

# THERAPEUTIC EFFECTS OF ENHANCED EXTERNAL COUNTER PULSATION (EECP) ON CLINICAL SYMPTOMS, ECHOCARDIOGRAPHIC MEASUREMENTS, PERFUSION SCAN PARAMETERS AND EXERCISE TOLERANCE TEST IN CORONARY ARTERY DISEASE PATIENTS WITH REFRACTORY ANGINA

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## ABSTRACT

**Background:** The purpose of this study was finding relationship between the therapeutic effects of Enhanced External Counterpulsation on treatment resistant angina among the patients, who are unsuitable for invasive interventions.

**Aims & Objective:** To study the therapeutic effects of Enhanced External Counter Pulsation (EECP) on clinical symptoms, echocardiographic measurements, perfusion scan parameters and exercise tolerance test in coronary artery disease patients with refractory angina.

**Material and Methods:** In an interventional study 50 patients (34 men and 16 women) under EECP therapy were investigated for one year. This machine is composed of three pairs of cuffs which work by attaching cuffs to lower limbs and it is contracted during diastole from distal to proximal and makes pressure to vessels of lower limbs. Treatment effects of EECP on clinical signs were evaluated on the base of Canadian cardiovascular society classification for angina severity, drugs consumption and SF36 quality of life questionnaire. Para clinical assessments including echocardiography, perfusions scan and exercise tolerance test parameters were also assessed prior to EECP, at the end of the treatment and at 12 months thereafter. Any differences in background measurements were recorded and analyzed.

**Results:** Decrement of angina severity and improvement of life quality before and after one month EECP therapy was significant ( $p < 0.001$ ,  $p = 0.01$ ). The rate of nitrate consumption and other medications causes no significant difference concerning dosage decrease ( $p > 0.05$ ). There was significant difference between ejection fraction of before, one month and one year after treatment only in severe IHD ( $p = 0.016$ ,  $p = 0.038$ , respectively). Left ventricle end diastolic and end systolic diameters were also significantly decreased after one month ( $p = 0.031$ ), and this improvement remained up to one year. Difference between ischemia severity in perfusion scan before and one month afterwards was significant as well ( $p = 0.044$ ). The exercise tolerance test duration after one month also increased ( $p < 0.001$ ) and did not change statistically after one year.

**Conclusion:** This study demonstrated that EECP is a useful method, while effective and safe for patients with severe refractory angina pectoris resistant to drug therapy and aggressive interventions such as PCI or CABG are not suitable.

**KEY-WORDS:** Enhanced External Counter Pulsation (EECP); Refractory Angina; Coronary Artery Disease; Coronary Artery Bypass Grafting Surgery; Ischemia

## Introduction

Patients with CAD (coronary artery disease) who have chronic ischemic symptoms that are unresponsive to both conventional medical therapy and revascularization techniques have refractory angina pectoris (RAP). It has been estimated that greater than 100,000 patients each year in the US may be diagnosed as having this condition.<sup>[1,2]</sup> Patients with refractory angina pectoris (RAP) have marked limitation of ordinary

physical activity or are unable to perform any routine physical activity without discomfort (CCS functional class III/IV).<sup>[3]</sup>

Despite optimal medical therapy and invasive procedures, such as angioplasty and cardiac bypass surgery, there are an estimated 300,000 to 900,000 patients in the U.S. who have RAP.<sup>[4]</sup>

Concerning the patients with RAP who are not candidate for CABG (Coronary artery bypass grafting surgery) and PCI (Percutaneous coronary

intervention), because of specific anatomy of coronary arteries or despite maximum medical therapy are still symptomatic; other kinds of treatments such as enhanced external counter pulsation (EECP) could be considered as a good alternative.<sup>[5]</sup>

In general, this device is composed of three pairs of cuffs and monitoring system. It works by attaching of cuffs to lower limbs and it contracts during diastole from distal to proximal respectively and pressures to the vessels of lower limbs.<sup>[6]</sup>

Recent evidence suggests that EECP therapy may improve symptoms and decrease long-term morbidity via more than one mechanism including; improvement in endothelial function, promotion of collateralization, enhancement of ventricular function, improvement in oxygen consumption, regression of atherosclerosis, and peripheral training effects similar to exercise.<sup>[4]</sup>

EECP therapy represents the only truly non-invasive technique for which both a reduction of angina symptoms, improvement in objective measures of myocardial ischemia, and improvement in left ventricular function (both systolic and diastolic) have been shown in many studies.<sup>[7-9]</sup>

Nevertheless, the issue of EECP therapy in the ischemic heart disease or patients with heart failure has somewhat controversial scientific aspects.

