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Prior Revascularization Increases the Effectiveness of Enhanced External Counterpulsation

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Summary

Background and hypothesis: Enhanced external counterpulsation (EECP) is an effective noninvasive treatment for chronic angina. However, its usefulness has been felt to be limited in patients with angiographically demonstrated triple-vessel coronary artery disease (CAD), in accord with the hypothesis that a patent vessel is necessary for transmission of the EECP-augmented coronary artery pressure and volume to the distal coronary vasculature.

Methods: The effect of revascularization [coronary artery bypass grafting (CABG)] prior to EECP was examined in 60 patients with CAD and chronic angina (35 without and 25 with prior CABG). Patients were grouped by the extent of CAD (single-, double-, triple-vessel disease in the unrevascularized group) and by the extent of residual disease (number of stenotic native vessels unbypassed or supplied by a stenotic graft in the CABG group). Significant CAD or graft stenoses were defined as stenoses demonstrating ≥ 70% luminal diameter narrowing. Benefit was assessed by improvement in post-EECP treatment over pretreatment radionuclide stress testing.

Results: Radionuclide stress testing demonstrated a comparable favorable response (80 vs. 71%; p = NS) in patients with prior CABG versus unrevascularized patients. Enhanced external counterpulsation was highly and comparably effective in patients with unrevascularized native single- and double-vessel CAD and in patients with CABG with residual single-and double-vessel CAD (88 vs. 80%; p = NS). Most notably, CABG significantly increased the beneficial response to EECP in those patients with triple-vessel CAD and stenotic grafts compared with unrevascularized patients with triple-vessel CAD (80 vs. 22%; $p < 0.05$ by chi-square test).

Conclusion: The results suggest a new role for EECP as an effective treatment for post CABG ischemia, despite extensive CAD and even in the presence of stenotic grafts.

Key words: external counterpulsation, coronary artery disease, revascularization, coronary artery bypass grafting

Introduction

Enhanced external counterpulsation (EECP) is an effective noninvasive treatment for chronic angina. By increasing venous return, producing diastolic augmentation and systolic unloading, it may increase cardiac output and coronary blood flow. Treatment with EECP has been shown to decrease anginal symptoms and to improve both exercise tolerance and exercise-induced myocardial perfusion defects in the majority of patients.[1,2] The improvement in exertional ischemia by radionuclide stress testing has been shown to be maintained in a majority of patients over a 3-year follow-up period. At 5-year follow-up, the revascularization and event rates of EECP-treated patients are comparable with those observed in patients treated with angioplasty and surgical revascularization.[3,4] The improvement in exercise myocardial perfusion appears to be most reliably predicted by the presence of an open artery as documented by pretreatment coronary angiography.[5]

Prior surgical revascularization [coronary artery bypass grafting (CABG)] would be expected to enhance the effectiveness of EECP by providing additional conduits as per the "patent conduit" hypothesis. The present study was undertaken to confirm this postulate and to examine whether the response rate of patients with CABG can be predicted similarly to that of unrevascularized patients based on the presence of one or more patent conduits (i.e., does graft stenosis have an impact similar to that of native coronary artery stenosis on the response rate to EECP?).

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Materials and Methods

All patients receiving EECP and meeting the entry criteria during the reported period were enrolled in sequence and included in the analysis. Eligibility criteria included stable, functionally limiting angina in patients with angiographic evidence of coronary artery disease (CAD) (≥ 70% stenosis) and a baseline maximal treadmill radionuclide stress test demonstrating a reversible perfusion defect or defects treated with a course of EECP. The patients received EECP for 1 to 2 h daily for a total of 35 h of treatment. Within 1 week after the last EECP treatment, each patient repeated a treadmill radionuclide stress test performed to the same workload as baseline. The coronary angiograms were reviewed by two trained angiographers prior to patient entry. The radionuclide stress tests were evaluated and interpreted by two physicians trained in nuclear cardiology. The interpreting physicians were blinded to the patient's identity, clinical status, or order of the studies. The radionuclide studies were evaluated in a semiquantitative fashion with the results agreed upon between the two interpreting physicians. A decrease in the radionuclide stress defect was defined as an improvement in the radionuclide perfusion image over baseline.

