Clin. Cardiol. Suppl. II, Vol. 25, II-3–II-5 (2002)

A Historical Overview of Enhanced External Counterpulsation

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Summary: Angina remains a significant health problem in the United States and the world. Although there are a variety of pharmacologic and interventional therapies to treat angina, many patients are not adequately helped by these treatments. Enhanced external counterpulsation (EECP) is an effective, noninvasive technique designed to decrease the frequency and duration of anginal episodes, as well as increase exercise duration in patients with acute angina. Since the early 1960s, the technology of EECP has been thoroughly refined. In addition, a number of important clinical trials have provided evidence for its effectiveness. Continuing research is needed to determine the best patients for EECP and its appropriate clinical application.

Key words: angina pectoris, coronary artery disease, enhanced external counterpulsation, exercise duration, time-to-ST-segment depression

Introduction

Despite interventional techniques and drugs, angina pectoris remains a major medical problem in society. The prevalence is 213 cases for every 100,000 persons over the age of 30.[1] According to Framingham Heart Study guidelines, 350,000 new cases are diagnosed every year.[2]

Even when patients undergo conventional or interventional therapies, many continue to have angina. The Bypass Angioplasty Revascularization Investigation (BARI) trial demonstrated significant clinical and functional status impairment 5 years after bypass surgery and angioplasty in patients with multivessel coronary disease.[3] Following coronary revascularization, 30% of patients were unable to return to work due to their angina. Among the subjects in the trial, 15 to 20% rated their health as fair to poor following revascularization.

There are a variety of treatment options for symptomatic coronary artery disease. Pharmacologic options include beta blockers, calcium blockers, and long-acting nitrates. Interventional techniques are percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG). Some patients may not be candidates for some of these options, while other patients may have tried them all and still have angina. It is these patients for whom new therapeutic options are needed. One of these new options is a class of drugs known as FOX inhibitors. These are antianginal drugs designed to alter metabolic pathways within the myocardium. Another developed treatment is transmyocardial revascularization with laser. However, one of the most exciting, noninvasive approaches is enhanced external counterpulsation (EECP).

Early Research on Enhanced External Counterpulsation

The whole concept of counterpulsation can be traced back to the late 1960s with the work of W. C. Birtwell. This work involved inserting catheters into the femoral arteries of animals and withdrawing blood during systole. This blood was then reinjected during diastole in an attempt to reduce arterial wall stress and to facilitate diastolic coronary flow. While the procedure was very effective from a physiologic point of view, it was not feasible from a practical standpoint due to the enormous hemolysis and other attendant problems.

Ultimately, this research led to intra-aortic balloon counterpulsation, based on the same concept. Afterload reduction by rapid deflation of a balloon in the aorta during systole was combined with diastolic augmentation by reinflation of the balloon in diastole. This was found to enhance both hemodynamics and, in particular, myocardial energetics and oxygen demand in coronary blood flow.

Although this refinement in the procedure was very effective, an intra-aortic balloon represented an invasive and some-

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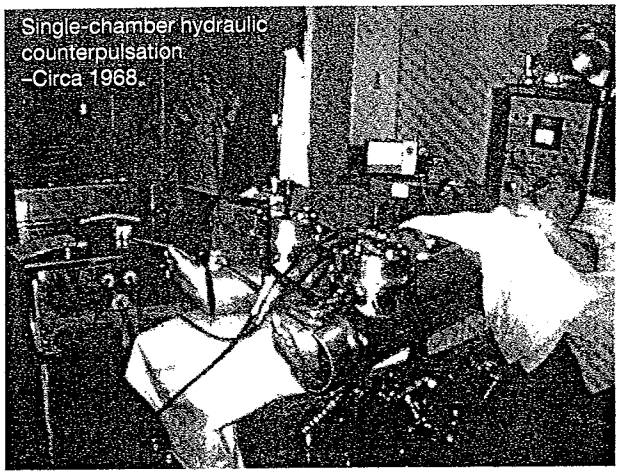
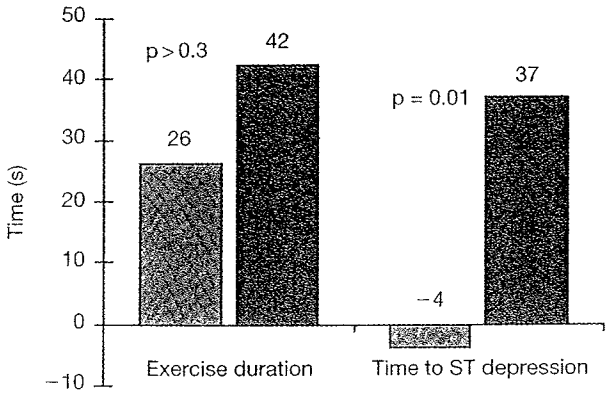


FIG. 1 An early enhanced external counterpulsation pressure apparatus used on a patient in 1968. Reprinted with permission from C. Richard Conti, M.D.

what complex procedure. Researchers gravitated to the last step along the pathway, namely external counterpulsation. By exerting external pressure on the legs and buttocks in diastole, then rapidly removing it in systole, one could essentially duplicate the physical effects. By 1968, a pressure apparatus was developed and used on patients (Fig. 1).

