Acute and Chronic Hemodynamic Effects of Enhanced External Counterpulsation in Patients With Angina Pectoris

Rohit Romesh Arora, Michael Louis Carlucci, Andrea Michele Malone, and Nicole Vanessa Baron

ABSTRACT

Background: **Enhanced external counterpulsation (EECP) is an effective noninvasive treatment for patients with angina pectoris. However, the hemodynamic effects of EECP are still unknown and have been theorized to simulate the clinical use of the intra-aortic balloon pump, enhancing cardiac output, stroke volume, and retrograde aortic diastolic flow.**

Methods: **Twelve hemodynamic parameters were measured, using the BioZ System (CardioDynamics International Corporation, San Diego, Calif) after 1 hour (n=22) and after 35 hours (n=16) of EECP treatment compared with baseline. The BioZ System noninvasively measures hemodynamic parameters using the thoracic electrical bioimpedance method.**

Results: **One hour of EECP treatment revealed a significant decrease in cardiac output, stroke volume, contractility, afterload, preload, and myocardial energy production, but systolic time ratios and thoracic fluid content were unchanged. However, after 35 hours of therapy, stroke volume ($P \leq 0.05$), index of contractility ($P \leq 0.05$), and thoracic fluid content ($P \leq 0.01$) were decreased.**

Conclusions: **The acute reduction in contractility, preload, and concurrent bradycardia may have favorable hemodynamic effects for patients with angina pectoris. Further studies are needed to elucidate the mechanism of EECP therapy and its efficacy for patients with angina pectoris. (J Investig Med 2001;49:500–504) Key Words: enhanced external counterpulsation • hemodynamic effects**

INTRODUCTION

Counterpulsation, a form of cardiac assistance, has been extensively reviewed in the last half of the twentieth century. Initial counterpulsation studies involved insertion of a cannula in the femoral artery that is connected to an extracorpeal pump. Timed by ECG signals, this pump drew blood from the coronary circulation during systole and returned that same amount of blood during diastole.[1] Counterpulsation decreased left ventricular work and oxygen consumption and increased collateral flow to ischemic areas of the heart.[2–5]

Preceding studies focused on the immediate hemodynamic effects of enhanced external counterpulsation (EECP) (before vs during treatment).[6,7] However, the effects of EECP therapy on patients' various hemodynamic parameters require further investigation. This study was conducted to examine the hemodynamic effects of EECP both before and after 1 hour of therapy and before and after 35 hours of EECP therapy using the thoracic electrical bioimpedance (TEB) method.

MATERIALS AND METHODS

Subjects

Thirty-one patients diagnosed with chronic stable angina with a Canadian Cardiovascular Society angina level of II, III, or IV were considered for enrollment. Twenty-two men (n=20) and women (n=2) with an average age of 68.4±9.1 years were included in the study of hemodynamic parameters before and after 1 hour of EECP treatment. Sixteen men (n=14) and women (n=2) with an average age of 69.2±8.7 years composed the subject population to examine the hemodynamic effects of EECP after thirty-five hours of treatment. The long-term arm of the study used six fewer subjects because of subject inability to complete the 7 weeks of treatment, primarily as a result of scheduling conflicts.

From the Division of Cardiology, Department of Medicine, University of Medicine and Dentistry of New Jersey, Newark (R.R.A., M.L.C., A.M.M.), and New York Presbyterian Hospital, New York, NY (N.V.B.).

Address correspondence to: Rohit R. Arora, MD, 185 South Orange Avenue, MSB, I-536, Newark, NJ 07103-2714. E-mail aroraso@umdnj.edu

All patients went through an initial evaluation to indicate candidacy for the EECP procedure. Patients were eligible if they had evidence of coronary artery disease by one of the three criteria: 1) one or more angiographically proved sternosis >70% in at least one major artery, 2) history of myocardial infarction documented by characteristic creatine kinase elevation, and/or 3) development of Q waves on the electrocardiogram or positive nuclear stress test for myocardial infarction or ischemia.

This study was approved by the institutional review boards at our institution. Enrollment was conditional upon subjects giving written informed consent.

Measurement of Hemodynamic Parameters

Thoracic electrical impedance. The BioZ System™ (CardioDynamics, International Corporation, Calif) uses the noninvasive TEB method to determine the mechanical activity of the heart. Recent studies have favorably compared TEB with more invasive procedures (ie, catheterization) as an effective means of determining cardiac output and other hemodynamic factors.[8–10] TEB is based on the principal that blood is the most electrically conductive substance in the body. As blood travels through the thorax, volume changes result in a change in the electrical conductivity of the thorax. TEB measures the change in electrical conductivity with every heartbeat. By measuring the thoracic conductivity and impedance, the BioZ System calculates a number of hemodynamic parameters.