Therefore, in the present study we aimed to evaluate the effects of EECP on different clinical indicators such as ; (1) angina severity, (2) drugs consumption, (3) quality of life as well as para clinical indices including; (a) left ventricle function, (b) myocardial perfusion status and (c) exercise tolerance test among the patients who were candidate for treatment by EECP.

## Materials and Methods

The study was set as pre and post interventional without control group. This research was carried out on the referred patients to physical medicine and rehabilitation ward of Educational Center of Imam Reza and Shahid Madani Hospitals from July

2008 to March 2010. Of course regarding to follow up one year after treatment, the study all of patients was finished by March 2011. Sampling method was simple numerical (accessible).

All of patients with coronary artery ischemic disease with required qualifications for this study were included to the research. Since some of the cases had no criteria for including to this research or their unwillingness, they were excluded from the study.

Inclusion Criteria were: (1) patients with minimal CAD and unsuitable response to medical treatment, (2) patients with Diffuse CAD with unsuitable response to medication, (3) CAD patients who were not eligible for CABG and PTCA (percutaneous trans coronary angioplasty), (4) patients with micro vascular disease angina, (5) Symptomatic patients with previous PTCA and no other visible vessel for revascularization, and (6) Symptomatic CABG patients with no other visible vessel for revascularization.

Exclusion Criteria were: (1) Arrhythmias which lead to functional disorders, (2) prone to bleeding, (3) active thrombophlebitis, (4) proved aortal aneurysm needed for surgery, (5) pregnancy, (6) patients with Severe AI (Aortic insufficiency), severe AS (Aortic stenosis) and severe MS (Mitral stenosis).

It should be mentioned that written consent was obtained from all patients before the study and this research was approved by regional ethics committee of Tabriz University of Medical Sciences.

Ultimately, 50 patients were enrolled and participated in this study. The prepared checklists by researcher were used for collecting data.

In this research, patients with coronary artery disease who had inclusion criteria, after determining of angina functional class in according CCS (Canadian cardiovascular society classification) by cardiologist were referred to outpatient cardiac rehabilitation ward. In CCS grading, angina is classified to four classes: Class 0: Asymptomatic; Class 1: Angina with strenuous exercise; Class 2: Angina with moderate exertion;

Class 3: Angina with mild exertion; Class 4: Angina at any level of physical exertion.<sup>[2]</sup>

Firstly, all demographic information, the existence of other diseases such as diabetes, chronic renal failure, history of CABG or PCI, amount and sort of consumed drugs were noted in a check list. Results of echocardiography parameters and exercise tolerance test and also myocardial perfusion scan were taken from the patients before EECP treatment and recorded in check list. SF36 standard life quality questionnaire was prepared in native language and was given to the patients before and after the treatment. They have to answer to different questions and finally a total score was given to them, before and after treatment.

Frequency of coronary artery diseases which included in the research and their gender classifications are presented in table 1.

**Table-1: Frequency of Diseases included in the Research and their Gender Classifications EECP Therapy Performance**

Patients with Following Inclusion Criteria, Enrolled in the Research	Gender		Total
	Male	Female	
1VD <sup>1</sup>	2	-	2
2VD	3	-	3
3VD	8	6	14
Minimal CAD <sup>2</sup>	2	3	5
Microvascular	2	-	2
Post CABG <sup>3</sup> patent grafts	8	4	12
Post CABG occluded grafts	7	1	8
Post PCI <sup>4</sup> patent stents	2	2	4
<b>Total</b>	<b>34</b>	<b>16</b>	<b>50</b>

