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Original Article

Can enhanced external counter pulsation as a non-invasive modality be useful in patients with ischemic cardiomyopathy after coronary artery bypass grafting?

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ABSTRACT

Background: Angina symptom in patients with ischemic cardiomyopathy (ICM) after coronary artery bypass grafting (CABG) surgery is a major challenging problem in practice. The choice among different treatment modalities available can be judged by different parameters especially measuring the risk/cost ratio to achieve the benefit. Enhanced external counter pulsation (EECP) is one of safest noninvasive modality for treatment of angina as well as it has an anti-failure effect.

Patients and method: 42 patients with ICM after CABG were suffering from stable angina and were treated at Al-Hayat Cardiology Centre in Tanta City (ACC). 20 patients of them (group A) received 35 sessions of EECP plus their anti-ischemic and anti-failure treatment, while the other 22 patients (group B) received only medical treatment and were followed up for 3 months regarding their angina class, functional class, frequency of angina attack, frequency of sublingual nitrate and rate of rehospitalization when needed during follow up period.

Results: Despite both groups had nearly similar severity of symptoms regarding the CCS class and NYHA class, yet patients in group A experienced significant improvement in comparison to patients in group B (p-value = .005, p-value = .002 respectively), and this was reflected on frequency of angina and need for sublingual nitrates per week which showed significant decrease in group A (p-value = .001).

Conclusion: As a non-invasive treatment modality EECP is very effective in improving the symptoms of angina and heart failure when combined with medical treatment in patients with ICM after CABG.

1. Introduction

The negative impact of angina and heart failure symptoms after CABG on patient's quality of life is a well-known problem.[1]

The re-intervention by per cutaneous intervention (PCI) or redo CABG is not without high perioperative risk to treat such patients and sometimes such intervention is not feasible.[2]

Transmyocardial laser revascularization, Angiogenic therapy through the intracoronary or intramyocardial administration of growth factors or through gene therapy, or spinal cord stimulation all are different modalities have been studied in clinical trials to assess their efficacy in treating refractory angina.[3–5]

Prior studies have demonstrated the effectiveness of EECP in treating the refractory angina and improving the CCS class to the patients.[6]

Our objective in this study is see how much effective is the EECP as a non-invasive modality in improving angina and functional class in patients with ischemic cardiomyopathy after CABG in comparison to medical treatment only.

2. Patients and methods

From January 2015 to January 2017, a prospective, controlled and randomized study was carried out at Al-Hayat cardiology Centre (ACC); a private medical Centre specialized in cardiac patients care and registered at Ministry of health in Tanta city, Arab Republic of Egypt.

42 patients with angina and poor functional class due to ICM after CABG had their medical consultation and treatment at the Centre.

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Patients included in this study (n = 42) were allocated into two groups, group A (n = 20) included patients who received 35 sessions of EECP (Patients are treated for a one-hour daily program for a total of 35 sessions over 7 weeks according to recommendation of European Society of Cardiology) plus their medical treatment, and group B (n = 22) included patients who received medical treatment only.

Direct consultation with the patients at the Centre was used to assess angina and heart failure classification. The Canadian Cardiovascular Society Functional (CCS) Classification was used to stratify the degree of angina. Heart failure status was assessed using the New York Heart Association (NYHA) Functional Classification. All of them were classified in NYHA class III or IV, their left ventricular function were impaired (ischemic cardiomyopathy) i.e. which is defined as the presence of left ventricular dilatation and systolic dysfunction with ejection fraction less than 45%.[7] LV EF for patients in group A was 40.85 ± 5.29%, and in group B was 43.00 ± 6.05%.

All patients included in this study had a clear data of having complete revascularization during their CABG surgery, under full and optimal anti angina and anti-failure medical therapy. ECG study was done daily before each session.

All patients must have echocardiographic study and whole arterial and venous duplex for lower limbs and carotid arteries as well as the abdominal aorta using (MySono U6 Samsung Medison machine) equipped with a multi frequency 2.5–4.0 MHz phased array transducer, the Duplex examination was performed using Linear transducer 5–10 MHz.

The ejection fraction "EF%" was calculated using biplane Simpson method. Diastolic dysfunction was assessed by tissue Doppler imaging which was used to measure mitral annular velocities. The peak systolic "S", early diastolic "E", atrial diastole "A" velocities were measured at both the mitral septal and lateral annulus, and the mean was taken E/E (Ratio between mitral flow E Velocity & Mitral annular E velocity). However, we did not take the diastolic dysfunction as a point of research in this study.

We excluded any patient with arterial aneurysms, deep vein thrombosis, severe aortic regurgitation which considered a contraindication for EECP and their INR should not exceed 1.5 if patients on warfarin.

