Clin. Cardiol. 30, 223–228 (2007)

Clinical Investigations

Portable Enhanced External Counterpulsation for Acute Coronary Syndrome and Cardiogenic Shock: A Pilot Study

JOSHUA COHEN, M.D.,* WILLIAM GROSSMAN, M.D.,* ANDREW D. MICHAELS, M.D., M.A.S.†
*Division of Cardiology, Department of Medicine, University of California at San Francisco Medical Center, San Francisco, California, USA; †Division of Cardiology, Department of Medicine, University of Utah, Salt Lake City, Utah, USA

Summary

Background: Enhanced external counterpulsation (EECP) currently is used as an outpatient therapy for patients with refractory chronic angina.

Hypothesis: We sought to determine the safety and feasibility of a portable EECP unit to treat patients with acute coronary syndrome and/or cardiogenic shock in the coronary care unit (CCU).

Methods: Ten patients with acute coronary syndrome and/or cardiogenic shock who were not considered candidates for invasive intra-aortic balloon counterpulsation (IABP) by the treating cardiologist were prospectively enrolled in this single-center study. Each patient received 2–4 one-hour EECP treatments performed at the bedside in the CCU. Anticoagulation or recent femoral access was not an exclusion criterion.

Results: The mean age was 58 ± 19 years (range 28–81), and half were women. Patients had either acute coronary syndrome alone (n = 4), cardiogenic shock alone (n = 3), or both (n = 3). The cardiac indications for study enrollment included: acute inferior wall ST-segment elevation myocardial infarction with cardiogenic shock (n = 2), non-ST-segment elevation myocardial infarction with postinfarction angina (n = 2) or heart failure (n = 1), unstable angina with refractory rest angina (n = 2), cardiogenic shock from ischemic cardiomyopathy with severe mitral regurgitation (n = 1), and cardiogenic shock from nonischemic cardiomyopathy (n = 2). No adverse events were recorded during or as a consequence of EECP therapy, including no bleeding complications, no heart failure exacerbations, and no skin breakdown. The portable EECP unit did not interfere with ongoing critical care nursing.

Conclusions: EECP is safe and feasible for acute bedside therapy of critically ill patients with acute coronary syndrome and/or cardiogenic shock who are not candidates for IABP.

Key words: coronary artery disease, heart failure, external counterpulsation, acute coronary syndrome, cardiogenic shock

Clin. Cardiol. 2007; 30: 223–228.

Introduction

In current clinical practice, enhanced external counterpulsation (EECP) is used for the outpatient treatment of refractory angina and heart failure. EECP has an antianginal effect in outpatients with exercise-induced myocardial ischemia.[1–5] EECP increases diastolic aortic pressure, thereby increasing coronary artery perfusion. Cuff deflation at the onset of systole decreases left ventricular afterload by systolic unloading.[6] These acute hemodynamic effects achieved with EECP are comparable to those with invasive intra-aortic balloon counterpulsation (IABP).[6]

While the use of IABP in acute coronary syndromes (ACS) and cardiogenic shock is well-established, there are situations when its application is limited due to

Address for reprints:

Andrew D. Michaels, M.D., M.A.S.
Division of Cardiology
University of Utah
Health Science Center
30 North 1900 East, Room 4A100
Salt Lake City
Utah 84132-2401
USA
e-mail: andrew.michaels@hsc.utah.edu

Received: October 9, 2006
Accepted with revision: November 30, 2006

Published online in Wiley InterScience
(www.interscience.wiley.com).
DOI:10.1002/clc.20074

the potential complications of lower extremity ischemia, bleeding, and infection.[7,8] For patients with IABP contraindications, EECP presents a potential noninvasive method for increasing coronary perfusion and ventricular unloading.

While early EECP devices using a hydraulic water compression system showed limited efficacy for cardiogenic shock[9–12] and acute myocardial infarction,[13] there have been no studies using the pneumatic EECP devices in these clinical situations. This pilot study sought to determine the safety and feasibility of a portable EECP device to treat acutely ill patients in the coronary care unit (CCU) with ACS and/or cardiogenic shock.