<sup>1</sup> one vessel disease; <sup>2</sup> coronary artery disease; <sup>3</sup> coronary artery bypass grafting surgery; <sup>4</sup> percutaneous coronary intervention

Three pairs of pressuring cuffs of EECP were attached to pelvis, femur and calves of patients by related therapists and supervising of physiatrists. As already mentioned the cuffs are inflated during diastole, the venous return eases and deflated at the beginning of systole. This rhythmic inflation and deflation was continued for an hour by ECG controlling and monitoring. The number of sessions was 35 each one hour for every patient.<sup>[4,6]</sup> All of side effects and unexpected incidences such as occurrence of myocardial infarction (MI), hospitalization, arrhythmias, skin complications and so on were noted during one year.

EECP device, which was used for treatment of selected patients in this study, is shown in the figure 1.



**Figure-1A:** Enhanced External Counter Pulsation (EECP) therapy device in Shahid madani hospital, Physical Medicine and Rehabilitation Research center, Tabriz University of Medical Sciences



**Figure-1B:** Device is composed of three pairs of cuffs and monitoring system. By attaching of cuffs to lower limbs and pelvis during diastole it contracts from distal to proximal respectively and pressures to the vessels of lower limbs. Cuffs are inflated during diastole, the venous return eases and deflated at the beginning of systole.

### **Myocardial Perfusion Scan**

All candidate patients for EECP therapy were referred to nuclear medicine center for myocardial perfusion scan. For achieving optimal heart rate during stress test, 24- 48 hours before scan, the patients discontinued beta- blockers and calcium antagonists. Myocardial perfusion scan was carried out in one day rest-stress protocol. First, following 4 hours fasting, rest state scan was done by triple head Marconi IRIX gamma camera system 30 minute after intravenous injection of 8

millicurie (mCi)  $^{99m}\text{Tc}$ -MIBI (in ECG-gated SPECT (single photon emission computed tomography) mode. Four hours later stress phase scan was done in same mode following intravenous injection of 20 mCi  $^{99m}\text{Tc}$ -MIBI in the peak of stress (exercise test by Bruce protocol or pharmacologic stress with dipyridamole or dobutamine).<sup>[9]</sup> Obtained scan images of patients were interpreted by nuclear medicine specialist using advanced softwares (Autoquant and Emory tool box), qualitatively and quantitatively.

Measured variables by perfusion scan were assessed in three categories as follows:

1. *Severity of Myocardial Ischemia*: this variable was graded according to reduction of mean count density in involved segment at stress phase relative to mean count density in same segment at rest phase. There were four grades. Grade 1: Normal (no difference); Grade 2: Mild ischemia (< 10%); Grade 3: Moderate ischemia (10-15%); Grade 4 (>15%)
2. *Extent of Ischemic Myocardium (Number of Reversible Defects)*: this variable was the summed of reversible segments, which showed reversible perfusion defect between stress and rest phases images. Left ventricle was divided into 20 segments for assessment of this variable.<sup>[1]</sup>
3. *Extent of Infarcted Myocardium (Fixed Perfusion Defect)*: this variable was the summed of segments without radiotracer uptake, which showed no reversible perfusion defect between stress and rest phases images. For assessment of this variable left ventricle also was divided into 20 segments as mentioned above.

These obtained data concerning ischemia severity and extent were recorded before and one month after EECP therapy.

### **Method of Echocardiography**

Echocardiography was performed on the patients before EECP, one month and one year after EECP by fellowship of echocardiography professor using GE Vivid 7 echocardiography with medical transducer phased array for taking M-Mode (2D) images as well as trans thoracic doppler echocardiography and following variables including EF (ejection fraction), left ventricle end

diastolic and end systolic diameters and MPI (myocardial performance index) were measured and the results were compared together.