Having a coronary angiographic study to determine the exact coronary lesion at the time of medical consultation was discussed with all patients, but patients included in this study preferred to try a non-invasive protocol of management either patients in group A or group B. Those who decided to have angiographic study and treated invasively were excluded.

The study was approved by the Human Ethics Committee and patient consent was waived.

2.1. The mechanism of action of EECP machine

The EECP machine used at ACC is the one manufactured by PSK Company (Chongqing PSK-Health Sci-tech Development Co., Ltd).

Our EECP machine model is (T1- touch screen); it consists of a treatment table, an air compressor, a console, two sets of three cuffs and pulse oximetry. Patient's calves, lower thighs and upper thighs are wrapped in 3 compressive pneumatic cuffs during the EECP session.

It works like the intra-aortic balloon regarding the mechanism of action which is based on trigger induced by electrocardiogram (ECG), where the sequential compression of the leg vessels through the cuffs started from distal to proximal in early diastole and then rapid deflation to the cuffs at the onset of systole.

The diastolic pressure (diastolic augmentation) increased by 93% due to rapid inflation, increasing perfusion pressure and myocardial perfusion. The Peak coronary flow velocity was measured in other clinical studies and it increases by 109%. A decrease in systolic pressure (systolic unloading) by 15% in the aorta and coronary arteries and improved ventricular unloading is induced by the rapid cuff deflation which promotes lower extremity arterial "runoff". Unlike the IABP, EECP also increases venous return, further promoting an increase in cardiac output.[8]

Patients in group A completed 35 sessions of treatment, each session is one hour per day for 5 days per week for 7 weeks, the pressure applied in this study was 220–250 mmHg. During the sessions, the patients are monitored by the responsible nurse staff and a cardiologist at the Centre.

2.2. Statistical analysis

The collected data were organized, tabulated and statistically analyzed using the Statistical Package for the Social Sciences software (SPSS, Chicago) version 22. For quantitative data, the range, mean and standard deviation were calculated. For qualitative data, the comparison between two groups and more was done using Chi-square test ($\chi 2$). For comparison between means of two groups of parametric data, student t-test was used.

3. Results

There were 42 patients included in the study, 20 patients in group A and 22 in group B. Both groups were comparable and showed no significant differences in demographic data, patient's risk factors, and a number of grafts in their CABG surgery (Table 1).

Table 2 summaries the changes in clinical variables regarding LVEF, the frequency of angina attacks per week, the frequency for sublingual nitrates per week; CCS and NYHA class at the start of the treatment and after 3 months follow up in each group.

Table 3 shows the comparisons between both groups regarding the same clinical variables as well as the rate of hospitalization if needed for any of the patients in either group during the period of follow up.

Figs. 1 and 2: summaries the clinical changes in CCS and NYHA class between patients in both groups.

4. Discussion

Medical treatment only for patients with angina and ICM who survived complex or diffuse coronary artery disease after CABG is associated with poor prognosis and poor quality of life during their follow up period.[9–11]

The selection of patients with severe ischemic cardiomyopathy for surgical revascularization is complex and involves the consideration of many clinical variables with a good estimation of both expected morbidity and mortality outcome especially in re-intervention scenarios.[12]

In our practice, when we discuss the available lines of treatment in such group of patients, they always asking for a none or less invasive treatment modality with zero or lowest side effects to improve their angina symptoms and their functional class especially those who experienced morbid out come after surgery.

In our study, we decided to study the effect of EECP in our patients with ischemic cardiomyopathy and suffering from angina in comparison to another group of patients who received the medical treatment only in the form of nitrates, beta-adrenoreceptor antagonists, calcium channel blockers, diuretic, ACI and aspirin.

Despite EECP is a U.S. Food and Drug Administration approved therapy as noninvasive therapy for patients with coronary artery disease and suffering from refractory angina as well as it received Class II a recommendation in European Society of Cardiology Guidelines for the Management of Stable Coronary Artery Disease, 2013,[13,14] yet in Egypt there is a very few centres haves such a

Table 1
Demographic and clinical data of the patients Qualitative data were described using number and percent, quantitative data was expressed in mean ± SD and was compared using student t-test.

