Enhanced External Counterpulsation in Patients with Coronary Artery Disease-Associated Erectile Dysfunction. Part I: Effects of Risk Factors

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ABSTRACT

Introduction. Recently it has been demonstrated that enhanced external counterpulsation (EECP) could improve erectile dysfunction (ED) in patients with refractory ischemic heart disease (IHD).

Aim. To assess the effect of risk factors on the efficacy and the satisfaction rate of EECP in patients with coronary artery disease (CAD)-associated ED.

Main Outcome Measures. To assess the effect of risk factors on EECP efficacy and satisfaction rate, we compared the pre- and post-EECP responses to erectile function domain, Q3, and Q4 in patients with and without risk factors. Overall satisfaction and global efficacy question (GEQ) were also assessed.

Methods. A total of 44 male consecutive patients with intractable angina caused by coronary insufficiency which cannot be controlled by conventional therapy were enrolled in this study. Patients were screened and followed up for ED using erectile function domain of the International Index for Erectile Function. A thorough sexual, medical, and psychosocial history was taken from all patients.

Results. All patients had severe diffuse triple vessels disease. They all had class III or IV angina. They were receiving the maximal antianginal pharmacotherapy. The mean age ± SD was 57.1 ± 5.6 years. Of the patients, 63.9% were below 60 years, and 86.4% were current or ex-smokers. There were significant differences between pre- and post-EECP regarding erectile function domain, Q3, and Q4. The sociodemographic variables were not significantly different among the studies groups and had not affected the GEQ or overall satisfaction. Overall satisfaction and GEQ were negatively influenced by smoking and presence of more than two risk factors. However, diabetes, hypertension, dyslipidemia, myocardial infraction, and obesity have not had such effects.

Conclusions. The efficacy and satisfaction rate of EECP in patients with CAD-associated ED were negatively influenced by presence of risk factors; however, the global efficacy and the overall patients' satisfaction were encouraging. **El-Sakka A, Morsy A, and Fagih B. Enhanced external counterpulsation in patients with coronary artery disease-associated erectile dysfunction. Part I: Effects of risk factors. J Sex Med 2007;4:771–779.**

Key Words. Erectile Dysfunction; Risk Factors; EECP

Introduction

Epidemiological studies had shown that both erectile dysfunction (ED) and ischemic heart disease (IHD) share the same principal risk factors, namely aging, hypertension, diabetes, smoking, and dyslipidemia [1–4]. Most patients with ED are known to have at least one significant cardiovascular risk factor [1–4]. Because atherosclerosis is a systemic disease, it is now clear that, in many cases, the pathological processes of ED are similar to those involved in many vascular diseases [5]. Therefore, vasculogenic ED may be ultimately a result of a systemic vasculopathic state, such as IHD. Furthermore, it is not a coincidence that ED patients have symptomatic or asymptomatic IHD.

Refractory angina pectoris is a clinical diagnosis which is characterized by chronic angina due to

coronary artery insufficiency in patients who are refractory to conventional forms of treatment [6]. Enhanced external counterpulsation (EECP) is a noninvasive outpatient treatment used for patients with intractable angina refractory to aggressive surgical and medical treatment. A significant number of patients with IHD cannot be successfully managed, even with optimization of conventional treatment [6]. Although data indicated improvement in angina in patients undergoing EECP, the role of EECP in improvement of vascular status has not yet been well defined. EECP was reported to improve conditions other than IHD, such as symptoms of restless legs syndrome and renal excretory function in healthy volunteers as well as in patients with liver cirrhosis [7,8].

It was shown that coronary artery risk factors are significantly associated with ED [9]. Recently it has been demonstrated that EECP could improve erectile function in ED patients with refractory angina [10]. These findings prompted us to assume that ED risk factors could have an impact on the efficacy and the satisfaction rate of EECP on patients with IHD-associated ED.