Procedure. BioZ measurements were taken immediately before and immediately after EECP treatment. Patients were in the supine position, and movement was kept to a minimum to reduce artifacts. Four dual sensors were placed on each side of the neck and thorax. The color-coded dual electrodes were attached bilaterally to the root of the neck and to the thorax (xiphoid process at midaxillary line). As long as adequate ECG and impedance signals were present, monitoring began after the first 16 heartbeats and every 16 beats thereafter.

Hemodynamic parameters. The BioZ System passes a low-magnitude, high-frequency current though the thorax to assess conductivity and impedance of thoracic blood flow.[10] In the study, the BioZ system was used to measure/calculate the hemodynamic parameters listed in the Appendix.

EECP Procedure

EECP uses compressed air to inflate and deflate a series of cuffs wrapped around the patient's calves, lower thighs, and upper thighs. Pressure is applied sequentially from the patient's lower legs, lower thighs, and upper thighs and is synchronized with the cardiac cycle. Immediately after the aortic valve closes, at the onset of diastole, the cuffs sequentially inflate. This increase in blood flow is referred to as diastolic augmentation. At the onset of systole, the cuffs simultaneously deflate, allowing the compressed vessels to reconform, reducing vascular impedance. The pressure that can be applied to the cuffs can range from 0 to 300 mm Hg. In this study, the pressure applied ranged from 250 to 300 mm Hg. The effectiveness of EECP is measured by the ratios of peak systolic to peak diastolic pressures, and the ratio of area under the systolic waveform to the area under the diastolic waveform during counterpulsation. These ratios are calculated from the signals measured by finger plethysmography.

Statistical Analyses

Using a paired two-tailed t test, all hemodynamic parameters were observed before and after the EECP procedure with a 0.05 level of significance. Hemodynamic parameters were presented within one standard deviation from mean values.

RESULTS

Interestingly, 1 hour of EECP treatment revealed a significant decrease in cardiac output, stroke volume, contractility, afterload, preload, and myocardial energy production, but thoracic fluid content underwent no significant change. Also unexpectedly, after 35 hours of therapy, stroke volume ($P \leq 0.05$), index of contractility ($P \leq 0.05$), thoracic fluid content ($P \leq 0.01$), and thoracic fluid index (TFI) ($P \leq 0.05$) were decreased. These findings call into question the validity of the comparison between EECP and the intra-aortic balloon pump (IABP), given that the well-studied hemodynamic changes associated with the clinical application of IABP do not mimic the acute results reported in this study for EECP.

Note that the results reported are measurements taken immediately before and immediately after the first and thirty-fifth hour of EECP therapy. It is therefore useful to think of the hemodynamic differences between the first and the thirty-fifth treatments as chronic changes. Conversely, the two post-EECP hemodynamics values (immediately after the first and thirty-fifth sessions) provide a means for making acute comparisons with the hemodynamic results obtained immediately before the hourly EECP treatments. Both the acute and chronic hemodynamic changes are inconsistent with the currently accepted mechanism of EECP (ie, that it simulates the clinical application of IABP). The results of this study suggest the need for further review of the hemodynamic effects of EECP.

CONCLUSIONS

EECP has evolved as a specific noninvasive form of counterpulsation therapy for the treatment of angina pectoris. Previous studies indicate sustained benefits of EECP, such as a decrease in the frequency and intensity of angina episodes as well as an increase in exercise duration.[6] It has been assumed that these benefits result from effective diastolic augmentation and systolic unloading.[6–8] It is believed that the increase in diastolic flow may promote the formation or recruitment of collateral vessels responsible for enhancing coronary perfusion. The deflation of the cuffs during systole has been assumed to decrease cardiac workload, wall stress, and myocardial oxygen consumption.[8]

Our findings are not consistent with the above assumptions. For example, this study demonstrates that the long-term benefits of EECP treatment may not include an overall increase in cardiac output and stroke volume. Although previous studies indicate that during treatment these hemodynamic parameters are increased, the present study reveals that such effects are not prolonged after treatment. The acute results, therefore, do not simulate the clinical application of the IABP.

One recent study has compared the hemodynamic effects of IABP with those of EECP.[11] That limited study, in which only 1 hour of EECP therapy was provided to the subjects, revealed similar hemodynamic effects for the two treatment modalities. Specifically, vascular resistance decreased for both, and cardiac index underwent no significant change. The present findings differ from these results. As noted in Table 1, cardiac index decreased post-EECP. A major difference between the current study and the comparative one is the duration of EECP therapy. EECP, being noninvasive, is a less efficient means of achieving physiological changes than its invasive counterparts. This is why therapy is performed over the course of 7 weeks. One hour of EECP treatment is not enough to provide a therapeutic benefit.

