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Predictors of Adverse Outcomes in Treating Angina Patients with Enhanced External Counterpulsation

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Introduction

Enhanced external counterpulsation (EECP) is an effective, noninvasive angina treatment. EECP has been demonstrated to: increase stress exercise time, time to ST segment depression, and to improve stress radionuclide perfusion, findings that are paralleled by improvements in functional class, quality of life indices, and anginal symptoms. [1-4] Durability of benefit has been demonstrated for up to 5 years post treatment. [5-8]

While major adverse cardiovascular events (MACE), defined as death, myocardial infarction (MI), angioplasty (PCI), bypass (CABG) during treatment, are rare, it is nevertheless important to determine patient characteristics predicting unfavorable events. Characteristics, including patient demographics, cardiac history and function, medical treatment, were analyzed to determine their value in predicting MACE.

Methods

The International EECP Patient Registry (IEPR), administered by the Epidemiology Data Center of the University of Pittsburgh Graduate School of Public Health, was initiated in January 1998 to determine the patterns of use, safety, and efficacy of EECP. The Registry sequentially tracks, across a broad spectrum of participating providers (currently 102 participating centers), the demographics, entry characteristics, and outcomes of all angina patients

treated with EECP. The Registry generated database was used to analyze data from 2,899 consecutive patients, comparing the characteristics of patients with and without MACE during the treatment period.

Enhanced external counterpulsation was typically prescribed for 35 hours of treatment, one hour daily over a period of 7 weeks. An initial history and subsequent interval history of changes in angina, medication use, interim events (MACE) was obtained prior to treatment and at the end of therapy.

Statistical Analysis

The association of patient characteristics with MACE during EECP was analyzed by Chi-square tests. All patients were included whether or not they completed EECP treatment. Significance was defined as $p < 0.05$. Odds ratios of presence versus absence of risk factors were estimated for MACE using the multiple logistic regression model.

Results

The mean age of IEPR patients was 66.4∀ 10.7 years; 74.8% were male. The average duration of coronary artery disease (CAD) was 10.4 years with 65.5 % having had a prior MI, and 84.8 % having had prior revascularization, (63.3 % with PCI and 67.1 % with CABG). Only 20.2% were still considered candidates for either PCI or CABG and multivessel disease (MVD) was present in 77.5%.

At the time of treatment, 57.2% of patients had Canadian Cardiovascular Society (CCS) Class III angina, 24.1% had Class IV angina, and 2.6% had unstable angina. The mean left ventricular ejection fraction (LVEF) was 46.1 % with 18.2% of the patients having a LVEF of < 35% and 30.6 % of patients having a history of CHF. Cardiovascular risk factor prevalence was high, including: 76.3 % with family history of premature CAD, 42.4 % with diabetes mellitus (DM), 79.7% with hypertension, 78.4 % with hyperlipidemia, 71.4 % with a history of smoking, and non-cardiac vascular disease in 28.4%. Medications used by the IEPR patients included: Beta blockers (63.9%), Calcium channel blockers (47.3%), Angiotensin converting enzyme inhibitors (36.4%), Angiotensin receptor blockers (10.4%), Nitrates (74.1%), Lipid lowering medications (68.7%), Aspirin (71.4%).

Patients received a mean EECP treatment course of 34.1 hours with 83.3 % completing the course as prescribed. In 42.8% of incomplete EECP treatment cases, treatment was terminated at the patient's wishes. Overall CCS functional angina class improved one or more classes in 72.7% of patients, with a 7.3 mean decrease in anginal episodes/week, and discontinuation of nitroglycerin use in 54.3% of patients. Post EECP,

patients assessed improvement in their health in 62.1%, quality of life in 61.4%, and satisfaction with life quality in 66.1%.

Major adverse cardiovascular events (MACE) occurred in 2.0% of patients over the course of therapy including (not exclusive events): 0.3% death, 0.8% MI, 0.2% CABG, and 0.8% PCI. Exacerbation of heart failure was noted in 1.9%, skin breakdown in 1.3% and musculoskeletal complaints in 1.0% of patients.

Variables demonstrating some univariate association with MACE were: age, prior CABG/PCI, DM, non-cardiac vascular disease, class III/IV angina, left ventricular dysfunction (EF < 35%), multivessel CAD ($p < 0.2$). By multivariate analysis, however, the only significant independent predictors of MACE during the course of EECP treatment were diabetes mellitus (DM) and multivessel CAD (MVD), as shown in Table 1.

Table 1: Independent factors as predictors of adverse outcome during EECP therapy

Factor	MACE rate with factor	MACE rate without factor	Odds Ratio	Confidence Interval
DM	3.1	1.3	2.12	1.18-3.79
MVD	2.5	0.5	4.02	1.24-12.99

Discussion

Prior reports have demonstrated that angina patients may routinely be safely treated with EECP.

In the current study diabetes mellitus and multivessel CAD were potent predictors of MACE (death, MI, CABG, PCI) during the course of EECP treatment. Diabetics are known to be at greater risk of developing CAD and of having more diffuse disease on presentation. Diabetes has emerged as a strong adverse risk factor for revascularization success and long term prognosis in most medical, coronary bypass and angioplasty treatment registries to date[9]. Similarly, the extent of CAD has been shown to be an important predictor of events during medical treatment of angina.

In the present group of high risk, largely unrevascularizable patients treated with EECP, the overall risk of MACE was low, even in the diabetic and multivessel CAD groups. When treating these higher risk patients, however, the present study would support added vigilance in periprocedural monitoring (oximetry, hemodynamic, electrocardiographic) during counterpulsation and suggest that EECP be performed in an appropriate clinical setting.

Conclusions

EECP is a safe and effective treatment for angina. Reduction in angina and improvement in the quality of life are seen in the majority of

treated patients, including those who are no longer candidates for traditional revascularization. MACE (death/MI/CABG/PCI) occurs infrequently during treatment, even in patients with diabetes and multivessel coronary artery disease. However, the increase in MACE with DM and MVD supports increased vigilance during EECP treatment for these patient groups.

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