The later parameter is calculated as:  $\text{MPI} = (\text{IVRT} + \text{IVCT}) / \text{ET}$ , in which, IVRT is Isovolumic Relaxation Time, IVCT is Isovolumic Contraction Time and ET is ejection time.<sup>[2]</sup>

### **Exercise Test Method**

The patients were referred to exercise test before EECP, one month and a year after EECP.  $\beta$  blockers, Ca antagonists and Nitrates were cut 24-48 before exercise test. Exercise test was carried out 3-4 hours after empty stomach. This test was performed using RAM model 770 CE by Bruce protocol consisting of one minute warm up and 4 speed and steep increasing stages, each stage lasts 3 minutes. All of these stages were under direct supervision of cardiologist. The results were paraphrased by cardiologist. The rate of consumed oxygen was estimated on the basis of METs (Metabolic Equivalent) using the formula:  $\text{METs} = 1.11 + (0.016 \times \text{ETT time as second})$  and was recorded with METs coefficients.<sup>[7]</sup>

One month after finishing the treatment period by EECP, the obtained results from above assessments including functional class, life quality, drugs consumption, echocardiography parameters, exercise tolerance test and myocardial perfusion scan were totally recorded in check list by physiatrist. All of patients were visited by cardiologist during and after one year. The one-year follow ups were done for evaluation of stability and durability of therapeutic effects.

It should be mentioned myocardial scan was not performed again because of high expenses and possible complications.

### **Statistical Analysis**

The collected data were analyzed by SPSS version 15 and the results were expressed as Mean  $\pm$  SD. In order to comparing of quantitative variables of clinical symptoms, echocardiography findings, perfusion scan and exercise test before, one month and one year after EECP, Paired samples T-test was used. Chi Square statistical test was used for comparing of qualitative and ordinal variables. Normal distribution of data was evaluated by

kolmogorov - smirnov test. Confidence coefficient was 95% and P-value less than 0.05 was considered significant in this research.

## Results

### *Subjective Changes in Angina Severity Using Canadian Cardiovascular Society Scale*

Before treating by EECP, 2 patients (4%), were classified in class one, 26 patients (52%) in class two, 21 patients (42%) in class three and one patient (2%) classified in class four. One month after treatment it changed to 15 patients (30%) in class one, 26 patients (52%) in class two and 8 patients (16%) in class three (before first follow up there was one case of mortality). These variations and decrement in angina severity was completely significant by Chi Square test ( $p < 0.001$ ).

One year after treatment by EECP 16 patients (32%) were classified in class one, 18 patients (36%) in class two and 13 patients classified in class three (up to this time there was 3 mortalities). These variations were also significant in the comparison with the time before treatment by Chi Square ( $p = 0.001$ ). However, the difference of angina severity in these patients was not significant statistically after one year compared to one month after treatment ( $p = 0.229$ ).

### *Subjective Changes in Daily Drug Intake by Patients*

Mean of consumed nitrate dosage was  $7.97 \pm 6.85$  mg/day at the beginning of treatment. This amount reached to  $7.61 \pm 6.48$  mg/day one month after treating by EECP. This difference was not significant by Paired Sample T-Test ( $p = 0.344$ ). Mean of consumed nitrate dosage one year later was  $7.31 \pm 6.41$  mg/day which was not significantly different with beginning of treatment ( $p = 0.666$ ). Consumed  $\beta$  blockers mean at the start of treatment by EECP was  $47.30 \pm 36.39$  mg/day which reached to  $46.28 \pm 34.08$  mg/day. This was not significant by Paired Sample T-Test ( $p = 0.569$ ). The dosage mean after a year was  $46.65 \pm 34.66$  mg/day which represented no significant difference with the start of treatment ( $p = 0.568$ ). At the beginning of treatment mean of Ca blockers was  $4.28 \pm 6.35$  mg/day. One month after treating

by EECP it decreased to  $4.08 \pm 5.81$  mg/day. It was significantly different by Paired Sample T-Test ( $p = 0.322$ ). Also one year later, mean of consumed dosage of this drug group was  $4.14 \pm 5.90$  mg/day in patients and there was not any significant difference with the beginning of treatment ( $p = 0.323$ ). Mean of ACE inhibitor dosage was  $27.35 \pm 29.49$  mg/day for the onset of treatment. One month after treatment it decreased to  $26.84 \pm 29.31$  mg/day and there was no significant difference by Paired Sample T-Test ( $p = 0.322$ ). This mean reached to  $26.91 \pm 92.94$  mg/day after one year without any significant difference with the beginning of treatment ( $p = 0.323$ ).