Methods

Patients

This single-center study enrolled adult CCU patients admitted with ACS (Braunwald class IIIB/C unstable angina,[14] non-ST-segment elevation myocardial infarction, or ST-segment elevation myocardial infarction) and/or cardiogenic shock who were not candidates for IABP by the treating cardiology team. Exclusion criteria included severe aortic insufficiency, supraventicular tachyarrhythmias, thrombophlebitis, active femoral site bleeding or hematoma, and uncontrolled hypertension (>180/100 mmHg). Recent femoral vascular access and decompensated heart failure if the patient was intubated were not exclusion criteria. Patients or the surrogate decision-maker gave written informed consent prior to EECP, and the protocol was approved by the Committee on Human Research.

Study Procedures

EECP treatment was performed in the CCU (TS3 portable prototype model, Vasomedical, Inc., Westbury, NY). Patients received 2–4 one-hour EECP treatments over 24 h. Three sets of disposable lower-extremity pneumatic cuffs were connected by air hoses to the portable compressor unit (Fig. 1) in the CCU bed. The EECP device sequentially inflated the cuffs timed with the patient's cardiac cycle measured by electrocardiography. At the onset of systole, compressed air is released to reduce systolic aortic pressure. Counterpulsation was performed at cuff inflation pressures ranging from 80 to 300 mmHg. Noninvasive finger plethysmography was used to monitor the arterial waveforms. If systemic arterial and pulmonary artery catheters were used clinically, hemodynamic data was recorded before, during, and after each EECP treatment. Urine output prior to and during EECP was assessed using a Foley catheter. Patients were asked to report the severity of chest pain and dyspnea on a 0–10 scale before and during each EECP treatment. The cuff inflation pressure was started at low pressure (80 mmHg) and increased gradually over the 1-h treatment course as tolerated. Monitoring of the femoral access sites for vascular injury was performed.

Statistical Analysis

Continuous variables are presented as means standard deviations. Paired t-tests were used to compare continuous variables prior to and 30-min after initiation of EECP. Two-tailed probability (p) values <0.05 were considered significant. Statistical computations were performed using Stata version 9.2 (Stata Corporation, College Station, TX).

Results

Baseline Characteristics

Ten patients were enrolled (Table 1). The mean age was 58 ± 19 years (range 28–81), and half were women. Patients had either ACS alone (n = 4), cardiogenic shock alone (n = 3), or both (n = 3). The cardiac indications for study enrollment included: acute inferior wall ST-segment elevation myocardial infarction with cardiogenic shock (n = 2), non-ST-segment elevation myocardial infarction with postinfarction angina (n = 2) or heart failure (n = 1), class IIIB unstable angina with refractory rest angina (n = 2), cardiogenic shock from ischemic cardiomyopathy with severe mitral regurgitation (n = 1), and cardiogenic shock from nonischemic cardiomyopathy (n = 2). Two subjects had severe mitral regurgitation. Two others were intubated prior to study enrollment, and were continued on mechanical ventilation during the study period.

The decision not to treat the patients with IABP was made at the treating physicians' discretion. Reasons for selecting patients included preference for a noninvasive approach (n = 6), severe iliac tortuosity (n = 1), abdominal aortic ulcer (n = 1), recent abdominal aortic surgery (n = 1), and concern for infection one day following biventricular pacemaker implantation (n = 1).

Seven patients had femoral arterial access within 48 h of EECP. Four patients had current femoral arterial and/or femoral venous sheaths in place during EECP treatment.

EECP Therapy

Patients received an average of 2.5 ± 0.7 h of EECP therapy (range 2–4 h; Table 2). Patients were treated with antiplatelet and antithrombin agents including unfractionated intravenous heparin (n = 7), glycoprotein IIB/IIIA receptor blockers (n = 5), aspirin (n = 8), and clopidogrel (n = 7; Table 2). Arterial pressure was measured invasively in four patients, and noninvasively in sixs patients. During treatment, there was a significant increase in mean arterial pressure measured 30-min after starting EECP compared to baseline ($p = 0.0002$;