Material and Methods

Research Design

A total of 44 male consecutively and prospectively recruited 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. Patients were screened and followed up for ED using the erectile function domain of the International Index for Erectile Function (IIEF). The erectile function domain consists of questions 1–5 and question 15 for assessing the global erectile function. Scoring of the IIEF domain of erectile function allowed classification of each patient as having no (26–30), mild (17–25), moderate (11–16), or severe (0–10) ED. At the same visits they were assessed for ED, all patients were also interviewed for sociodemographic and relevant medical history. Sociodemographic data included age, obesity, and smoking habit. Medical history and risk factors for IHD included diabetes, hypertension, and dyslipidemia. Patients underwent routine laboratory investigations, total testosterone, and prolactin assessment. To assess the effect of risk factors and medical comorbidities on the efficacy and overall satisfaction of EECP, we compared the presence and absence of those risk factors on pre- and post-EECP responses to erectile function domain, Q3 (achieving erection), and Q4 (maintaining erection). 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 associated risk factors.

In the current study, EECP was used in patients with debilitating (functional Canadian classes III and IV) refractory angina pectoris "symptomatic despite being on maximal antianginal pharmacotherapy" and who were not candidates for revascularization, and have no contraindications to EECP use. IHD was diagnosed using the criteria of ≥1-mm horizontal ST-segment depression, during exercise/stress test. Severity of the CAD was evaluated by the degree of changes in exercise treadmill test, and angiography studies, in addition to the level of anginal syndrome, dyspnea, and whether or not the patient had undergone a myocardial infraction (MI).

Exclusion Criteria

Decompensated heart failure, usually stages C and D [11]

Left ventricular ejection fraction <30%

Arrhythmias that may interfere with triggering of EECP system (atrial fibrillation, flutter, and very frequent premature ventricular contractions)

Moderate to severe aortic insufficiency; aortic aneurysm or dissection

Severe hypertension >180/110 mm Hg; severe peripheral arterial disease

Technique

EECP (EECP®-MC2, Vasomedical, Inc., New York, USA), involves the use of three paired inflatable cuffs wrapped around the patient's lower extremities. The cuffs are sequentially inflated during diastole, in the calves followed by lower thighs followed by upper thighs. All pressure is released at the onset of systole. This sequential compression results in increased venous return and augmented diastolic pressure. Pressure within the cuffs is adjustable, and current EECP machines are capable of generating pressures up to 350 mm Hg, but pressures in the range of 250–275 mm Hg are usually applied. A treatment course consists of 35 1-hour sessions over a 7-week period (5 times/week) and is generally well tolerated with a low risk of adverse events.

Analysis of Data

The data were analyzed using the Statistical Package of Social Science (SPSS.11) software (SPSS, Inc, Chicago, IL, USA). Nonparametric patients' characteristics according to presence of risk factors were compared using the chi-square test and calculation of odds ratio and 95% confidential interval. Unpaired *t*-test and one-way ANOVA were used to compare means of each of the measured variables pre- and post-EECP.

Results

Demographics

A total of 44 male Saudi patients with intractable angina caused by CAD which cannot be controlled by conventional therapy were the subject of this study. The mean age ± SD was 57.1 ± 5.6 years (range 46–67). Of the patients, 63.9% were below 60 years. A total of 86.4% were current or ex-smokers, and the mean duration of smoking was 17.2 ± 6.8 years, with an average of 31.6 ± 14.3 cigarettes a day. According to the body mass index, 18.2% of the patients were healthy, 27.3% were overweight, and 54.5% were obese. Two patients had one risk factor, 6 patients had two risk factors, 16 patients had three risk factors, and 20 patients had more than three risk factors.