The patients were separated into two groups for analysis. One group had undergone prior surgical revascularization (CABG), the other had not. The unbypassed patients were further separated into groups with single-, double-, and triple-vessel CAD based on the presence of one or more major epicardial vessels with a stenosis ≥ 70%. Patients post CABG were similarly grouped (single-, double-, and triple-vessel CAD) by the extent of residual disease [number of unbypassed major epicardial vessel(s) or major stenotic vessel(s) supplied by a graft with a ≥ 70% stenosis]. The radionuclide stress test results for each patient were masked and graded as showing improvement in perfusion or not. The data were analyzed using the chi-square test, with significance at a level of $p < 0.05$.

Exclusion criteria were similar to those used in previous studies of EECP, including uncontrolled congestive heart failure; myocardial infarction within the preceding 3 months, or unstable angina; aortic valve insufficiency; severe peripheral vascular disease (arterial or thrombophlebitis); severe systemic hypertension (blood pressure > 180/110 mmHg); significant arrhythmia interfering with EECP timing (atrial fibrillation, frequent ectopy, pacemaker); and significant bleeding diathesis.

Results

Sixty patients (56 men and 4 women) with a mean age of 61 ± 8 years (range 45–74) were entered into this study. Cardiac angiography in the 35 unrevascularized patients demonstrated that 13 patients had native single-vessel CAD, another 13 had double-vessel CAD, and 9 had triple-vessel CAD. In the group of 25 patients with CABG, 7 had residual single-vessel disease, 5 had residual double-vessel disease, and 8 had residual triple-vessel disease. Reported frequency of anginal episodes decreased in all patients and most patients reported an improvement in angina-limited exercise tolerance. The post-EECP radionuclide stress test results for both groups are shown in Table I. Enhanced external counterpulsation was highly and comparably effective in 23 of 26 patients with unrevascularized native single- and double-vessel CAD and in 12 of 15 patients post CABG with residual single- and double-vessel CAD (88 vs. 80%; p = NS). Most notably, CABG significantly increased the beneficial response to EECP in those patients with triple-vessel CAD and stenotic grafts compared with unrevascularized patients with triple-vessel CAD (80 vs. 22%; $p < 0.05$ by chi-square test). The overall efficacy of EECP in patients with and without prior CABG is graphically illustrated in Figure 1. The effect of coronary disease extent on EECP response in patients with CAD and CABG is delineated in Figure 2.

TABLE I Percentage of unrevascularized and previously revascularized patients demonstrating improvement on post-enhanced external counterpulsation (EECP) radionuclide stress testing (by coronary artery disease extent in the unrevascularized patients and by residual coronary artery disease in the revascularized patients)

Unrevascularized (n = 35)		*Revascularized (n = 25)*	
CAD extent	Improved RN stress	Residual CAD	Improved RN stress
1- & 2-vessel (n = 26)	23/26 (88%)	1- & 2-vessel (n = 15)	12/15 (80%)
3-vessel (n = 9)	2/9 (22%)[a]	3-vessel (n = 10)	8/10 (80%)[a]
All (n = 35)	25/26 (71%)	All (n = 25)	20/25 (80%)

[a] Percentage of patients with triple-vessel CAD and stenotic grafts responding to EECP is significantly greater than that of patients with unrevascularized triple-vessel CAD ($p < 0.05$ by chi-square test).
Abbreviations: CAD = coronary artery disease, RN = radionuclide.

Enhanced external counterpulsation was well tolerated by all patients completing the course of therapy. By patient report, anginal symptoms (frequency, severity, ease of precipitation, and duration of episodes) decreased in all patients. Antianginal medications at baseline were maintained or decreased in all patients over the course of therapy.

Discussion

Despite the greater severity of native coronary disease, the response rate of patients with CABG to EECP overall is comparable with that of patients who have not undergone revascularization (80 vs. 71%). In patients who have not been revascularized, those with significant single- and double-vessel CAD are much more likely to benefit from EECP than those with triple-vessel disease (88 vs. 22%, $p < 0.05$). By contrast, the patients with CABG tend to respond in a manner similar to the unrevascularized patients with single- and double-vessel

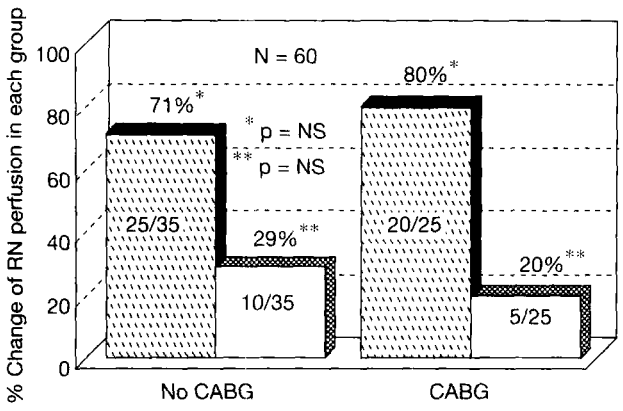

FIG. 1 Percentage of revascularized (CABG) and unrevascularized (no CABG) coronary artery disease patients showing improvement in myocardial perfusion by radionuclide stress testing after enhanced external counterpulsation (EECP). CABG = coronary artery bypass grafting, RN = radionuclide. ▨ = Improved perfusion, □ = unchanged perfusion.