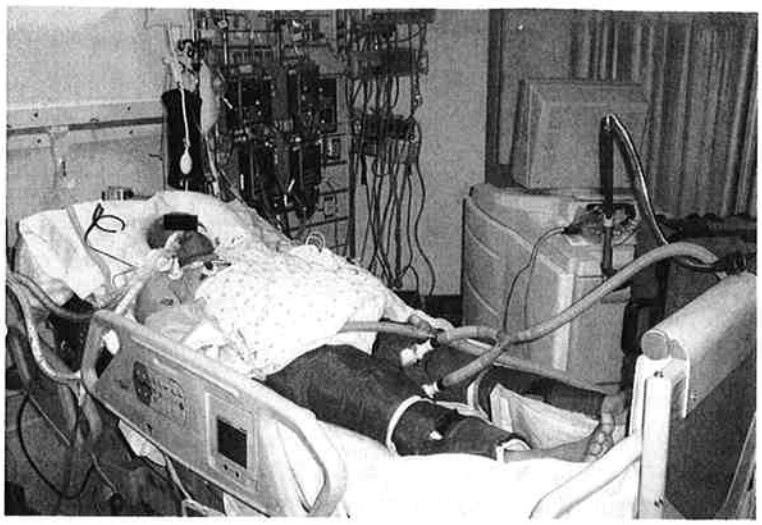

FIG. 1 Portable enhanced external counterpulsation on a critically ill patient in the coronary care unit. This patient remained in cardiogenic shock after successful right coronary artery stenting for acute inferior ST-segment elevation myocardial infarction. An intra-aortic balloon pump was not possible due to severe bilateral iliac artery tortuosity.

TABLE 1 Baseline demographics and clinical characteristics

Patient	Age (years)	Sex	ACS	Shock	Diabetes	HTN	CAD	PVD	Current smoker	Dyslipidemia	LVEF (%)	Mitral regurgitation
1	49	M	Y	N	Y	Y	Y	N	N	Y	74	Mild
2	45	M	Y	N	N	N	Y	N	N	Y	52	Trace
3	63	M	Y	Y	Y	Y	Y	N	Y	Y	40	Mild
4	81	F	Y	N	N	Y	Y	Y	N	Y	70	Moderate
5	76	M	Y	Y	Y	Y	Y	Y	N	Y	53	Trace
6	32	M	N	Y	Y	Y	N	N	N	N	21	Mild
7	74	F	Y	N	Y	Y	Y	N	N	Y	54	None
8	66	M	N	Y	N	N	Y	Y	N	Y	41	Severe
9	28	F	N	Y	N	N	Y	N	N	N	39	Severe
10	66	F	Y	N	N	Y	Y	N	N	Y	75	Trace

Abbreviations: ACS = acute coronary syndrome, HTN = hypertension; CAD = coronary artery disease, PVD = peripheral vascular disease, LVEF = left ventricular ejection fraction.

Table 3). There were no significant changes in heart rate, pulse oximetry, or urine output. While there was no significant change in chest pain severity, the severity of dyspnea improved during EECP ($p = 0.036$). No EECP-related adverse events were recorded during or as a consequence of EECP therapy, including no bleeding complications, no heart failure exacerbations, and no skin breakdown from the pneumatic cuffs. Potential concerns such as excessive noise from the air compressor units, moving the TS3 device into the CCU rooms, or interference with ongoing critical care nursing did not occur during this study.

EECP in Unstable Angina

Patient 4 was an 81-year-old woman hospitalized with Braunwald class IIIB unstable angina. Angiography showed occlusion of all native coronary arteries and all grafts from her two prior coronary bypass surgeries. She was not a candidate for further coronary revascularization, and was treated with intravenous antianginal agents with continued rest angina in the CCU. After two one-hour EECP treatments, the patient's angina appeared less frequent and less severe (from 8/10 down to 3/10). The patient was discharged with the plan to continue EECP as an outpatient.

EECP in Acute Myocardial Infarction

Patient 2 was a 45-year-old man who presented with an acute non-ST-elevation myocardial infarction. Urgent coronary angiography revealed critical stenoses of the left main, left anterior descending, and right coronary arteries with thrombolysis in myocardial infarction (TIMI) III flow. He was referred for coronary artery bypass grafting, but the timing of surgery was delayed due to the patient's clopidogrel exposure. He was admitted to the CCU where he developed recurrent

TABLE 2 EECP therapy

Patient	EECP duration (hrs)	Max EECP pressure (mmHg)	Femoral arterial access	Femoral venous access	Device closure	Asprin	Clopidogrel	GP IIB/IIIA inhibitor	Antithrombotic medications
1	3	280	Recent 6F	None	Angioseal	Y	Y	Y	UFH
2	2	280	Current 6F	Current 8F	None	Y	Y	Y	UFH
3	3	280	Recent 6F	Current 7F	Angioseal	Y	Y	Y	None
4	1	160	None	None	None	Y	Y	N	LMWH
5	2	160	Current 6F	Current 8F	None	Y	Y	Y	UFH
6	4	300	None	Current 7F	None	N	N	N	None
7	2	160	Recent 6F	None	Perclose	Y	Y	Y	None
8	2	160	Recent 8F	None	None	Y	N	N	UFH
9	2	300	Recent 8F	None	None	N	Y	N	UFH
10	2	280	None	None	None	Y	N	N	UFH

Abbreviations: GP IIB/IIIA = glycoprotein IIB/IIIA, UFH = unfractionated heparin, LMWH = low molecular weight heparin (enoxaparin).