EECP Efficacy on Erectile Function and Angina

All patients had angiographically proven severe diffuse triple vessels disease with coronary stenosis (>70%) in at least one major coronary artery. They all had class III or IV angina. They were receiving the maximal antianginal pharmacotherapy "β-blockers, Ca^{++} channel blockers, and nitrates." Additionally, statins, anticoagulants, antiplatelets, angiotensin type 1, diuretics, angiotensin-converting enzyme inhibitor, and insulin were used according to each patient's condition. In pre-EECP, all patients had either moderate or severe ED. Patients were followed up for 6 months post EECP. There was a significant post-EECP improvement in erectile function. There were significant differences between pre- and post-EECP regarding erectile function domain, Q3, and Q4 ($P < 0.05$ for each). In post-EECP, 34/44 patients (77.3%) reported improvement of anginal pain. Of them, 29/34 patients (85.3%) improved from class IV or III to class II, and the rest of them improved to class I. Four out of five patients who had improved to class I had pre-EECP class III angina. Further, 88.6% of the patients were using nitrate therapy on a daily base. Of them, 61.5% reported decrease of the weekly usage of nitrates. In total, 79.5% of the patients were overall satisfied regarding both anginal and sexual function improvement. There was a significant association between anginal improvement and sexual function ($P < 0.05$).

Evaluation of ED Risk Factors' Effects on the Efficacy and Satisfaction Rate of EECP

The sociodemographic variables were not significantly different among the studied groups and had not influenced the global efficacy or overall satisfaction rate. GEQ was significantly lower in older patients ($P < 0.01$). Further, the sociodemographic variables were not significantly different among patients with two or more risk factors in comparison with patients with less than two risk factors ($P > 0.05$ for each) (Table 1). Erectile function domain, Q3, and Q4 were not significantly different among patients with and without risk factors such as diabetes, hypertension, dyslipidemia, heart failure, MI, and obesity ($P > 0.05$ for each) (Table 2). Erectile function domain, Q3, and Q4 in pre- and post-EECP were negatively influenced by smoking. Presence of more than two risk factors had the same negative effect on erectile function domain, Q3, and Q4 in pre-EECP ($P < 0.05$ for each) (Table 2). EECP efficacy and overall satisfaction were higher in patients with heart failure ($P < 0.05$ for each) (Table 3). Overall satisfaction and global efficacy were negatively influenced by smoking and presence of more than two risk factors ($P < 0.05$ for each) (Table 3). However, diabetes, hypertension, dyslipidemia, MI, and obesity had no such effects on efficacy and overall satisfaction ($P > 0.05$ for each) (Table 3). There were no significant differences in testosterone or prolactin levels among patients with and without risk factors in the study groups ($P > 0.05$).

Discussion

Conventionally, little attention has been given to the association between ED and IHD. Recently, more studies have shown a significant association between the two conditions [1–4]. A generalized atherosclerotic process that affects the arterial blood flow is a common cause of impotence. 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 [12].

Table 1 Sociodemographic characteristics of the study population according to medical comorbidities, overall satisfaction, and GEQ

	Number of comorbidities (N = 44)			Overall satisfaction (N = 44)				GEQ (N = 44)		
Characteristics of ED	>2 (N = 36)	≤2 (N = 8)	*P* value*	Very satisfied (N = 20)	Satisfied (N = 15)	Unsatisfied (N = 9)	*P* value*	Yes (N = 37)	No (N = 7)	*P* value*
Age groups			>0.05				>0.05			<0.01
<60 years	23 (63.9%)	5 (62.5%)		14 (70.0%)	9 (60.0%)	5 (55.6%)		25 (67.6%)	3 (42.9%)	
≥60 years	13 (36.1%)	3 (37.5%)		6 (30.0%)	6 (40.0%)	4 (44.4%)		12 (32.4)	4 (57.1%)	
School education			>0.05				>0.05			>0.05
Less than secondary	20 (55.6%)	4 (50.0%)		11 (55.0%)	8 (53.3%)	5 (55.6%)		20 (54.1%)	4 (57.1%)	
Completed secondary	12 (33.3%)	3 (37.5%)		9 (45.0%)	4 (26.7%)	2 (22.2%)		14 (37.8%)	1 (14.3%)	
High education	4 (11.1%)	1 (12.5%)		0 (0%)	3 (20.0%)	2 (22.2%)		3 (8.1%)	2 (28.6%)	
Marital status			>0.05				>0.05			>0.05
One	31 (86.1%)	6 (75.0%)		18 (90.0%)	12 (80%)	7 (77.8%)		31 (83.8%)	6 (85.7%)	
More than one	5 (13.9%)	2 (25.0%)		2 (10.0%)	3 (20%)	2 (22.2%)		6 (16.2%)	1 (14.3%)	
Occupation			>0.05				>0.05			>0.05
Governmental	7 (19.4%)	1 (12.5%)		4 (20.0%)	2 (13.3%)	2 (22.2%)		7 (18.9%)	1 (14.3%)	
Private	22 (61.1%)	6 (75.0%)		14 (70.0%)	10 (66.7%)	4 (44.4%)		23 (62.2%)	5 (71.4%)	
Retired	6 (16.7%)	1 (12.5%)		2 (10.0%)	3 (20.0%)	2 (22.2%)		6 (16.2%)	1 (14.3%)	
No work	1 (2.8%)	0 (0%)		0 (0%)	0 (0%)	1 (11.1%)		1 (2.7%)	0 (0%)	

