S, Zhan C, Chen Y, Wo S, Chen G, Ma H, Chen P, Huang B, Nose Y: Sequential external counterpulsation (SECP) in China. *Trans Am Soc Artif Intern Organs* 1983;29:599–603
2. Soroff HS, Hui J, Ciron F: Current status of external counterpulsation. *Crit Care Clin* 1986;2:277–295
3. Xu Y, Hu D, Zheng ZS: External counterpulsation. *Chin Med J* 1990;103:768–771

4. Lawson WE, Hui JCK, Soroff HS, Zheng ZS, Kayden DS, Sasvary D, Atkins H, Cohn PF: Efficacy of enhanced external counterpulsation in the treatment of angina pectoris. *Am J Cardiol* 1992;70:859–862
5. Arora RR, Chou TM, Jain D, Fleishman B, Crawford L, McKiernan T, Nesto RW: The multicenter study of enhanced external counterpulsation (MUST-EECP): Effect of EECP on exercise induced myocardial ischemia and anginal episodes. *J Am Coll Cardiol* 1999;33:1833–1840
6. Masuda D, Nohara R, Hirai T, Kataoka K, Chen LG, Hosokawa R, Inubushi M, Tadamura E, Fujitani M, Sasayama S: Enhanced external counterpulsation improved myocardial perfusion and coronary flow reserve in patients with chronic stable angina. *Eur Heart J* 2001;22:1451–1458
7. Karim S, Sani A, Karo-Karo S, Kasim M, Basha A, Gunadhi I, Japaries W, Suwita R: Enhanced external counterpulsation in the treatment and rehabilitation of coronary patients in Indonesia. *Asian Cardiovasc Thorac Ann* 1995;3:26–28
8. Brown AS, Dodd D, Hevey D, Horgan JH: Enhanced external counterpulsation reduces angina frequency and improves exercise tolerance in patients with refractory angina (abstr). *Heart* 2000;83(suppl.1):4
9. Urano H, Ikeda H, Ueno T, Matsumoto T, Murohara T, Imaizumi T: Enhanced external counterpulsation improves exercise induced tolerance, reduces exercise-induced myocardial ischemia and improves left ventricular diastolic filling in patients with coronary artery disease. *J Am Coll Cardiol* 2001;37:93–99
10. Werner D, Hui JCK, Kropp J, Daniel WG: Pneumatische externe Gegenpulsation—Therapieoption bei Angina pectoris. *Z Kardiol* 1998;87(suppl. II):193–198
11. Suresh K, Simandl S, Lawson WE, Hui JCK, Lillis O, Burger L, Guo T, Cohn PF: Maximizing the hemodynamic benefit of enhanced external counterpulsation. *Clin Cardiol* 1998;21:649–653
12. Cohn PF: EECP—new data on possible mechanisms of action. *Eur Heart J* 2001;22:1363–1364
13. Conti CR: Alternative therapies for patients with persistent chronic stable angina. *Clin Cardiol* 1999;22:773–774
14. Huang W, Chen YC, Zheng ZS, Zhong WF, Lawson WE, Hui JCK: External counterpulsation increases capillary density during experimental myocardial infarction (abstr). *Eur Heart J* 1999;20(suppl. 1):168
15. Lawson WE, Hui JCK, Zheng ZS, Burger L, Jiang L, Lillis O, Oster Z, Soroff H, Cohn PF: Improved exercise tolerance following enhanced external counterpulsation: Cardiac or peripheral effect. *Cardiology* 1996;87:271–275
16. Werner D, Wonka F, Krinke HE, Klinghammer L, Daniel WG: Pneumatische externe Gegenpulsation—ein neues perfusionstechnisches Prinzip. *Biomed Tech* 1998;43(suppl. 1):344–345
17. Cai D, Wu R, Shao Y: Experimental study of the effect of external counterpulsation on blood circulation in the lower extremities. *Clin Invest Med* 2000;23:239–247
18. Taguchi I, Ogawa K, Oida A, Abe S, Kaneko N, Sakio H: Comparison of hemodynamic effects of enhanced external counterpulsation and intra-aortic balloon pumping in patients with acute myocardial infarction. *Am J Cardiol* 2000;86:1139–1141
19. Lawson WE, Kennard ED, Holubkov R, Kesley SF, Strobeck JE, Soran O, Feldbeck AM, IEPR investigators: Benefit and safety of enhanced external counterpulsation in treating coronary artery disease patients with a history of congestive heart failure. *Cardiology* 2001;96:78–84
20. Gorcsan J, Crawford L, Soran O, Wang H, Severyn D, de Lame PA, Schneider V: Improvement in left ventricular performance by enhanced external counterpulsation in patients with heart failure (abstr). *J Am Coll Cardiol* 2000;35:230
21. Stefanadis C, Dornellis J, Tsiamis E, Stratos C, Kallikazaros I, Toutouzas P: Aortic function in patients during intra-aortic balloon pumping determined by the pressure-diameter relation. *J Thorac Cardiovasc Surg* 1998;116:1052–1059
22. Werner D, Schneider M, Weise M, Nonnast-Daniel B, Daniel WG: Pneumatic external counterpulsation—a new non-invasive method to improve organ perfusion. *Am J Cardiol* 1999;84:950–952
23. Michaels AD, Kennard ED, Kelsey SE, Holubkov R, Soran O, Spence S, Chou TM: Does higher diastolic augmentation predict clinical benefit from enhanced external counterpulsation? Data from the International EECP Patient Registry (IEPR). *Clin Cardiol* 2001;24:453–456
24. Conti CR: EECP—Enhanced external counterpulsation. *J Am Coll Cardiol* 1999;33:1841–1842
25. Stys TP, Lawson WE, Hui JCK, Fleishman B, Manzo K, Strobeck JE, Tartaglia J, Ramasamy S, Suwita R, Zheng ZS, Liang H, Werner D: Effects of enhanced external counterpulsation on stress radionuclide coronary perfusion and exercise capacity in chronic stable angina pectoris. *Am J Cardiol* 2002;89:822–824
26. Arora RR, Chou TM, Jain D, Fleishman B, Crawford L, McKiernan T, Nesto R, Ferrans CE, Keller S: Effects of enhanced external counterpulsation on health-related quality of life continue 12 months after treatment: A substudy of the multicenter study of enhanced external counterpulsation. *J Invest Med* 2002;50:25–32