As indicated in Results, the TFI was significantly increased. TFI is a measure of the mean electrical impedance of the thoracic cavity. It can be assumed from these data that EECP affects the level of electrical impedance, which may contribute to the end values of the other hemodynamic parameters, measured before treatment. Because impedance is another term for electrical resistance, TFI is analogous to the more conventional hemodynamic parameter systemic vascular resistance. An increased TFI is therefore a sign of increased electrical resistance.

The acute reduction in contractility and preload and the concurrent bradycardia may have favorable hemodynamic effects in patients with angina pectoris. Reduction in the heart rate before and after 1 hour of treatment suggests EECP may be responsible for decreasing the demand of blood by the heart. Reduction in contractility reveals that

Table 1. Hemodynamic parameters before and after 1 hour of EECP treatment (n=22).

	Pre-EECP	±SD	Post-EECP	±SD	*P*
Heart rate	65.2	11.2	61.8	10.1	≤0.05
Acceleration index	1.2	0.5	1.0	0.5	≤0.05
End diastolic index	96.1	23.5	91.7	25.6	≤0.05
Left stroke index	72.7	27.7	64.2	25.3	≤0.05
Stroke volume	115.4	46.5	103.6	48	≤0.05
Systemic vascular resistance index	141.6	62.5	167.9	80	≤0.05
Systemic vascular resistance (afterload)	72.8	31.6	86.8	42.5	≤0.05
Stroke systemic vascular resistance index	141.5	62.2	168.2	79.5	≤0.05
Cardiac index	3.7	1.4	3.03	1.2	≤0.05
Cardiac output	7.0	2.7	5.9	2.5	≤0.05
Stroke index	58.9	23.1	52.5	23.3	≤0.05
Systolic time ratios	0.4	0.06	0.4	0.05	NS
Index of contractility	0.2	0.7	0.2	0.6	NS
Thoracic fluid index	26.3	6.8	25.2	5.7	NS
Thoracic fluid content	0.04	0.01	0.06	0.10	NS

Abbreviation: NS, not significant.

the normalized peak aortic flow decreased after 1 hour of treatment, therefore reducing the myocardial oxygen consumption.

The limitations of the present study include that the hemodynamic changes measured were not on line, that is continuously during the procedure. There were additional limitations of the BioZ system. Known conditions that limit the accuracy of the data are septic shock, aortic valve regurgitation, acute myocardial infarction, severe hypertension (mean arterial pressure >130 mm Hg), tachycardia of rates >180 beats per minute, patient's height less than 47 in (102 cm) or greater than 91 in (230 cm), patient's weight less than 66 lb (30 kg) or greater than 342 lb (155 kg), and patient movement. Specific to the present study, hypertension and patient movement may have contributed to inaccurate measurements (Table 2).

Although EECP has been found to be a clinically useful tool, its mechanism of action remains largely unknown. Collateral recruitment, nitric oxide release, and neoangiogenesis are other possible factors contributing to the clinical efficacy of EECP. Recent studies have investigated these phenomena, although not, as yet, in relation to EECP.[12,13] Some of the hemodynamic effects of EECP, including reduction in contractility and preload and concurrent bradycardia may have favorable effects on patients with angina pectoris. However, our results do not simulate the hemodynamics of IABP, suggesting that other mechanisms may be in play to explain the clinical benefits. Larger invasive hemodynamic studies may be necessary to pinpoint the exact hemodynamic changes associated with EECP therapy.[14]

APPENDIX: GLOSSARY OF TERMS

Acceleration Index (ACI) [sec^{-2}]—The measure of peak acceleration of aortic blood flow. The peak acceleration takes place approximately 15 to 30 ms after the opening of the aortic valve. ACI is a measure of the true inotropic state of the heart.

Afterload—Represents the forces that the ventricle must overcome to deliver blood into the systemic vasculature during contraction. The primary component of afterload is vasoactivity measured by systemic vascular resistance (SVR) [mm Hg $\times$ min $\times$ L^{-1}]. An indexed value of SVR was also calculated by dividing SVR by body surface area (BSA) to calculate the systemic vascular resistance index (SVRI) [mm Hg $\times$ minute $\times$ $L^{-1} \times m^2$]. A second measure of afterload is stroke systemic vascular resistance index (SSRI) [mm Hg $\times$ $mL^{-1} \times m^2$].

Base Impedance—The mean electrical impedance of the thoracic cavity, reported as the thoracic fluid index (TFI) [Ohm].

Cardiac Output (CO) [L $\times$ min^{-1}]—The volume of blood delivered by the heart into the vasculature in 1 min (CO = stroke volume $\times$ heart rate). The value of Cardiac Output indexed by the BSA is referred to as cardiac index (CI) [L $\times$ $min^{-1} \times m^{-2}$].

Table 2. Hemodynamic parameters before and after 35 hours of treatment (n=16).