*χ^2 at Significance level at $P < 0.05$; percentages are calculated for categorical parameters of comorbidities, overall satisfaction, and GEQ according to demographic data.
ED = erectile dysfunction; GEQ = global efficacy question.

Table 2 Comparison of erectile function domain, Q3, and Q4 before and after EECP in patients with and without medical comorbidities

	ED domain		Q 3		Q 4	
Medical comorbidities	Pretreatment Mean ± SD	Posttreatment Mean ± SD	Pretreatment Mean ± SD	Posttreatment Mean ± SD	Pretreatment Mean ± SD	Posttreatment Mean ± SD
Diabetes	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P < 0.05$	$P > 0.05$
Yes (N = 38)	10.6 ± 2.5	19.2 ± 3.3	2.2 ± 0.6	3.4 ± 0.5	2.1 ± 0.5	3.4 ± 0.6
No (N = 6)	12.7 ± 2.5	21.5 ± 3	2.8 ± 0.5	3.8 ± 0.5	3 ± 1.2	3.5 ± 0.6
Heart failure	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$
Yes (N = 32)	11.4 ± 2.7	20.4 ± 2.6	2.3 ± 0.6	3.5 ± 0.5	2.2 ± 0.7	3.5 ± 0.6
No (N = 12)	9.4 ± 1.8	17.1 ± 3.7	2.3 ± 0.5	3.3 ± 0.5	2.1 ± 0.3	3.3 ± 0.5
MI	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$
Yes (N = 30)	10.5 ± 2.7	19.3 ± 3.4	2.2 ± 0.6	3.4 ± 0.5	2.1 ± 0.5	3.4 ± 0.6
No (N = 14)	11.7 ± 2.4	20.1 ± 3.1	2.5 ± 0.5	3.6 ± 0.5	2.4 ± 0.8	3.6 ± 0.5
BMI	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$
<25 (N = 8)	11.3 ± 2.7	22.1 ± 3.4	2.4 ± 0.6	3.6 ± 0.8	2.4 ± 0.8	3.6 ± 0.7
25.1–27 (N = 12)	10.9 ± 2.4	21 ± 2.8	2.2 ± 0.8	3.5 ± 0.9	2.1 ± 0.9	3.4 ± 0.8
>27 (N = 24)	10.3 ± 2.8	19.7 ± 3.2	2 ± 0.7	3.4 ± 0.9	1.9 ± 0.7	3.3 ± 0.7
Smoking	$P = 0.02$	$P = 0.0001$	$P = 0.01$	$P = 0.003$	$P = 0.01$	$P = 0.01$
None (N = 6)	13 ± 2.3	22.5 ± 1.7	2.8 ± 0.7	3.8 ± 0.9	3 ± 1	4 ± 1.1
Ex-smoker (N = 9)	8.9 ± 2	15.14 ± 2.3	2 ± 0.6	3.1 ± 0.8	2 ± 0.6	3 ± 0.7
Current (N = 29)	11.1 ± 2.5	20.2 ± 2.5	2.2 ± 0.7	3.4 ± 0.8	2.1 ± 0.6	3.5 ± 0.8
Number of comorbidities	$P < 0.05$	$P > 0.05$	$P < 0.05$	$P > 0.05$	$P < 0.05$	$P > 0.05$
≤2 (N = 8)	12.3 ± 2.7	21.4 ± 3.3	2.6 ± 0.8	3.6 ± 0.9	2.5 ± 0.8	3.7 ± 0.9
>2 (N = 36)	10.2 ± 2.5	19.1 ± 3.1	2.1 ± 0.6	3.4 ± 0.8	2 ± 0.6	3.4 ± 0.8

