Historical Review of the Development of Enhanced External Counterpulsation Technology and its Physiologic Rationale

This review traces the evolution of external counterpulsation from its beginning to the early 1990s. The term counterpulsation derives from the dual hemodynamic goals of this treatment: to reduce the afterload of the left ventricle and to augment diastolic pressure. The studies summarized in this review demonstrate clinical benefits in the treatment of angina, acute myocardial infarction, and cardiogenic shock. It has been demonstrated that an external counterpulsation treatment system is highly effective when a series of 3 pneumatic cuffs is wrapped securely around the lower extremities and buttocks, inflating in a distal to proximal sequence, and deflating simultaneously timed to cardiac systole. Sequential inflation augments diastolic perfusion pressure; simultaneous deflation decreases peripheral vascular resistance, significantly decreasing cardiac workload. This method of counterpulsation, EECP, effectively increases myocardial oxygen supply by increasing coronary blood flow and diminishing myocardial oxygen requirements.

Harry S. Soroff, MD; John C.K. Hui, PhD; Fabio Giron, MD
From the Department of Surgery, SUNY at Stony Brook, Stony Brook, NY

Address for correspondence/reprint requests: Harry S. Soroff, MD, University Hospital at Stony Brook, Stony Brook, NY 11794

Initial Research

The creation of mechanical methods to assist the circulation in heart failure was inspired by the technology which was developing simultaneously for use in cardiac surgery. In 1953, Kantrowitz and Kantrowitz[1] showed that coronary blood flow in animals could be increased by 20%–40% if coronary arteries were perfused at an elevated pressure during diastole. In 1955, Newman et al[2] and Dennis et al[7] assisted the circulation of a patient with a failing heart by adopting the equipment and physiologic approach used in cardiac surgery in which venous blood is withdrawn into an oxygenator and returned to arterial circulation using a pump (veno-arterial bypass). However, this form of assisted circulation proved not to be effective in reducing myocardial oxygen consumption.

In 1958, Sarnoff et al[3] showed that duration of pressure or tension generated by the left ventricle is a major determinant of its oxygen consumption (Tension-Time Index). These findings were extended by Levine and Wegman's[4] study of the energetics of the human heart in 1962.

Initially, counterpulsation was carried out by cannulating the femoral artery. Soroff and his colleagues[5] showed that counterpulsation produced a significant reduction in left ventricular oxygen consumption as a result of reducing systolic pressure and increased coronary blood flow by increasing diastolic pressure.

In 1964, Birtwell et al,[6] Dennis et al,[7] and Giron et al[8] demonstrated that similar changes (i.e., reduced myocardial oxygen consumption and increased diastolic perfusion pressure) could be produced by applying external pressure to the arterial

ABBREVIATIONS AND ACRONYMS

EECP	Enhanced external counterpulsation
IABP	Intraaortic balloon pumping

system. Of equal importance was the profound effect that external counterpulsation had on venous return to the heart when the venous bed was compressed. Venous blood was pumped from the lower extremities to the heart, the valves in the venous system maintaining the position of the column of blood between cardiac cycles. These early findings led to the many studies in which the experimental and clinical effects of external counterpulsation were evaluated.[9-11] Reported results varied with the conditions of the experiments.

Initial External Counterpulsation Devices

The apparatus used in the early clinical studies performed by Soroff and Birtwell[12] consisted of two tapered, rigid cylinders that enclosed the legs from ankles to thighs. Between the legs and the cylinders were water-filled bladders that completely filled the intervening space. During cardiac systole, active suction was applied to the lower extremities in order to lower systolic pressure. During cardiac diastole, water was pumped synchronously into the bladders to compress the lower extremities. Because the inner bladders were distensible and the outer housing was rigid, the pressure generated within the water-filled chamber was directed against the vascular beds of the lower extremities, resulting in increased diastolic pressure and increased venous return to the heart.

In 1964, Osborn et al[13,14] were successful in producing counterpulsation using the trousers of an aviator's G-suit. However, the pressure on the lower abdomen and genitalia proved to be quite uncomfortable. When only the legs of the trousers were used, a higher external pressure was necessary to produce a significant change.

Sequential External Counterpulsation

In the late 1960s, members of the staff of the Artificial Devices Section of the National Institutes of Health proposed that the results of external counterpulsation could be improved if blood were expressed from the arterial and venous beds of the upper and lower extremities in a sequential manner. It was argued that sequenced pulsation, which produces a "milking" effect on the arterial and venous beds, would return more blood to the heart when pulsatile pressures were applied to the lower extremities with a distal to proximal sequence.

