Enhanced External Counterpulsation in Patients with Coronary Artery Disease-Associated Erectile Dysfunction. Part II: Impact of Disease Duration and Treatment Courses

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ABSTRACT

Introduction. Enhanced external counterpulsation (EECP) is a noninvasive outpatient treatment used for patients with intractable angina refractory to aggressive surgical and medical treatment. Recent results have demonstrated a positive impact of EECP on patients with ischemic heart disease (IHD)-associated erectile dysfunction (ED).

Aim. To assess the effect of IHD duration and number of EECP courses on efficacy and satisfaction rate of EECP on patients with IHD-associated ED.

Main Outcome Measures. We compared pre- and post-EECP responses to erectile function (EF) domain, Q3 and Q4 of the International Index of Erectile Function score in patients who received one or two courses of EECP and those who had <5- or ≥5-years duration of IHD.

Methods. As mentioned in part I a total of 44 male patients with intractable angina caused by coronary insufficiency were enrolled in this study. Treatment course of EECP consists of 35 1-hour sessions over 7 weeks. Another 35 1-hour sessions over another 7 weeks were offered to patients who received one course and required a second course because of no or minimal improvement from class IV to class III angina after the first course.

Results. Patients who received only one course (N = 34) had significantly higher EF domain, Q3 and Q4, in pre- and post-EECP results than patients who received two courses (N = 10) after they completed the first course. Patients who had <5-years duration of IHD had significantly higher pre- and post EECP than patients who had ≥5 years regarding EF domain, Q3 and Q4. Considering the global efficacy question, overall satisfaction, and angina, there were significant improvements of post EECP in patients with <5 years than in patients with ≥5-years duration of IHD.

Conclusion. The efficacy and satisfaction rate of EECP in patients with IHD-associated ED were negatively influenced by longer duration of IHD and requirement of a second course of EECP. **El-Sakka AI, Morsy AM, and Fagih BI. Enhanced external counterpulsation in patients with coronary artery disease-associated erectile dysfunction. Part II: Impact of disease duration and treatment courses. J Sex Med 2007;4:1448–1453.**

Key Words. Erectile Dysfunction; CAD Duration; EECP Courses

Introduction

Vasculogenic erectile dysfunction (ED) may be ultimately a result of a systemic vasculopathic state, as ischemic heart disease (IHD) [1]. Furthermore, it is not a coincidence that ED patients have symptomatic or asymptomatic IHD. A significant number of patients with IHD cannot be successfully managed, even with optimization of conventional treatment [2]. Enhanced external counterpulsation (EECP) produces an actual hemodynamic effect that is presumed to be similar to that produced by the invasive intra-aortic balloon pump [2]. Recently, EECP has been reported to improve conditions other than IHD such as restless legs syndrome and renal excretory function in healthy volunteers as well as in patients with liver cirrhosis [3,4]. However, the role of

EECP in improvement of vascular status has not yet been well defined.

Previous studies [5,6] confirmed that the severity and duration of IHD may negatively influence the vascular mechanism of erection. Further, recent investigation has demonstrated that EECP can improve anginal pain as well as IHD-associated ED despite presence of risk factors and medical comorbidity [7]. These factors prompted us to assume that other risk variables such as duration of IHD and the requirement for more EECP courses could have a negative impact on efficacy and the satisfaction rate of EECP in patients with IHD-associated ED.

Materials and Methods

Research Design

As mentioned in part I of this study, a total of 44 consecutive male patients with intractable angina caused by coronary insufficiency in the presence of coronary artery disease (CAD) which cannot be controlled by conventional therapy were enrolled in this study. The patients were prospectively recruited. They were screened and followed up for ED using the erectile function (EF) domain of the International Index of Erectile Function.

To assess the effect of number of EECP courses and IHD duration on response to EECP, we compared pre- and post-EECP responses to EF domain, Q3 (achieving erection) and Q4 (maintaining erection) in patients who received one course only and in patients who received two courses. Patients who received two courses were assessed at two time points: after they completed the first course (time point A) and after they completed the second course (time point B). Further, we compared the same variables in patients who had <5- or ≥5-years duration of IHD. Global efficacy question (GEQ, "Did treatment improve your erection?") and overall patient satisfaction question (Are you satisfied with the efficacy of your treatment?) were also addressed to assess EECP efficacy and satisfaction rate in patients with and without the examined variables.