### *Subjective Changes in Quality of Life Using SF36 Questionnaire*

Mean of SF36 questionnaire score for 50 patients at the onset of treatment was  $39.57 \pm 9.60$ . This rate increased to  $42.76 \pm 12.25$  and there was no significant difference by Paired sample T-Test statistical test ( $p = 0.010$ ). After one year this mean reached to  $45.74 \pm 12.36$  which indicated significant difference with first score on the basis of Paired sample T-Test ( $p > 0.001$ ). Furthermore, the results after one month was significantly different with those after one year ( $p = 0.014$ ).

### *Objective Changes in Ischemia Severity and Extent Using Myocardial Perfusion Scan*

From the viewpoint of ischemia severity, before treating by EECP 10 patients (20%) were in group I (no evidence of ischemia), 8 patients (16%) in group II (mild ischemia), 12 patients (24%) in group III (moderate ischemia) and 16 patients (32%) in group IV (severe ischemia). One month later, previous 12 patients presented in group I, 12 patients (24%) in group II, 12 patients in group III and 12 patients presented (24%) in group IV. This decline was significant by Paired Sample T-Test ( $p = 0.044$ ).

Mean extent of ischemic myocardial tissue in the participant patients before treatment was  $3.46 \pm 2.72$  segments, which was decreased to  $3.02 \pm 2.55$  segments after EECP. This difference was not significant by Paired Sample T-Test ( $p = 0.105$ ). Extent of scar tissue (fixed perfusion defects) was  $1.89 \pm 2.63$  segment in patients before treatment, which reached to  $1.74 \pm 2.61$  one month after

treatment. The difference was not significant by Paired Sample T-Test ( $p=0.051$ ).

### **Objective Changes in Ejection Fraction and End Diastolic and Systolic Diameters of Left Ventricle Using Echocardiograph**

Mean of EF before treatment was  $43.55 \pm 11.60$  that one month after EECP treatment increased to  $45.35 \pm 11.30$ . This difference was statistically significant by Paired Sample T-Test ( $p=0.016$ ). This mean was  $45.74 \pm 11.52$  one year after treatment which was significant in the comparison with EF amount before treatment by Paired Sample T-Test ( $p=0.038$ ). In addition to above investigation, we categorized patients in two groups: 1) patients with EF less than 40% (17 patients) and 2) patients with EF equal or higher than 40% (33 patients). Only in first group statistical tests emphasized on significant changes of EF ( $p=0.029$ ).

Diameter of left ventricular in end diastole (LVEDD) was  $5.03 \pm 0.96$  cm. It was  $4.85 \pm 0.89$  cm after one month which was significant based on Paired Sample T-Test ( $p=0.031$ ). One year after treatment mean of LVEDD was  $4.85 \pm 0.89$  cm which was not significant in comparison with first follow up measurement ( $p=0.164$ ).

Mean of end systolic diameter in left ventricle (LVESD) was  $3.84 \pm 0.94$  at the beginning of research. This amount reached to  $3.68 \pm 0.9$  and it was significant by Paired Sample T-test ( $p=0.032$ ). LVESD mean one year after onset of treatment was  $3.61 \pm 0.93$ , which was not different from one month after treatment ( $p=0.129$ ).

Mean of myocardial performance index (MPI) before treatment period was  $0.67 \pm 0.31$  that reached to  $0.65 \pm 0.26$  which was not significant by Paired Sample T-Test ( $p=0.204$ ). This mean was  $0.68 \pm 0.28$  one year after beginning of treatment and it was not different with the onset of treatment as well ( $p=0.459$ ).

### **Objective Changes in Consumed Energy and ST Depression in Exercise Tolerance Test**

Mean of exercise test duration before treatment was  $344.86 \pm 150.84$  sec. This amount increased to  $387.23 \pm 148.47$  sec which was completely significant by Paired Sample T-Test ( $p<0.001$ ).

One year after, this mean did not change significantly rather than before treatment and was  $387.00 \pm 158.96$  ( $p=0.087$ ).