Lueptow et al[15] published elegant studies of patterns of flow that occur in circulatory models when subjected to pulsatile pressures. They attempted to simulate the heart and arterial and venous systems by creating a model made of tubes filled with an aqueous solution of glycerin. Their experiments compared flow patterns obtained when external pressure was applied in four different ways to the "legs" of the model during cardiac diastole.

In their view,[15] compression from distal (calves) to proximal (thighs to buttocks) was more effective than uniform compression to the entire lower extremities. These fluid dynamic studies also showed that, when the system is depressurized only to atmospheric pressure, the significant diastolic augmentation is obtained at the expense of a small increase in systolic afterload.

Cohen et al[16] studied sequential external counterpulsation and compared it with the effects of IABP in experimental animals before and after the induction of cardiogenic shock. The sequential external pressure device increased cardiac output by an average of 25%, compared with 4% for IABP. This effect presumably was due to the increase in venous return caused by the effect of external pressure on the venous vasculature.

A later study of sequenced external pressure by Langou and Cohen[17] suggested that, in normal baboons and in baboons with induced cardiogenic shock, not only was cardiac output significantly increased, but also the ratio of diastolic pressure to systolic pressure was increased. Cohen et al[16] also compared sequenced and nonsequenced counterpulsation. With their device, they found that, although diastolic augmentation was equivalent in the two states, cardiac output rose by 17% when the pressure was sequenced and did not rise significantly when the pressure was applied uniformly. In seven normal human subjects, the actual diastolic pressure increases were modest and cardiac output rose by 12%.[17]

Zheng et al[18], at the Division of Assisted Circulation and the Departments of Medicine, Physiology and Anatomy of the Zhongshan Medical College of China, published their results of several studies on the effects of sequential external counterpulsation using cuffs around the upper and lower extremities and around the buttocks. They compared hemodynamic effects in the following three modes of external pressurization in 16 normal volunteers and in 16 selected patients with coronary heart disease: nonsequenced leg counterpulsation, nonsequenced four-limb counterpulsation, and sequenced four-limb

counterpulsation with and without upper thigh cuffs, which exert pressure on the vascular bed of the buttocks. Although the nonsequenced leg counterpulsation was shown to be effective in raising diastolic pressure, the sequenced four-limb counterpulsation was apparently more effective, and produced diastolic augmentation 46% higher than that obtained with nonsequenced external counterpulsation. Sequenced four-limb counterpulsation alone and with upper thigh cuffs greatly increased the ratio of diastolic pressure to systolic pressure. The addition of upper thigh cuffs increased diastolic augmentation by 44% and resulted in a reduced systolic pressure.

These studies strongly suggest that the effect on diastolic pressure depends on the size of the vascular bed that is activated; in other words, pressurization of four limbs plus buttocks produced greater diastolic augmentation than pressurization of the lower extremities alone. Inclusion of the upper thigh with its large muscle mass and large vascular bed is critical to achieving effective counterpulsation.

External Counterpulsation in Acute Myocardial Infarction

Three studies of patients with uncomplicated myocardial infarction were published between 1980 and 1983 each showing a strongly suggestive or significant reduction in mortality in the groups of patients treated with external counterpulsation in the first hours after onset of infarct. The study by Triulzi et al[19] was carried out in three parts. External counterpulsation was applied to two groups of 10 patients each within the first 10 hours after onset of symptoms of an anterior myocardial infarction. External counterpulsation was applied either for 1 or 2 hours. An attempt was made to map the ischemic area by precordial ST segment mapping. During the period of external counterpulsation, there was a reduction in size of the ischemic area that was not observed either during the control period or 2 hours after stopping external counterpulsation.

In the third part of this study, investigators evaluated 131 patients with acute myocardial infarction who were not in shock. Although incidences of life threatening arrhythmias and of persistent heart failure were lower in the treated group (72 patients) than in the control group (59 patients), differences were not statistically significant.

The second study was undertaken in 25 institutions by cardiologists who evaluated the efficacy of external counterpulsation in the treatment of acute myocardial infarction.[11] All patients were randomized, had mild ventricular failure, and all received circulatory assist within 24 hours after onset of symptoms. The control group of 116 patients and the treatment group of 142 patients were virtually the same with regard to all characteristics. Although mortality in the entire group of 142 treated patients was lower, it was not significantly lower. External counterpulsation for 3 and 4 hours also was associated with a significant lessening of morbidity as manifested by recurrent chest pain, progression of heart failure, occurrence of ventricular fibrillation, change in heart size, and clinical cardiac function at discharge. This study appears to support the findings of Triulzi et al[19]: that the beneficial effect of external counterpulsation is transitory unless applied, as in the above study, for 3 or more hours.