EECP was used in the enrolled patients who had debilitating (functional Canadian classes III and IV) refractory angina pectoris "symptomatic despite being on maximal anti-anginal pharmacotherapy" and who were not candidates for revascularization, and have no contraindications to EECP use. The inclusion and exclusion criteria as well as the EECP technique were described in part I of this study. The institutional review board approved the study. IHD was diagnosed using the criteria of 1 mm or more horizontal ST-segment depression, during exercise/stress test. The duration since that diagnosis was considered as the duration of IHD in this study. Severity of the CAD was evaluated by the degree of changes in exercise treadmill test, angiography studies in addition to the level of anginal syndrome, dyspnea, and whether or not the patient had undergone a myocardial infarction.

EECP Courses

A treatment course consisted of 35 1-hour sessions over a 7-week period (five times/week) for patients who received only one course. Another 35 1-hour sessions over another 7-week period were instituted for patients who received one course and required a second because of no or minimal improvement from class IV to class III angina after the first course. Courses were directly consequential and were generally well tolerated with low risk of adverse events.

Analysis of Data

The data were analyzed using the Statistical Package of Social Science (SPSS.11) software program. Nonparametric EECP and IHD duration according to GEQ, overall satisfaction, and improvement of angina were compared using chi-squared test. Paired sample *t*-test (two-tailed) and one-way analysis of variance were used to compare means of each of the measured variables pre- and post EECP.

Results

Effects of Number of EECP Courses and IHD Duration on Global Efficacy and Satisfaction Rate

The mean EF domain increased from 11.0 ± 2.5 in pre-EECP to 19.2 ± 3.0 in post EECP in patients who received only one course (N = 34). The mean EF domain increased from 9.7 ± 1.4 in pre-EECP to 14.7 ± 1.9 at time point A and to 19.1 ± 2.8 at time point B in patients who received two courses (N = 10) (Table 1). Patients who received only one course had significantly higher EF domain, Q3 and Q4 in pre- and post-EECP results, than patients who received two courses at time point A ($P < 0.05$ for each) (Table 1). Those significant differences were not demonstrated between patients who had received one course and those who had completed the two courses (time point B) ($P > 0.05$ for each) (Table 1). About 52.9% of the patients who required only one

Table 1 Comparison of EECP number of courses and IHD duration according to means of EF domain, Q3 and Q4