TABLE 3 Hemodynamic and Clinical Effects during the first hour of EECP

	Mean arterial pressure (mmHg)		Heart Rate (bpm)		Pulse oximetry saturation (%)		Urine output (cc/hour)		Chest severity (0–10 scale)		Dyspnea severity (0–10 scale)	
Patient	Prior	During	Prior	During	Prior	During	Prior	During	Prior	During	Prior	During
1	99	112	55	56	98	98	50	50	4	3	0	0
2	80	88	66	79	97	98	40	40	1	1	0	0
3	68	74	107	108	95	94	35	35	0	0	4	2
4	99	104	67	67	99	99	60	60	5	5	0	0
5	71	77	69	70	99	99	30	25	Intub	Intub	Intub	Intub
6	49	60	110	110	97	97	20	100	Intub	Intub	Intub	Intub
7	80	90	88	88	95	95	35	35	0	0	5	4
8	71	77	94	92	93	95	20	20	0	0	6	3
9	68	68	89	87	95	96	25	25	0	0	7	3
10	92	97	57	57	94	94	50	50	0	0	2	1
Total	78 ± 16	85 ± 16*	80 ± 20	81 ± 19	96 ± 2	96 ± 2	36 ± 14	44 ± 23	1.3 ± 2.1	1.1 ± 1.9	3.0 ± 2.9	1.6 ± 1.6†

Abbreviations: Intub = intubated patient.
* denotes paired t-test p-value <0.001 compared to baseline.
† denotes paired t-test p-value <0.05 compared to baseline.

angina. His angina improved after treatment with EECP therapy.

Patient 5 was a 76-year-old man with history of three-vessel coronary artery disease and diabetes who underwent EECP in the CCU 16 h after right coronary artery stenting for acute inferior ST-segment elevation myocardial infarction (Fig. 1). The patient remained in cardiogenic shock from extensive right ventricular infarction, and was hypotensive despite dopamine and dobutamine. The patient did not receive an IABP due to severe bilateral iliac artery tortuosity. He was discharged from the hospital on day 6, and did well at 8-month follow-up.

EECP in Cardiogenic Shock

Patient 6 was a 32-year-old man with nonischemic cardiomyopathy with a left ventricular ejection fraction of 21%. One day prior to enrollment, he underwent biventricular pacemaker defibrillator implantation. Shortly thereafter, he was intubated for pulmonary edema. He remained hypotensive with poor urine output despite treatment with intravenous furosemide, dopamine, dobutamine, and norepinephrine. He started EECP 16 h after intubation, and subsequently his urine output increased from 20 cc/h to 100 cc/h, beginning 30-min after initiation of EECP. He was extubated 3 days later, but died two weeks later from a respiratory arrest. Patient 8 had low urine output (20 cc/h) prior to EECP. This patient had cardiogenic shock from an ischemic cardiomyopathy and severe mitral regurgitation. This subject had no improvement in urine output during EECP.

Patient 9 was a 28-year-old woman on intravenous milrinone and furosemide awaiting heart transplantation for dilated cardiomyopathy. She tolerated EECP well