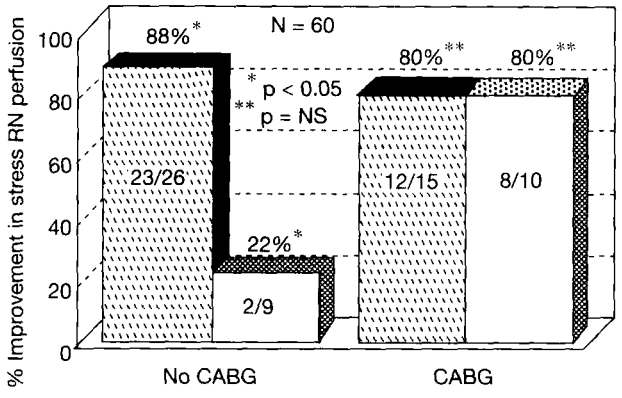

FIG. 2 Percentage of unrevascularized (no CABG) and revascularized (CABG) patients with coronary artery disease (CAD) showing improved myocardial perfusion by radionuclide stress testing after EECP treatment by CAD extent (single- and double-vessel vs. triple-vessel CAD in the group with no CABG; patients post CABG are categorized into single- and double-vessel residual vs. triple-vessel residual CAD as described in the text). Abbreviations as in Figure 1. ▨ = Single- and double-vessel CAD, □ = triple-vessel CAD.

CAD despite triple-vessel CAD and stenotic grafts. Comparison of the response of patients post CABG with triple-vessel CAD and stenotic grafts with the response of unrevascularized patients with triple-vessel CAD demonstrated a significantly greater response rate in the patients with CABG (80 vs. 22%; $p < 0.05$).

Prior revascularization may provide additional conduits, allowing EECP diastolic augmented pressure and volume to be transmitted to the distal coronary vasculature. It has been shown with the intra-aortic balloon pump that proximal vessel patency is a requisite for transmission of the augmented diastolic pressure and flow to the distal coronary vasculature.[6,7] Revascularized patients with patent grafts would thus be expected to respond similarly to unrevascularized patients with single- and double-vessel CAD.[8] In unrevascularized patients, the differential effectiveness of EECP in single- and double-vessel versus triple-vessel CAD supports the patent vessel hypothesis. The effectiveness of EECP in patients with triple-vessel CAD and stenotic grafts suggests that a stenotic graft may still allow EECP-augmented diastolic flow to be transmitted to the distal coronary vasculature.[9,10] This may be because vein grafts are often considerably greater in diameter than the coronary artery to which they are anastomosed; consequently, a ≥ 70% stenosis may not limit flow as much as it would in a native coronary. Alternatively, the additional number of conduits provided by CABG may affect distal perfusion through a summation effect. Because of its demonstrated benefit, EECP thus has a role as an effective treatment for the common and progressive problem of post-CABG myocardial ischemia.

Limitations

Prior revascularization significantly improves the response to treatment with EECP. The number of patients treated in this study, however, is small and the results will need to be confirmed in larger groups. The radionuclide perfusion analysis, while sufficient to demonstrate differential benefits between baseline and treated groups, would benefit from more rigorous quantitative analysis. This will also require a larger and angiographically defined treatment group.

Conclusions

Enhanced external counterpulsation can be used effectively to intervene at several stages in the clinical progression of CAD. It is highly effective in lessening ischemic symptoms and burden and in improving exercise tolerance in unrevascularized patients, particularly in those with single- or double-vessel disease. In the previously surgically revascularized patient, recurrent angina and ischemia become increasingly prevalent and troubling with the passage of time from surgery. It is of importance that EECP is effective in previously revascularized patients, including in those with stenotic grafts. It may therefore be expected to be of particular usefulness as a treatment alternative in this group of older, higher-risk patients with prior CABG and limited graft availability.

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