Variables	EF domain (mean ± SD)	Q3 (mean ± SD)	Q4 (mean ± SD)
Pretreatment*	$P < 0.01$	$P < 0.01$	$P < 0.01$
EECP I (N = 34)	11.0 ± 2.5	2.3 ± 0.5	2.2 ± 0.6
EECP II (N = 10)	9.7 ± 1.4	1.7 ± 0.5	1.8 ± 0.5
Post treatment	$P < 0.001$	$P < 0.001$	$P < 0.001$
EECP I (N = 34)	19.2 ± 3.0	3.5 ± 0.5	3.5 ± 0.5
EECP I for II (N = 10)	14.7 ± 1.9	3.0 ± 0.1	3.1 ± 0.5
Post treatment	$P > 0.05$	$P > 0.05$	$P > 0.05$
EECP I (N = 34)	19.2 ± 3.0	3.5 ± 0.5	3.5 ± 0.5
EECP II (N = 10)	19.1 ± 2.8	3.4 ± 0.5	3.4 ± 0.5
Post treatment	$P < 0.001$	$P < 0.001$	$P < 0.001$
EECP I for II (N = 10)	14.7 ± 1.9	3.0 ± 0.1	3.1 ± 0.5
EECP II (N = 10)	19.1 ± 2.8	3.4 ± 0.5	3.4 ± 0.5
EECP I (N = 34)	$P < 0.001$	$P < 0.001$	$P < 0.001$
Pretreatment	11.0 ± 2.5	2.3 ± 0.5	2.2 ± 0.6
Post treatment	19.2 ± 3.0	3.5 ± 0.5	3.5 ± 0.5
EECP I for II (N = 10)	$P < 0.001$	$P < 0.001$	$P < 0.001$
Pretreatment	9.7 ± 1.4	1.7 ± 0.5	1.8 ± 0.5
Post treatment	14.7 ± 1.9	3.0 ± 0.1	3.1 ± 0.5
EECP II (N = 10)	$P < 0.001$	$P < 0.001$	$P < 0.001$
Pretreatment	9.7 ± 1.4	1.7 ± 0.5	1.8 ± 0.5
Post treatment	19.1 ± 2.8	3.4 ± 0.5	3.4 ± 0.5
Pretreatment	$P < 0.01$	$P < 0.001$	$P < 0.001$
IHD <5 years (N = 16)	11.7 ± 2.3	2.4 ± 0.6	2.2 ± 0.5
IHD ≥5 years (N = 28)	9.4 ± 1.2	1.6 ± 0.5	1.7 ± 0.5
Post treatment	$P < 0.001$	$P < 0.001$	$P < 0.01$
IHD <5 years (N = 16)	20.2 ± 2.6	3.6 ± 0.5	3.5 ± 0.6
IHD ≥5 years (N = 28)	14.4 ± 2.4	3.2 ± 0.6	3.3 ± 0.5
IHD <5 years (N = 16)	$P < 0.001$	$P < 0.001$	$P < 0.001$
Pretreatment	11.7 ± 2.3	2.4 ± 0.6	2.2 ± 0.5
Post treatment	20.2 ± 2.6	3.6 ± 0.5	3.5 ± 0.6
IHD≥5 years (N = 28)	$P < 0.001$	$P < 0.001$	$P < 0.001$
Pretreatment	9.4 ± 1.2	1.6 ± 0.5	1.7 ± 0.5
Post treatment	14.4 ± 2.4	3.2 ± 0.6	3.3 ± 0.5

*Pretreatment for EECP II is the same for EECP I for II.
Paired sample *t*-test (two-tailed) and one-way analysis of variance were used to calculate significance level at $P < 0.05$; regarding mean ± SD for EECP courses and IHD duration, according to EF domain, Q3 and Q4.
EECP I = who received only one course; EECP I for II = after first course for those who received two courses (time point A); EECP II = after second course for those who received two courses (time point B); IHD = ischemic heart disease; EECP = enhanced external counterpulsation; EF = erectile function.

course and all patients who required a second course had ≥5-years duration of IHD, respectively. Patients who had <5-years duration of IHD had significantly higher pre- and post EECP than patients who had ≥5 years regarding EF domain, Q3 and Q4 ($P < 0.05$ for each) (Table 1).

Considering the GEQ, overall satisfaction, and angina, there were significant improvement of post EECP in patients with <5 years than in patients with ≥5-years duration of IHD. Further, patients who received one course only had significant improvement in those variables than patients who received two courses at time point A ($P < 0.05$ for each) (Table 2). About 88.2% of the patients who received only one course reported improvement of angina. Of the 10 patients who received two courses, at time point A, 4/10 (40%) reported improvement from class IV to class III. At time point B, 7/10 (70%) reported improvement from classes IV and III to class II ($P < 0.001$). The sociodemographic variables such as age, obesity, and number of comorbidity negatively influenced the improvement of angina ($P < 0.05$ for each) (Table 3).

Discussion

A generalized atherosclerotic process that affects the arterial blood flow is a common cause of ED. It has been proposed that the smaller penile arteries (diameter 1–2 mm) suffer obstruction plaque burden earlier than the larger coronary (3–4 mm), carotid (5–7 mm), or iliofemoral (6–8 mm) arteries; hence, ED may be symptomatic before a coronary event. Vessel occlusive atherosclerosis is a major contributing factor to the pathophysiology of IHD; therefore, the likelihood for many ED patients to have IHD is high [4,8–10]. As the survival of patients with primary coronary events continues to increase, the number of patients with CAD unsuitable to further revascularization and symptoms refractory to medical treatment also

Table 2 Comparison of GEQ, overall satisfaction, and improvement of angina according to EECP number of courses and IHD duration