Mean of consumed energy during exercise test was  $5.41 \pm 3.07$  METs before start of EECP treatment. One month later this time increased to  $6.34 \pm 3.12$  which was completely significant by Paired Sample T-Test ( $p<0.001$ ). After one year follow up, this mean was  $6.21 \pm 3.24$  that in the comparison with primary measurements indicated decrement, however, it was not significant ( $p=0.075$ ).

Mean of ST variations in ETT before treatment was  $0.41 \pm 0.76$  mm which one month after treatment was  $0.44 \pm 0.73$  mm, in spite of this increment, it was not significant by Paired Sample T-Test ( $p=0.723$ ). One year after treatment ST segment variations mean was  $0.43 \pm 0.68$  mm which indicated no significant difference ( $p=0.878$ ).

Changes in all of above mentioned clinical and paraclinical variables at baseline and after one-month EECP therapy are summarized in table 2.

**Table-2: Changes in Clinical and Paraclinical Variables between Baseline and After One Month EECP Therapy among Study Patients**

Variables	Before EECP	1 Month After EECP	p value
<b>Clinical Symptoms</b>			
Daily nitrates intake (mg/day)	$7.97 \pm 6.85$	$7.61 \pm 6.48$	0.34
Quality of life SF35 score	$39.57 \pm 9.60$	$42.76 \pm 12.25$	0.01
CCS <sup>a</sup> grading	42% in class III	16% in class III	<0.001
<b>Perfusion Scan</b>			
Ischemia severity grading	32% in group IV	24% in group IV	0.04
Extent of ischemic myocardium	$3.46 \pm 2.72$ segment	$3.02 \pm 2.55$ segment	0.10
Extent of infarcted myocardium	$1.89 \pm 2.63$ segment	$1.74 \pm 2.61$ segment	0.05
<b>Echocardiography</b>			
EF <sup>b</sup> (%)	$43.55 \pm 11.60$	$45.35 \pm 11.30$	0.01
LVEDD <sup>c</sup> (cm)	$5.03 \pm 0.96$	$4.85 \pm 0.89$	0.03
LVESD <sup>d</sup> (cm)	$3.84 \pm 0.94$	$3.68 \pm 0.9$	0.03
MPI <sup>e</sup>	$0.67 \pm 0.31$	$0.65 \pm 0.26$	0.20
<b>Exercise Tolerance Test</b>			
Exercise duration (sec)	$344.86 \pm 150.84$	$387.23 \pm 148.47$	<0.001
Consumed energy (METs)	$5.41 \pm 3.07$	$6.34 \pm 3.12$	<0.001
ST segment variations	$0.41 \pm 0.76$ mm	$0.44 \pm 0.73$ mm	0.72

<sup>a</sup> Canadian cardiovascular society classification; <sup>b</sup> Ejection fraction; <sup>c</sup> Left ventricle end diastolic diameter; <sup>d</sup> Left ventricle end systolic diameter; <sup>e</sup> myocardial performance index

## Discussion

Our investigations revealed that an EECP therapy cycle in CAD patients can increase the quality of their life efficiently. This increment has been obtained both in short term and long term life quality. Moreover, it was shown that EECP decreases angina severity on the basis of CCS in short term remarkably and its effect remained up to one year. Though, improvement of life quality and one year CCS angina class of patients can be attributed to placebo effects of EECP to some extent. But since these groups of patients do not respond to common treatments, any kind of treatment which, decreases chest pain of patients without any side effects could be considered rational.

Based on the perfusion scan findings in our research, EECP decreases the severity of ischemia in myocardial tissue significantly; in contrast, it did not have any considerable effects on ischemic tissue extent and size of scar or infarcted myocardium.

It was revealed by echocardiography parameters that EECP treats efficiently EF of patients in short term and this effect remains up to one year relatively.

Furthermore it was demonstrated that EECP therapy, in the cases with EF lower than 40% is definitely better. On the other hand, in patients with EF higher than 40%, no significant changes were observed.

Also end diastolic diameter of left ventricle was decreased significantly in short term, however, long term variations were not remarkable. Similar alterations were true about end systolic diameter of left ventricle. But EECP did not affect distinctly on the rate of left ventricular septum movement. Moreover, Myocardial Performance Index (MPI) did not show considerable changes in this study.