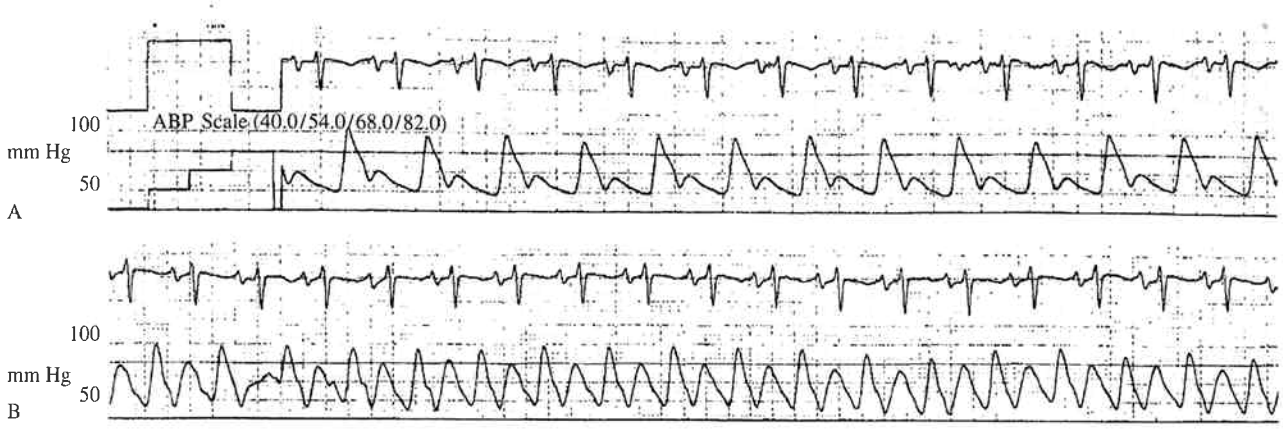

FIG. 2 Radial arterial tracing from patient 9 at baseline (a) and during enhanced external counterpulsation at a cuff inflation pressure of 300 mmHg (b). The patient is a 28-year-old woman on intravenous milrinone and furosemide who was awaiting heart transplantation for dilated cardiomyopathy.

with improvement in her hemodynamics (Fig. 2). She underwent orthotopic heart transplantation and was doing well at 9-month follow-up. Both patients with severe mitral regurgitation reported an improvement in their rest dyspnea during EECP.

Discussion

In current practice, EECP is limited to the outpatient management of refractory angina and heart failure. EECP systems are essentially fixed in place and cannot routinely be transported. This pilot study demonstrated the safety and feasibility of a portable prototype EECP system to provide bedside treatment to critically ill CCU patients. Observations suggested that acute inpatient EECP therapy may improve cardiovascular performance and possibly clinical outcomes in patients with ACS and/or cardiogenic shock.

Research regarding the hemodynamic and clinical effects of external counterpulsation began in the 1960s using hydraulic-driven, water-filled compression chambers. Soroff first applied external counterpulsation in man.[9,10] Among 20 patients with cardiogenic shock treated with external counterpulsation, the mortality rate of 65% was reported to be lower than historical rates for IABP.[11]

External counterpulsation prevented the hypotension caused by nitroprusside vasodilator therapy, providing left ventricular systolic unloading pharmacologically while maintaining coronary perfusion by external counterpulsation.[15] In a multicenter study, 258 acute myocardial infarction patients were randomized to external counterpulsation within 24 h of presentation or usual care.[13] External counterpulsation patients had a trend toward lower hospital mortality rate (8.4%) compared with controls (14.7%; $p = 0.12$). Counterpulsation patients had lower rates of recurrent angina, heart failure, and ventricular fibrillation.

There were limitations of early external counterpulsation devices.[9–13,15] The leg compression bags were not sufficiently powerful to provide effective systolic unloading. Studies of cardiac metabolism showed that IABP decreased myocardial oxygen consumption, while external counterpulsation increased consumption. In studies measuring coronary sinus blood flow during atrial pacing, early external counterpulsation devices had no acute beneficial metabolic or hemodynamic effects.[16,17]

The modern pneumatic cuff EECP system augments intracoronary pressure and flow.[6] Improving coronary perfusion pressure in addition to left ventricular systolic unloading makes EECP a potentially useful hemodynamic assist device. A recent trial showed that EECP was superior to medical therapy alone in stable outpatients with left ventricular systolic dysfunction, resulting in improved exercise tolerance, heart failure class, and quality of life.[18] In two of our patients with severe mitral regurgitation, patient-reported severity of dyspnea improved during EECP. In this pilot study, we observed no harmful effect from increased venous return in patients with heart failure.

This study is limited by its small size and single-center design. As a safety and feasibility study, it was not designed to evaluate the efficacy of portable EECP compared to other treatments. We could not report changes in aortic and diastolic arterial pressure because six of the ten subjects had noninvasive measures of systemic pressure. The subjective measures of chest pain and dyspnea severity were aimed at assessing safety.

In conclusion, portable EECP is a safe and feasible treatment for critically ill patients suffering from acute coronary syndrome and/or cardiogenic shock who are not candidates for IABP therapy. The acute hemodynamic effects of increased coronary perfusion and left ventricular systolic unloading with EECP are favorable for these patient groups, suggesting that acute EECP may result in improved clinical outcomes in those with acute coronary syndrome and/or cardiogenic shock.