	GEQ			Overall satisfaction			Improvement angina		
Variables	Yes	No	*P* value*	Yes	No	*P* value*	Yes	No	*P* value*
EECP I (N = 34)	31 (91.2%)	3 (8.8%)	<0.01	30 (88.2%)	4 (11.8%)	<0.01	30 (88.2%)	4 (11.8%)	<0.001
EECP I for II (N = 10)	6 (60%)	4 (40%)		5 (50%)	5 (50%)		4 (40%)	6 (60%)	
EECP I (N = 34)	31 (91.2%)	3 (8.8%)	>0.05	30 (88.2%)	4 (11.8%)	>0.05	30 (88.2%)	4 (11.8%)	<0.05
EECP II (N = 10)	8 (80%)	2 (20%)		8 (80%)	2 (20%)		7 (70%)	3 (30%)	
EECP I for II (N = 10)	6 (60%)	4 (40%)	<0.05	5 (50%)	5 (50%)	<0.05	4 (40%)	6 (60%)	<0.05
EECP II (N = 10)	8 (80%)	2 (20%)		8 (80%)	2 (20%)		7 (70%)	3 (30%)	
IHD duration			<0.01			<0.05			<0.01
<5 years (N = 16)	15 (93.7%)	1 (6.3%)		14 (87.5%)	2 (12.5%)		14 (87.5%)	2 (12.5%)	
≥5 years (N = 28)	22 (78.6%)	6 (21.4%)		21 (75%)	7 (25%)		20 (71.4%)	8 (28.6%)	

*χ^2 significance level at $P < 0.05$; percentages are calculated for categorical parameters of EECP I, EECP I for II, EECP II, and IHD according to GEQ, overall satisfaction, and improvement of angina.
EECP I = who received only one course; EECP I for II = after first course for those who received two courses (time point A); EECP II = after second course for those who received two courses (time point B); IHD = ischemic heart disease; EECP = enhanced external counterpulsation; GEQ = global efficacy question.

continues to rise. Likewise, the incidence of ED continues to increase in association with age and in concurrence with CAD.

Recent investigation demonstrated that EECP could improve EF in ED patients with refractory IHD [7]; our aim in the current study was to assess the impact of IHD duration and the number of EECP courses on the efficacy and the satisfaction rate of EECP in patients with IHD-associated ED. This might ultimately establish the role of EECP in the armamentarium of ED treatment of those patients. For that purpose, we compared pre and post-EECP responses to EF domain, Q3, Q4, GEQ, and overall satisfaction in patients with and without impairment of those risk variables.

EECP was developed approximately 40 years ago [11,12], at the same time as intra-aortic balloon pump, and was expected not only to be a less invasive treatment, but also to have the same degree of effectiveness in hemodynamic improvement. Subsequently, the EECP device was improved and a better effect was obtained [13,14]. EECP enhances diastolic augmentation and systolic unloading by means of a pressurized air cuff around the patient's legs that is maintained at approximately 300 mm Hg during diastole. In previous studies, the effectiveness of this method in chronic angina has been reported, and its effectiveness has been confirmed in a large-scale clinical trial [15,16]. In our study, all patients had severe diffuse triple vessels disease, and they were receiving the maximal anti-anginal pharmacotherapy as mentioned in part I of this study. They could be classified as a high-risk category according to

Table 3 Comparison of IHD duration and improvement of angina according to risk factors

	IHD duration			Improvement of angina		
Variables	<5 years (N = 16)	≥5 years (N = 28)	*P* value*	Yes (N = 34)	No (N = 10)	*P* value*
Age groups			>0.05			<0.05
<60 years (N = 28)	9 (32.1%)	19 (67.9%)		24 (85.7%)	4 (14.3%)	
≥60 years (N = 16)	7 (43.7%)	9 (56.3%)		10 (62.5%)	6 (37.5%)	
Smoking			<0.05			>0.05†
None (N = 6)	4 (66.7%)	2 (33.3%)		5 (83.3%)	1 (16.7%)	
Ex-smoker (N = 9)	4 (44.4%)	5 (55.6%)		5 (55.6%)	4 (44.4%)	
Current (N = 29)	8 (27.6%)	21 (72.4%)		24 (82.8%)	5 (17.2%)	
BMI			<0.01			<0.05‡
<25.0 (N = 8)	5 (62.5%)	3 (37.5%)		7 (87.5%)	1 (12.5%)	
25.1–27.0 (N = 12)	6 (50%)	6 (50%)		9 (75%)	3 (25%)	
>27.0 (N = 24)	5 (20.8%)	19 (79.2%)		18 (75%)	6 (25%)	
Number of comorbidities			>0.05			<0.05
≤2 (N = 8)	2 (25%)	6 (75%)		7 (87.5%)	1 (12.5%)	
>2 (N = 36)	14 (38.9%)	22 (61.1%)		27 (75%)	9 (25%)	