During the late 1960s, there was continuous progress and refinement of the equipment needed to do EECP. In the early 1970s, EECP was found to be beneficial for patients with cardiogenic shock, stable angina, and acute myocardial infarction. Despite these emerging benefits, EECP technology did not receive significant widespread attention during this time. Considerable interest was generated in China, however, particularly in terms of its favorable cost effectiveness.



*Adjusted mean of change from baseline

FIG. 2 Results from the MUST-EECP multicenter study showing exercise duration and time to ST-segment depression for the active counterpulsation (CP) group and the inactive (sham) CP group. ▨ = Sham, ▩ = active. Adapted from Ref. No. 4 with permission.

The MUST-EECP Study

The pivotal turn of events in EECP came in 1999 with the publication of the Multicenter Study (MUST)-EECP trial.[4] This randomized trial looked at the effect of EECP on exercise-induced myocardial ischemia and anginal episodes. Subjects were given 35 h of either active or inactive counterpulsation (CP) over a 4- to 7-week period. Exercise duration increased in both groups, although the difference was not statistically significant (Fig. 2). Time to ST-segment depression, however, increased significantly from baseline in the active CP group (Fig. 2). These subjects also experienced a decrease in anginal episodes compared with the inactive CP group (Fig. 3).

Despite the impressive results of the MUST-EECP trial, controversy and doubt remained. Most of this uncertainty centered on the role placebo played in the study, as well as on the training component. Since this trial, additional studies have been published that have added to the body of evidence. One of these, published in 2001, used thallium scintigraphy before and after EECP.[5] All exercise parameters improved after EECP therapy. Positron emission tomography scans also demonstrated a decrease in the prevalence of exercise-induced reversible perfusion defects, as well as an improvement in left ventricular diastolic filling.

Conclusion

Today, EECP technology has been refined to a significant extent. It has progressed from early, rapidly inflating, water-filled balloons around the lower torso to separate air-filled bladders that sequentially inflate from the calves all the way up to the pelvis. There is an increasing body of evidence to support its use in patients with angina. A variety of clinical issues continue to be discussed and debated. What are the possible mechanisms behind EECP? How should patients be selected for EECP? How can counterpulsation be optimized? Where does EECP stand in relation to other therapies for angina? Is

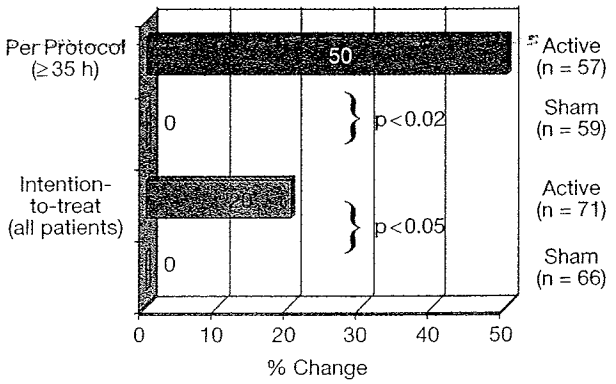


FIG. 3 Daily episodes of angina in the MUST-EECP multicenter study based on per protocol and intent-to-treat (ITT) analysis. Sham = inactive. Adapted from Ref. No. 4 with permission.

there a role for EECP in the treatment of congestive heart failure? What are the results of recent clinical trials? Many of these questions are expected to be answered from ongoing and future studies.

Discussion

Participant: Have any of you thought about combined counterpulsation with internal and external counterpulsation in patients with cardiogenic shock? What would the mechanism of improvement be, and is there any synergistic improvement?

DeMaria: Yes, actually I have been trying to persuade Dr. Hui to look at it as an orphan technique because you should be able to maintain close to a normal or adequate pressure to perfuse the head, the heart, and the kidneys. You are increasing the venous return, and you could sequentially use the intra-aortic balloon pump. It should have a dramatic effect. Also, there is some question of use in septic shock as well, where you have got tremendous vasodilation. There was some talk of working with one of the balloon pump companies at one point.

Participant: If you have a patient who fails an initial course of EECP therapy, would you offer them a second course of therapy? If a patient has a benefit, and 8 months or a year later they have recurrent symptoms, would you offer them a second course of EECP therapy? In patients who live a distance away, we have sometimes done 2-hour courses. Do you think this is acceptable?

DeMaria: I would say yes to all three of your questions. Your questions are very relevant, and we all experience this. We have done a few persons 6 months later; I don't know if we have done them beyond that.

References

1. Elveback LR, Connolly DC, Melton LJ III: Coronary heart disease in residents of Rochester, Minnesota. VII. Incidence, 1950 through 1982. *Mayo Clin Proc* 1986;61:896–900
2. Kannel WB, Feinleib M: Natural history of angina pectoris in the Framingham study. Prognosis and survival. *Am J Cardiol* 1972;29: 154–163
3. Writing Group for the Bypass Angioplasty Revascularization Investigation (BARI) Investigators: Five-year clinical and functional outcome comparing bypass surgery and angioplasty in patients with multivessel coronary disease. A multicenter randomized trial. *J Am Med Assoc* 1997;277:715–721
4. 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
5. Urano H, Ikeda H, Ueno T, Matsumoto T, Murohara T, Imaizumi T: Enhanced external counterpulsation improves exercise 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