In the third study, Zheng et al[18] reported that, when sequential external counterpulsation was applied to 52 patients with acute myocardial infarction, chest pain and shock, symptoms were quickly relieved during the first 1–2 hours of external counterpulsation. These authors correlated beneficial effects of external counterpulsation with the degree to which diastolic pressure was augmented.

External Counterpulsation in Cardiogenic Shock

Soroff et al[10] treated 20 patients in cardiogenic shock with external counterpulsation. Response to external counterpulsation was good to excellent in 16 patients, fair in 3, and poor in 1 patient. Sequential analysis of the survivor data allowed the authors to reason that if the survival rate in a group of cardiogenic shock patients using standard therapy is only 15%, then an improved survival rate of 45% using external counterpulsation is statistically significant ($p<0.01$).

External Counterpulsation in Treatment of Angina

Banas et al[21] and Clap et al[20] working with Soroff and Giron, studied 21 patients with angina, who had frequent and incapacitating pain. Repeat coronary angiography was performed in 11 patients,

4–8 weeks after external counterpulsation. There was a definite increase in vascularity in 5, equivocal changes were noted in 4, and no change was visible in 2. Four of the 17 patients, who improved, experienced a recurrence of their symptoms, which were again improved with repeat external counterpulsation.

This group then studied 18 patients by subjecting them to a sham period of external counterpulsation for 2 hours daily for 5 days, followed by active external counterpulsation for 2 hours daily for 5 days.[20] No improvement in symptoms or exercise tolerance occurred after sham pumping. Eleven of the 18 patients showed significant improvements after effective pumping. The patients who improved had at least one vessel open on coronary angiography. It was postulated that pressure produced by external counterpulsation is transmitted to the coronary vascular bed around an area of obstruction through another coronary vessel which is open.

Solignac et al[22] studied 10 patients with angina pectoris prior to and during external counterpulsation, and during right atrial pacing before and after 4 consecutive 2 hour sessions of external counterpulsation. These authors did not find that external counterpulsation was helpful. This was also the experience of Loeb et al[23] with respect to treatment of patients with anginal symptoms, but they did note a modest improvement in exercise tolerance.

Willerson et al[24] studied a very heterogenous group of 13 patients, 10 men and 3 women ranging in age from 39–62 years, 8 of whom had angina and 5 of whom had acute coronary insufficiency. Three of the latter group of 5 patients experienced acute coronary insufficiency 4–8 days after a documented inferior myocardial infarction. Five patients underwent cardiac catheterization, revealing significant triple vessel disease in 4 patients and single vessel disease in 1 patient. They concluded that external counterpulsation for short periods did not help these patients. No mention was made of the effect on symptomatology associated with ischemic heart disease. In view of earlier studies by Banas et al[20] suggesting that there must be at least one vessel open to influence coronary blood flow or development of collateral channels, it would not be expected that these patients would benefit from short periods of counterpulsation.

Zheng et al[18] evaluated the effect of prolonged periods of EECP in 200 angina patients. The patients were treated 1 hour daily for 12 days. In 97% of the 200 cases, sequential external counterpulsation provided long term symptomatic relief, compared with a 72% incidence of relief in a medically treated control group of 40 patients. Sixty-three percent of the patients showed improvements in their electrocardiograms, compared with 40% in the control group. Relapse of symptoms occurred "minimally" in the group treated with external counterpulsation, in contrast to 20–40 cases in the control group after drug therapy was discontinued. Exercise tolerance also was measured in a group of 15 stable angina patients. Sham sequential external counterpulsation produced no improvement, compared with improved exercise tolerance in 15 patients receiving sequential external counterpulsation.

Use of external counterpulsation is an extremely attractive treatment because it is noninvasive. The hypothesis is that counterpulsation increases pressure in the coronary vascular bed during diastole, promoting development of collateral channels. It is, however, extremely difficult to evaluate the efficacy of treatment for angina, even with controlled or randomized studies. This difficulty is due to factors such as the variability of the symptoms of angina and the difficulty in many patients in correlating anatomic abnormalities seen on angiography with symptoms. The studies reviewed here in which external counterpulsation was studied in patients with angina demonstrated different degrees of improvement in either symptoms or exercise tolerance.

In summary, external counterpulsation, since its inception in 1962, has been shown to be effective in the treatment of various manifestations of ischemic heart disease. Additional studies will no doubt elucidate the mechanism of its action, its effect on the central nervous system, and the indications for the use of EECP in other forms of vascular insufficiency.

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