*χ^2 significance level at $P < 0.05$; percentages are calculated for categorical parameters of age, smoking, BMI, and number of comorbidities according to IHD duration and improvement of angina.
†Smoking = none vs. ex-smoker and current.
‡BMI = <25.0 vs. 25.1–27.0 and >27.0.
IHD = ischemic heart disease; BMI = body mass index.

Princeton II guidelines [17]. The high association between IHD and ED in the study population could be referred to the postulation that a generalized atherosclerotic process of the arterial tree is the common underlying etiology of both conditions. Regarding GEQ, overall satisfaction, and improvement of angina, there were significant differences in post EECP between patients with <5- or ≥5-years duration of IHD. An improvement in the health-related quality of life measures (perform activities of daily living, ability to work, body pain, confidence in health, energy, ability to engage in social activities with family and friends, anxiety, and depression) has been reported in a follow up analysis of patients at 1-year post EECP [18,19]. Extrapolation of the cardiac positive impact of EECP on EF could be a potential explanation of post-EECP ED improvement.

It was reported that the EECP effect was due to both cardiac and peripheral effects. With exposure to the augmented blood flow and endothelial shear stress, there is elaboration of nitric oxide, prostacycline, β fibroblast growth factor, and vascular endothelial growth factor from the arterial bed and a decrease in brain natriuretic peptide and endothelin-1 concentrations that ultimately improve endothelial function and vascular remodeling [20,21]. This may help explain the long-term sustained benefits of EECP even after discontinuation of treatment.

To assess the impact of IHD duration and number of EECP courses on the efficacy of EECP, no treatment for ED was offered to the patients during the study period. In the current study, there were significant differences in pre- and post EECP between patients who received one course only and those patients who required a second course because of the less improvement of anginal class after the first course and between patients with <5 years and those patients with ≥5-years duration of IHD regarding EF domain, Q3 and Q4. Those results could be expected because those patients who required a second course of EECP sessions could have severe and longstanding IHD. Differences were not demonstrated between those patients who received one course and those who had completed the second course because they attained a comparable outcome. These results indicate that the efficacy of EECP treatment may be more obvious in patients with the most disabling angina. The reason for this is not known; however, the importance of shear stress role in endothelial function cannot be ignored; the shear stress forces may be stronger in patients with severe angina as compared with patients with mild angina [20,21]. Further, patients may appreciate improvement from higher classes of angina (IV or III), as compared to lower classes. Consistent with our findings, previous studies have shown an improvement in up to 74% of patients with angina undergoing EECP especially in the younger patients who had a greater likelihood of improvement [15,16]. Supporting the positive impact of EECP, previous studies had reported that EECP therapy was effective in the treatment of chronic stable angina with lowering in Canadian Cardiovascular Society Classification. Furthermore, other studies have reported that post-EECP benefit in pain and health-related quality of life measures continued for years [18,19].

Limitations of our study are the relatively small number of patients, the lack of long-term follow-up data, and lack of control group. Therefore, the possibility of placebo effect of the device cannot be ruled out in this type of cohort study. Although our preliminary results indicated an improvement in EF, however, the possibility of EECP effects on patients' well-being and confidence cannot be excluded.

Conclusions

The results of the current study indicate that the efficacy and satisfaction rate of EECP were negatively influenced by longer duration of IHD and requirement of a second course of EECP; however, the global efficacy and overall patient satisfaction were promising. Although our preliminary results indicated an improvement of IHD-associated ED, large-scale trials and long-term data are needed.

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Statement of Authorship

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