		Group A	Group B	P-value
Age	Range	44–65	47–70	.082
	Mean ± S.D	55.25 ± 7.69	59.64 ± 8.2	
Sex	Male (%)	8 (40%)	8 (36.4%)	.808
	Female (%)	12 (60%)	14 (63.6%)	
No. of grafting vessels	2 (%)	7 (35%)	3 (13.6%)	.448
	3 (%)	8 (40%)	12 (54.5%)	
	4 (%)	3 (15%)	4 (18.2%)	
	5 (%)	2 (10%)	3 (13.6%)	
Smoker	Yes (%)	2 (10%)	4 (18.2%)	.449
	No (%)	18 (90%)	18 (81.8%)	
D M	Yes (%)	16 (80%)	14 (63.6%)	.241
	No (%)	4 (20%)	8 (36.4%)	
HTN	Yes (%)	13 (65%)	19 (86.4%)	.104
	No (%)	7 (35%)	3 (13.6%)	
Hypercholesterolemia	Yes (%)	14 (70%)	12 (54.5%)	.449
	No (%)	6 (30%)	10 (45.5%)	

*: Statistically significant at $p \leq .05$
Group A: Patients treated by medical treatment plus EECP.
Group B: Patients treated medically only.

Table 2
Clinical evaluation of the patients at the start of the treatment and after 3 months follows up, comparison between both groups. Continuous variables were expressed as mean ± SD and was compared using student t-test, categorical variables were number (%) and was compared using Chi-square test.

		Group A	Group B	P. value
LVEF at the start of treatment		40.85 ± 5.29	43.00 ± 6.05	.229
LVEF after 3 months follow up		43.15 ± 3.22	43.55 ± 4.85	.760
Angina frequency at the start of treatment		9.90 ± 2.67	9.55 ± 2.28	.646
Angina frequency after 3 months follow up		1.40 ± 2.06	6.86 ± 3.44	.001*
Frequency of SL nitrate use at the start of treatment		6.86 ± 3.44	9.05 ± 2.01	.106
Frequency of SL nitrate use after 3 months follow up		0.65 ± 0.93	6.59 ± 2.99	.001*
Admission to hospital		0.10 ± 0.31	0.95 ± 1.13	.002*
		Group A	Group B	P. value
CCS at the start of treatment	II (%)	1 (5%)	0 (0%)	.236
	III (%)	11 (55%)	17 (77.3%)	
	IV (%)	8 (40%)	5 (22.7%)	
CCS after 3 months follow up	I (%)	11 (55%)	3 (13.6%)	.005*
	II (%)	7 (35%)	8 (36.4%)	
	III (%)	2 (10%)	11 (50%)	
NYHA at the start of treatment	III (%)	13 (65%)	9 (40.9%)	.118
	IV (%)	7 (35%)	13 (59.1%)	
NYHA after 3 months follow up	I (%)	11 (55%)	2 (9.1%)	.002*
	II (%)	7 (35%)	7 (31.8%)	
	III (%)	2 (10%)	9 (40.9%)	
	IV (%)	0 (0%)	4 (18.2%)	

Group A: Patients treated by medical treatment plus EECP.
Group B: Patients treated medically only.
* Statistically significant at $p \leq .05$.

machine. And our study considered the first one in Egypt which considered this topic.

During the follow-up period in our study, there was no mortality in either group but there were 3 patients in group B who needed to be hospitalized due to uncontrolled symptoms in outpatient treatment. Such observation can be supported by significant improvement in CCS class and NYHA class in group A in comparison to group B after 3 months follow up.

The symptoms of heart failure improved despite the LVEF showed no significant increase in either group.

Also in our study, the frequency of angina attacks and the need for sublingual nitrates decreased dramatically and significantly in group A in comparison to group B, despite no significant ECG changes in patients who received EECP treatment.

Our results are in agreement with a lot of previous studies and the MUST_EECP (Multicentre study of enhancing external counterpulsation) which is the first multicentre study published approved the efficacy of EECP in controlling the symptoms of refractory angina.[15]

In another study done by Lawson et (2003) who used a more objective tool of judgment as they proved the significant improvement in the perfusion defects by the radionuclide stress testing after using the EECP.[16]

Another studies also proved the significant effect of EECP on functional capacity and quality of life in patients with congestive heart failure.[17,18]

The non-significant changes in LVEF in our patients after EECP was also in agreement with study by Myavari et al. in 2007 who

Table 3
Clinical evaluation of the patients at the start of the treatment and after 3 months follows up in each group. Continuous variables were expressed as mean ± SD and was compared using student t-test, categorical variables were number (%) and was compared using Chi-square test.