Unpaired *t*-test and one-way ANOVA were used to compare means of each of the measured variables pre- and post-EECP.
BMI = body mass index; ED = erectile dysfunction; EECP = enhanced external counterpulsation; GEQ = global efficacy question; MI = myocardial infraction.

The association between ED and CAD is multifactorial. It has been shown that both ED and IHD have the same principal risk factors, namely aging, hypertension, diabetes, smoking, and dyslipidemia [1,9,12–15]. Considering the increase in life expectancy and the high incidence of both ED and IHD in aging populations, a further increase in patients with IHD and ED would be expected. Therefore, the need for further connecting the ED and cardiovascular research fields becomes urgent.

Despite an increasing success of conventional medical treatment and the continued development and improvement of mechanical revascularization approaches, a significant number of patients with IHD and angina pectoris cannot be successfully managed, even with optimization of medical treatment. Many of these patients are not candidates for revascularization with angioplasty or surgery for myriad reasons [6]. As the survival of patients with primary coronary events continues to increase, the number of patients presenting with CAD unsuitable to further revascularization and symptoms refractory to medical treatment also continues to rise. Further, it has been reported that up to 15% of patients with angina pectoris meet the criteria for refractory angina. This necessitates the search for alternative therapies, such as spinal cord stimulation, left stellate ganglion blockade, thoracic epidural anesthesia, and EECP [16]. Likewise, the incidence of ED is significantly increasing with age and in concurrence with CAD.

Following the recent investigation which demonstrated that a non-invasive method of assisting the circulation "EECP" could improve erectile function in ED patients with refractory IHD [10], the current study aimed to assess the impact of ED risk factors on the efficacy and satisfaction rate of EECP in patients with CAD-associated ED and ultimately might 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 erectile function domain, Q3, and Q4 in patients with and without those risk factors. GEQ and overall patients' satisfaction were also addressed.

All patients had severe diffuse triple vessels disease, and they were receiving the maximal antianginal pharmacotherapy "β-blockers, Ca^{++} channel blockers, and nitrates." It is conceivable that those medications were used in patients with no drug-contraindications and were adjusted according to their tolerance.

It was confirmed that the mechanism involved in spontaneous ischemia during intercourse is similar to the mechanism responsible for ischemia produced in the exercise laboratory [17]. EECP enhances diastolic augmentation and systolic unloading by means of a pressurized air cuff around the patient's legs that is maintained at

Table 3 Comparison of overall satisfaction and GEQ in patients with and without medical comorbidities