It should be noticed that EF, LVEDD and LVESD are extremely volume dependent parameters that can justify the differences between several studies in this field. Since MPI is a completely independent parameter of patient volume status, so it can describe effects of EECP treatment on

cardiac performance better than above mentioned parameters. In this study there was no significant difference between MPI of before, one month and one year later in our patients.

In a comprehensive study by Urano et al. in Japan, EECP improved exercise endurance, reduced perfusion defects and improved left ventricular diastolic function via increasing of filling rate in thallium scan of patients with stable CAD.<sup>[4]</sup>

In our research EECP increased exercise endurance and decreased myocardial tissue ischemia in short term significantly. However, it did not have any considerable effects on decreasing of perfusion defects in ischemic or infarcted myocardium.

In a study performed by Holubkov et al., two treatment methods of PCI and EECP were compared each other. The overall results indicated that EECP could be considered as an alternative treatment for PCI candidates. This study recommends EECP as a proper choice for suitable CAD patients.<sup>[5]</sup>

Our study results confirm above findings and suggest EECP as an appropriate alternative treatment in the cases that PCI does not have suitable efficacy.

In a research by Petterson et al., on 55 patients with refractory angina, the beneficial effects of EECP was proved again. A notable point is that patients with severe ischemic problems and higher functional class of angina (class III/IV) achieved better outcome than the others.<sup>[6]</sup>

In present research 50 patients were participated. Regarding to improvement of clinical and echocardiography parameters, decreasing of ischemia severity and increasing of exercise test endurance; EECP could be considered as useful procedure for such patients. EECP effects on severe angina were more effective in our study as well.

In an another study performed by Loh et al. on 58 patients with chronic refractory angina resistant to treatment, short and long term positive effects of EECP were revealed. Most of cases obtained

better angina functional class.<sup>[10]</sup> Amount of nitrates' consumption and frequency of angina attacks were also decreased. This study recommends EECP as a beneficial and safe treatment method for patients who do not respond to routine interventions.<sup>[10]</sup>

Our study demonstrated that positive effects of EECP on CAD patients in short and long term too. Mean of exercise time also increased, but the amount of nitrate consumption did not decrease markedly.

Ozlem Soran et al., evaluated 363 patients with LV ejection fraction  $\leq 35\%$ . After a treatment period by EECP these effects were observed in most of patients: life quality improvement, decrement of nitrate consumption and relative improvement of angina severity.<sup>[11]</sup>

In a research by Yavari et al. carried out in Iran, EECP had beneficial clinical effects. The results of this study on 67 patients, revealed that improvement in the field of exercise test and functional class of angina. However, this study did not prove the improvement of echocardiography parameters including EF and LV end diastolic diameters.<sup>[12]</sup>

A research by Kumar et al. on 47 patients with RAP, indicated that clinical symptoms such as angina pain and dyspnea decreased and not only life quality but also the walking distance in 6 minutes walking test improved significantly. Of course, similar to above mentioned study, there was not detected any significant relation between EF, LVEED and LVESD with treatment process.<sup>[13]</sup>

In the present survey, in addition to improvement of life quality factors, exercise duration and resistance of patients were increased. These results are in agreement with Kumar et al. findings. However, our study revealed that EECP could be completely beneficial for patients with severe disease and EF less than 40%.

Erliding and colleagues demonstrated that EECP could be more effective in patients with more severe angina (based on CCS). Moreover, its long term effects would be useful and relatively persistent.<sup>[14]</sup>

Our findings also verified positive effects of EECP in short term and somewhat in long term in the field of refractory angina treatment.

One of the last studies in this regard which was carried out by Kozdog et al., have shown beneficial effects of EECP in CAD patients again. Results of this research demonstrated improvement of clinical and some of biochemical parameters, which are mostly prognostic markers in patients with symptomatic CAD and chronic heart failure.<sup>[15]</sup>

## Conclusion

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This study clarified that EECP is a profitable, effective and yet a safe method for patients with severe angina and resistant to medical treatment who are not appropriate for PCI and CABG interventions.

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