		At the start of treatment	After 3 months follow up	P. value
LVEF A		40.85 ± 5.29	43.15 ± 3.22	.105
LVEF B		43.00 ± 6.05	43.55 ± 4.85	.741
Angina frequency A		9.90 ± 2.67	1.40 ± 2.06	.001*
Angina frequency B		9.55 ± 2.28	6.86 ± 3.44	.004*
Frequency of SL nitrate use A		8.10 ± 1.65	0.65 ± 0.93	.001*
Frequency of SL nitrate use B		9.05 ± 2.01	6.59 ± 2.99	.003*
		At the start of treatment	After 3 months follow up	P. value
CCS A	I (%)	0 (0%)	11 (55%)	.001*
	II (%)	1 (5%)	7 (35%)	
	III (%)	11 (55%)	2 (10%)	
	IV (%)	8 (40%)	0 (0%)	
CCS B	I (%)	0 (0%)	3 (13.6%)	.001*
	II (%)	0 (0%)	8 (36.4%)	
	III (%)	17 (77.3%)	11 (50%)	
	IV (%)	5 (22.7)	0 (0%)	
NYHA A	I (%)	0 (0%)	11 (55%)	.001*
	II (%)	0 (0%)	7 (14%)	
	III (%)	13 (65%)	2 (10%)	
	IV (%)	7 (35%)	0 (0%)	
NYHA B	I (%)	0 (0%)	2 (9.1%)	.003*
	II (%)	0 (0%)	7 (31.8%)	
	III (%)	9 (40.9%)	9 (40.9%)	
	IV (%)	13 (59.1)	4 (18.2%)	

Group A: Patients treated by medical treatment plus EECP.
Group B: Patients treated medically only.
* Statistically significant at $p \leq .05$.

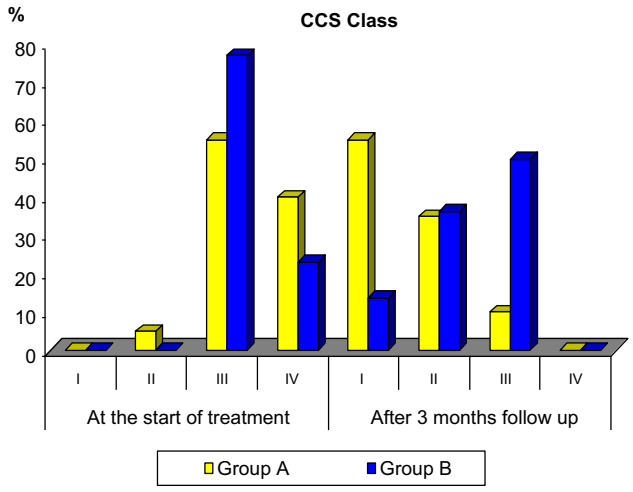

Fig. 1. Comparison as regard changes in CCS class between both groups at the start of treatment and after 3 months follow up.

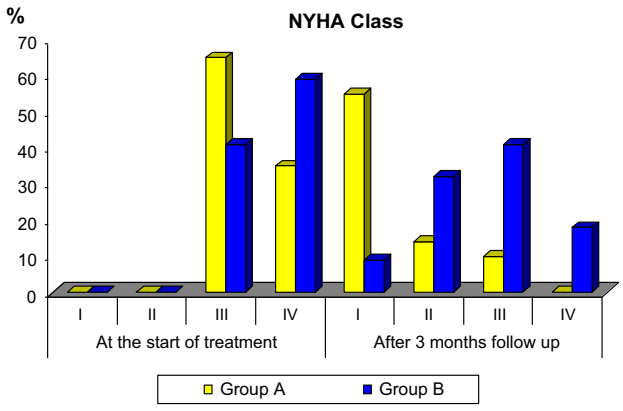

Fig. 2. Comparison as regard changes in NYHA class between both groups at the start of treatment and after 3 months follow up.

proved no differences in LVESD, LVEDD and ejection fraction before and after EECP treatment.[19]

On the contrary, Kozdag et al. (2012), proved significant improvement in LVEF using EECP in patients with ischemic heart failure.[20]

Such superior and adding benefits of EECP to our patients over medical treatment only as proved in our study cannot be explained only by the placebo effect as was claimed before by Springer et al. about the psychosocial effect of EECP in angina patients.[21]

Bonetti et al. proved that the long-term effect of EECP mediated through shear stress on vascular endothelium which triggers angiogenesis and improves vascular endothelial function.[22]

Also in a recent study by Darren et al. (2015), who proved that the improvement in heart failure class after EECP due to ventricular- vascular interactions through a reduction in central blood pressure, aortic pulse pressure, wasted left ventricular energy, and myocardial oxygen demand.[23]

Exposure to smoking or other causes, results in the release of vasoactive substances that negate the effect of shear stress may be the cause of impairment of the long-term effect of EECP and possibility of recurring some angina symptoms to the patients.[24,25]

5. Conclusion

As a non-invasive treatment modality, EECP is very effective in improving the symptoms of angina and heart failure when combined with medical treatment in patients with ICM after CABG.

6. Conflicts of interest

None.

7. Notes

Our results does not under estimate the value of PCI or re -do CABG in treating patients with angina and ICM after CABG, but rather prove that offering a non-invasive treatment modality without major complications in such patients could be a good choice.

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