References

1. Arora RR, Chou TM, Jain D, Fleishman B, Crawford L, et al.: 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
2. Arora RR, Chou TM, Jain D, Fleishman B, Crawford L, et al.: 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 Investig Med* 2002;50:25–32
3. Lawson WE, Hui JCK, Soroff HS, Zheng ZS, Kayden DS, et al.: Efficacy of enhanced external counterpulsation in the treatment of angina pectoris. *Am J Cardiol* 1992;70:859–862
4. Lawson WE, Hui JCK, Zheng ZS: Three-year sustained benefit from enhanced external counterpulsation in chronic angina pectoris. *Am J Cardiol* 1995;75:840–841
5. Stys TP, Lawson WE, Hui JC, Fleishman B, Manzo K, et al.: 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
6. Michaels AD, Accad M, Ports TA, Grossman W: Left ventricular systolic unloading and augmentation of intracoronary pressure and Doppler flow during enhanced external counterpulsation (EECP). *Circulation* 2002;106:1237–1242
7. Meco M, Gramegna G, Yassini A, Bellisario A, Mazzaro E, et al.: Mortality and morbidity from intra-aortic balloon pumps. Risk analysis. *J Cardiovasc Surg* 2002;43:17–23
8. Sirbu H, Busch T, Aleksic I, Friedrich M, Dalichau H: Ischaemic complications with intra-aortic balloon counter-pulsation: incidence and management. *Cardiovasc Surg* 2000;8:66–71
9. Soroff HS, Birtwell WC, Giron F, Collins JA, Deterling RA Jr: Support of systemic circulation and left ventricular assist by synchronous pulsation of extramural pressure. *Surg Forum* 1965;16:148–150
10. Giron F, Birtwell WC, Soroff HS, Ruiz U, Collins JA, et al.: Assisted circulation by synchronous pulsation of extramural pressure. *Surgery* 1966;60:894–901
11. Cohen LS, Mullins CB, Mitchell JH: Sequenced external counterpulsation and intraaortic balloon pumping in cardiogenic shock. *Am J Cardiol* 1973;32:656–661
12. Mueller H: Are intra-aortic balloon pumping and external counterpulsation effective in the treatment of cardiogenic shock? *Cardiovasc Clin* 1977;8:87–102
13. Amsterdam EA, Banas J, Criley JM, Loeb HS, Mueller H, et al.: Clinical assessment of external pressure circulatory assistance in acute myocardial infarction: report of a cooperative clinical trial. *Am J Cardiol* 1980;45:349–356
14. Gersh BJ, Braunwald E, Rutherford JD: Chronic coronary artery disease. In *Heart Disease: A Textbook of Cardiovascular Medicine* (6th ed.) (Eds. Braunwald E, Zipes DP, Libby P). Philadelphia, PA: Saunders, 2001
15. Parmley WW, Chatterjee K, Charuzi Y, Swan HJ: Hemodynamic effects of noninvasive systolic unloading (nitroprusside) and diastolic augmentation (external counterpulsation) in patients with acute myocardial infarction. *Am J Cardiol* 1974;33:819–825
16. Solignac A, Ferguson RJ, Bourassa MG: External counterpulsation: coronary hemodynamics and use in treatment of patients with stable angina pectoris. *Cathet Cardiovasc Diagn* 1977;3:37–45
17. Kern MJ, Henry RH, Lembo N, Park RC, Lujan MS, et al.: Effects of pulsed external augmentation of diastolic pressure on coronary and systemic hemodynamics in patients with coronary artery disease. *Am Heart J* 1985;110:727–735
18. Feldman AM, Silver MA, Francis GS, Abbottsmith CW, Fleishman BL, et al.: PEECH Investigators: Enhanced external counterpulsation improves exercise tolerance in patients with chronic heart failure. *J Am Coll Cardiol* 2006;48:1198–1205

Volume 30
5 '07

Clinical Cardiology®

An International Indexed and Peer-Reviewed Journal for Advances in the Treatment of Cardiovascular Disease

Cardiology in China

Coronary Ectasia

Parasites and Myocardial Disease

EECP for ACS

AMI, PCI Stent and QT Dispersion

Prognosis, Effort Tolerance and Cardiac Rehabilitation

ACS, Diabetes and In-Hospital Mortality

Biomarkers in Ischemic and Dilated Cardiomyopathies

(see inside for complete Table of Contents)

May 2007