	Pre-EECP	±SD	Post-EECP	±SD	*P*
Heart rate	66.1	12.9	65.5	14.6	NS
Acceleration index	1.2	·0.5	1.1	0.4	NS
End diastolic index	92.6	25.3	86.3	23.8	NS
Left stroke index	67.7	27.6	59.1	18.6	NS
Stroke volume	107.7	45.5	93.8	32.6	≤0.05
Systemic vascular resistance index	153.7	72.7	166.5	58.0	NS
Systemic vascular resistance (afterload)	79.7	36.8	86.9	32.9	NS
Stroke systemic vascular resistance Index	153.6	72.5	166.6	58.2	NS
Cardiac index	3.5	1.5	3.1	1.3	NS
Cardiac output	6.9	3.0	6.1	2.6	NS
Stroke index	55.6	22.9	51.5	19.1	NS
Systolic time ratios	0.4	0.06	0.39	0.06	NS
Index of contractility	0.05	0.02	0.04	0.02	≤0.05
Thoracic fluid index	25.6	7.3	28.0	7.8	≤0.05
Thoracic fluid content	0.04	0.01	0.04	0.01	≤0.05

End Diastolic Volume (EDV)—The volume of blood in the ventricle at the end of diastole. The EDV is presented as the End Diastolic Index (EDI) [mL × m^{-2}], which is a measure of EDV/BSA.

Heart Rate (HR) [beats × min^{-1}]—The number of beats performed in the heart in 1 minute.

Index of Contractility (IC) [sec^{-1}]—A measurement of the normalized peak aortic flow. IC is a preload/volume-dependent measure of contractility.

Left Cardiac Work Index [kg × m × m^{-2}]—A value of the measure of work that the left ventricle must expend to pump blood indexed by the BSA. This value parallels the myocardial oxygen consumption.

Left Stroke Work Index [g × m × m^{-2}]—Related to myocardial energy production during every heartbeat and/or myocardial oxygen consumption per beat.

Preload—The end effect of the forces of the returning blood during diastole, which stretch the myocardial fibers. Preload is measured through the value of end diastolic index (EDI).

Stroke Volume (SV) [mL]—The volume of blood delivered by the heart to the vasculature in one heart beat.

Thoracic Fluid Content (TFC) [Ohm^{-1}]—The total conductivity of the thorax, representing parallel conductivity contributions of three compartments: intravascular, intra-alveolar, and interstitial.

REFERENCES

1. Jacobey JJ, Taylor WJ, Smith GT, Gorlin R, Harken DE. A new therapeutic approach to acute coronary occlusion. Am J Cardiol 1963; 11:218. Abstract.

2. Rosenweig J, Chatterjee S. Mechanical augmentation of coronary circulation in the ischemic heart: Angiographic and hemodynamic correlation with prolonged survival. J Thorac Cardiovasc Surg 1967;54: 839–847.

3. Hahnloser PB, Gallo E, Schenk WG. The hemodynamics of counterpulsation. J Thorac Cariovasc Surg 1966;51;366–378.

4. Schenk WC, Gallo E, Hahnloser PB. Current status of counterpulsation in cardiac assistance. A summary of experimental experience in the dog. Can Med Assoc J 1966;95;664–665.

5. Rosenweig J, Chatterjee S. Treatment of acute myocardial perfusion by counterpulsation: Experimental rationale and clinical experience. J Thorac Cardiovasc Surg 1970;59;243–250.

6. Arora RR, Chou TN, 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.

7. Krishnamurthy S, Simandl S, Lawson WE, Hui J, Lillis O, Burger L, Guo T, Cohn PF. Maximizing the hemodynamic benefit of enhanced external counterpulsation. Clin Cardiol 1998;21:649–653.

8. Soran O, Crawford LE, Schneider VM, Feldman AM. Enhanced external counterpulsation in the management of patients with cardiovascular disease. Clin Cardiol 1999;22:173–178.

9. Raisinghani A, Diaco NV, Sageman SW, Spiess BD, Williams BR, Bellot P, Ohmori K, DeMaria AN. The cost study: A multi-center trial comparing measurement of cardiac output by thoracic electrical bioimpedance with thermodilution. Presented at the American College of Cardiology 47th Annual Scientific Sessions, April 1, 1998, Atlanta, GA.

10. Deleted in proof.

11. 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.

12. Mason IJ. The ins and outs of fibroblast growth factors. Cell 1994;78:547–552.

13. Deleted in proof.

14. Belardinelli R, Ciampini N, Costantini C, Blandini A, Purcaro A. Comparison of impedance cardiography with thermodilution and direct Fick methods for noninvasive measurement of stroke volume and cardiac output during incremental exercise in patients with ischemic cardiomyopathy. Am J Cardiol 1996;77:1293–1301.