	Overall satisfaction				GEQ		
Medical comorbidities	Very satisfied (N = 20)	Satisfied (N = 15)	Unsatisfied (N = 9)	*P* value*	Yes (N = 37)	No (N = 7)	*P* value*
Diabetes				*P* = 0.7			*P* = 0.4
Yes (N = 38)	18 (90.0%)	12 (80.0%)	8 (88.9%)	OR = 1.1 (95% CI –2.4–2.4)	32 (86.5%)	6 (85.7%)	OR = 1.2 (95% CI –2.2–2.2)
No (N = 6)	2 (10.0%)	3 (20.0%)	1 (10.1%)		5 (13.5%)	1 (14.3%)	
Heart failure				*P* = 0.006			*P* = 0.001
Yes (N = 32)	17 (85.0%)	12 (80.0%)	3 (33.3%)	OR = 2.4 (95% CI 0.7–4.2)	30 (81.1%)	2 (28.6%)	OR = 2.5 (95% CI 0.6–4.4)
No (N = 12)	3 (15.0%)	3 (20.0%)	6 (66.7%)		7 (18.9%)	5 (71.4%)	
MI				*P* = 0.5			*P* = 0.3
Yes (N = 30)	16 (80.0%)	8 (53.3%)	6 (66.7%)	OR = 0.04 (95% CI –1.3–2)	26 (70.3%)	4 (57.1%)	OR = 0.9 (95% CI –0.9–2.6)
No (N = 14)	4 (20.0%)	7 (46.7%)	3 (33.3%)		11 (29.7%)	3 (42.9%)	
BMI				*P* = 0.3			*P* = 0.2
<25 (N = 8)	4 (20.0%)	2 (13.3%)	2 (22.2%)	OR = 0.9 (95% CI –0.9–2.6)	6 (16.2%)	2 (28.6%)	OR = 0.8 (95% CI –0.8–2.4)
25.1–27 (N = 12)	6 (30.0%)	3 (20.0%)	3 (33.3%)		10 (27.0%)	2 (28.6%)	
>27 (N = 24)	10 (50.0%)	10 (66.7%)	4 (44.4%)		21 (56.8%)	3 (42.9%)	
Smoking				*P* = 0.001			*P* = 0.001
None (N = 6)	3 (15.0%)	2 (13.3%)	1 (10.1%)	OR = 2.5 (95% CI 0.7–4.4)	6 (16.2%)	0 (0%)	OR = 2.2 (95% CI 0.8–3.4)
Ex-smoker (N = 9)	3 (15.0%)	2 (13.3%)	4 (44.4%)		6 (16.2%)	3 (42.9%)	
Current (N = 29)	14 (70.0%)	11 (73.3%)	4 (44.4%)		25 (67.6%)	4 (57.1%)	
Number of comorbidities				*P* = 0.01			*P* = 0.4
≤2 (N = 8)	4 (20.0%)	3 (20.0%)	1 (11.1%)	OR = 1.8 (95% CI 0.8–2.2)	7 (18.9%)	1 (16.7%)	OR = 1.1 (95% CI –2.1–2.2)
>2 (N = 36)	16 (80.0%)	12 (80.0%)	8 (88.9%)		30 (81.1%)	6 (83.3%)	

*Chi-square test and calculation of odds ratio and 95% confidential interval.
Significance level at $P < 0.05$; percentages are calculated for categorical parameters of overall satisfaction and GEQ according to medical comorbidities.
BMI = body mass index; GEQ = global efficacy question; MI = myocardial infraction.

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 [17–20]. It has been concluded that the increase in coronary blood flow by EECP treatment is mainly through diastolic augmentation.

The hemodynamic effects of EECP have been theorized to simulate the clinical use of the intra-aortic balloon pump, enhancing cardiac output, stroke volume, and retrograde aortic diastolic flow. EECP produces hemodynamic changes that reduce myocardial oxygen demand in addition to potential for increased transmyocardial pressure to open collaterals. 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 [21–24]. This may help explain the long-term sustained benefits of EECP in our patients even after discontinuation of treatment. Supporting to that notion were the previous studies that clearly demonstrated the role of downregulation of nitric oxide synthase in vasculogenic ED, in addition to the restoration of erectile function following intracavernosal injection of vascular endothelial growth factor in animal model for arteriogenic ED [25,26].

In the current study, 63.9% of the patients were below the age of 60 years, 86.4% were current or ex-smokers, and more than 80% were overweight or obese. GEQ was significantly lower in older patients. Erectile function domain, Q3, and Q4 in pre- and post-EECP were negatively influenced by smoking. The influence of age, smoking, and obesity on both the prevalence and severity of ED and IHD is well established [2,16]. All patients had intractable angina not responding to the maxim pharmacotherapy, and all of them had moderate or severe ED. The high prevalence of severe ED in our patients could be explained by the postulation that a generalized atherosclerotic process that affects the arterial blood flow is a common cause of ED in patients with IHD. In the past, all patients had tried different modalities of ED treatment (90.9% had tried phosphodiesterase type 5 [PDE5] inhibitors, and 31.8% had tried intracavernosal injection of prostaglandin E1). Currently, 88.6% of the patients were using nitrate therapy on a daily base; therefore, there was no chance to use PDE5 inhibitors. To assess the impact of risk factors on the efficacy of EECP, no treatment for ED was offered to the patients during the study period.

There were significant differences in the severity of ED in pre- and post-EECP. There was a significant improvement of post-EECP anginal pain in 34/44 (77.3%) of the patients. Of them, 29/34 patients (85.3%) improved from class IV or III to class II, and the rest of them improved to class I. Four of five patients who had improved to class I had pre-EECP class III angina. It was noted that there was a significant decrease in the frequency of anginal episodes and nitrate usage. However, post-EECP objective assessment could better validate the results of the current study. In 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 [18,19]. EECP efficacy and overall satisfaction were not hindered by heart failure. These results indicated 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 [21,22]. Also, it might be easier for a patient to experience an improvement from class IV to III, as compared with lower classes.

Overall satisfaction and global efficacy were negatively influenced by smoking and presence of more than two risk factors. Diabetes, hypertension, dyslipidemia, MI, and obesity had no such effects on efficacy and overall satisfaction. However, the number of patients who had two risk factors or less is small to draw final conclusion. The sociodemographic variables were homogenous, and there were no significant differences between the studied groups regarding level of education, occupation, or marital status. This will eliminate the statistical effect of these factors on the efficacy of EECP and enable to draw the difference in response to EECP in both groups.

There were significant differences in erectile function domain, Q3, and Q4 between pre- and post-EECP application. In total, 79.5% and 84.1% of the patients were overall satisfied and answer positively regarding the global efficacy of EECP on sexual function.

Supporting to 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, several studies have reported that post-EECP benefit in pain and health-related quality-of-life measures continued for years [27–29].

We hypothesize that the efficacy rate of EECP in our study is somewhat high; this could be: (i) due to a more homogenous sample population, consisting exclusively of patients with CAD-associated ED; (ii) because we excluded all patients with decompensated heart failure, usually stages C and D, and patients with left ventricular ejection fraction <30%. A good portion of our patients had heart failure (stages A and B), and most of them had ED risk factors which pointed severe ED complaint, thus those patients might appreciate even a moderate improvement of their erectile function as a significant progress; and (iii) because collaboration with cardiologists allowed for modifications of patients' treatment (e.g., β-blockers, thiazide diuretics) and control of risk factors, as smoking, obesity, and sedentary lifestyle could also be important factors. However, further studies are warranted to assess the impact of controlling risk factors and medical comorbidities on the efficacy and the satisfaction rate of EECP in patients with CAD-associated ED.

In summary, the efficacy and satisfaction rate of EECP in patients with CAD-associated ED were negatively affected by presence of risk factors; however, the global efficacy and the overall patients' satisfaction were encouraging. Extrapolation of the cardiac positive impact of EECP on erectile function could be a potential explanation of post-EECP ED improvement. The mechanistic pathways are very interesting target for further research to delineate the influence of risk factors on the efficacy of EECP in patients with ED.

A potential methodological limitation of our study is the small number of patients and the lack of long-term follow-up data in this cohort group. Our results indicated that the efficacy and satisfaction rate of EECP in patients with CAD-associated ED, although were high, were negatively affected by presence of risk factors; however, the role of EECP in the treatment of those patients with IHD-associated ED has not yet been well defined. Large-scale trials and long-term data are needed to address the importance and limitation of incorporating this technique into the armamentarium of ED treatment in that selected group of patients.

Conclusions

The results of the current study demonstrated that the efficacy and the satisfaction rate of EECP in patients with CAD-associated ED were negatively affected by presence of risk factors; however, the global efficacy and the overall patients' satisfaction were encouraging. Large-scale trials and long-term data are warranted to address the role and limitations of EECP in patients with CAD-associated ED.

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