Section: Cardiology

Original Research Article

EFFICACY OF TREATMENT WITH ENHANCED EXTERNAL COUNTER PULSATION IN CORONARY ARTERY DISEASE OR HEART FAILURE: FINDINGS FROM AN INDIAN REGISTRY-BASED STUDY

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Abstract

Background: The present study evaluated the efficacy of enhanced external counterpulsation (EECP) in patients with coronary artery disease or heart failure who were unable or not willing to undergo coronary artery bypass graft or percutaneous coronary intervention. **Materials and Methods:** This was a retrospective, registry-based study conducted in a healthcare setting in Western India. Medical charts of patients already treated with EECP between January 2017 and October 2022 from patient medical records were reviewed. The results were statistically analysed, and $p<0.05$ was considered significant. **Result:** The mean age of the 181 patients included in this study was 56.56 ± 10.01 years, with a majority belonging to the male gender (83%). More than 35% patients had hypertension and diabetes mellitus each. A statistically significant difference was observed in the presence and absence of angina ($p<0.0001$), and dyspnea ($p=0.0416$), and LVEF (44.53 ± 14.45 % vs 49.14 ± 12.02 %), TMT time (7.07 ± 3.93 s vs 9.44 ± 3.76 s), VO_{2max} (19.05 ± 9.92 mL/kg/min vs 24.59 ± 10.71 mL/kg/min) and MET values (5.44 ± 2.83 vs 7.03 ± 3.05) before and after EECP. **Conclusion:** The findings of this registry-based study suggest that EECP therapy may be considered an effective non-invasive alternative therapy for patients with coronary artery disease or heart failure who are unable to undergo coronary artery bypass graft or percutaneous coronary intervention.

INTRODUCTION

Heart failure (HF) continues to remain a major health issue worldwide. It is a major cause of cardiac disease in around 8–10 million people across the globe; nearly 120,000 to 200,000 deaths per year (accounting for 15–20% of all deaths) in India are attributable to first-time heart attacks. Compared with the Western population, Indian patients with HF are younger, sicker, with greater morbidity and mortality rates.[1] After the age of 45, the lifetime risk of HF remains significantly high, varying between 20% and 45% amongst racial and ethnic groups. Secular trends have shown that, while the incidence of HF with intact ejection fraction (EF) is rising, that with reduced EF is declining.[2] Despite an abundance of recent diagnostic and therapeutic advancements, those suffering from HF continue to receive suboptimal care.[3]

Enhanced external counterpulsation (EECP), a non-invasive external counterpulsation device, has gradually become more popular as a treatment for chronic angina over the past several years.[4] The United States Food and Drug Administration (US FDA) initially approved the use of EECP in 2002 for the treatment of patients with congestive heart failure, stable or unstable angina pectoris, acute myocardial infarction, or cardiogenic shock.[5] EECP is an outpatient, non-invasive treatment involving ECG-gated successive leg compression with hemodynamic outcomes that are identical to those of an intraaortic balloon pump (IABP). Over the years, EECP has demonstrated improvements in exercise-induced myocardial perfusion, angina symptoms, exercise tolerance, as well as quality of life in patients with coronary artery disease (CAD). Furthermore, EECP has also been shown to be well-tolerated and efficient in people with severe left ventricular dysfunction (LVD) and angina.[4]

EECP employs three sets of pneumatic cuffs that result in sequential contraction during diastole, raised aortic diastolic pressure, coronary blood flow, and central venous return. This technique seems to enhance myocardial perfusion by augmenting coronary vasodilation and angiogenesis, which are stimulated by nitric oxide and vascular endothelial growth factor (VEGF).[3,6] Moreover, research has shown that EECP therapy acts by increasing shear stress on the endothelium and activating mechanoreceptors and their signalling pathways

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which regulate endothelial function and morphology. This can, in turn, prevent future cardiovascular events.[7]

The coronary artery bypass graft (CABG) and percutaneous coronary intervention (PCI) have been the primary treatments for revascularization in stable CAD. However, there are many situations where these therapies are deemed unsuitable in several CAD patients.[8-10] In such scenarios, the EECP can be used as an alternative therapy. Nevertheless, there is little evidence in India evaluating the effect of EECP in coronary conditions where CABG or PCI cannot be considered an option. The present study was therefore conducted with an aim to evaluate the efficacy of EECP in patients with CAD or HF where CABG or PCI were not feasible.

MATERIALS AND METHODS

This retrospective, registry-based study was conducted in an advanced healthcare centre in Western India. In this study, we reviewed medical charts of patients with CAD already treated with EECP from patient medical records between January 2017 and October 2022. The study conduct complied with Good Clinical Practice Guidelines, the Declaration of Helsinki, and applicable local laws in India.

Patients

The target population consisted of patients diagnosed with CAD or HF who could not undergo CABG or PCI. The inclusion criteria for this study were patients of all age groups, both genders, those who had CAD or HF, post-CABG and post-PCI patients with angina, patients in whom CABG or PCI were not feasible and those unwilling to undergo PCI or CABG. Patients with significant aortic regurgitation (AR), DVT, uncontrolled arrhythmia, uncontrolled hypertension, aortic aneurysms and pregnant women were excluded from the study.

Statistical Analysis

Medical records between January 2017 and October 2022 revealed data for 181 patients with CAD/HF who did not undergo CABG or PCI and were hence treated with EECP. Quantitative variables were calculated as mean ± standard deviation (SD) or median (range; first quartile, third quartile). Qualitative variables were summarized as proportions and frequencies. All tests were two-sided, and $p<0.05$ was considered significant (unless otherwise specified). All statistical analyses were performed using SAS version 9.4 (SAS Institute, Inc., Cary, NC, USA).

RESULTS

A total of 181 patients were included in this study. The baseline demographic characteristics of our study population is summarized in [Table 1]. The youngest patient enrolled was aged 27 years and the eldest was 83 years old. The median number of EECP sessions required were 35 and ranged between 35 and 45.

[Table 2] compares various parameters before and after EECP in the study population. A significant difference was observed in the presence and absence of angina, dyspnea, LVEF, TMT time, VO2max and MET values [Figure 2] before and after EECP.

Table 1: Patient demographic characteristics

Parameter	Values
Age (years), mean ± SD	56.56 ± 10.01
Gender, n (%)	
Males	151 (83.43)
Females	30 (16.57)
Previous cardiovascular interventions, n (%)	
CABG	8 (4.42)
PTCA	35 (19.34)
Coronary artery disease, n (%)	
Yes	177 (97.79)
No	4 (2.21)
Comorbidities, n (%)	
Diabetes mellitus	63 (34.81)
Hypertension	67 (37.02)
Chronic kidney disease	5 (2.76)

Table 2: Comparison of parameters before and after EECP

Parameter	Pre-EECP	Post-EECP	p-value
Angina class, n (%)			<0.0001*
Yes			
I	23 (12.71)	72 (39.78)	
II	90 (49.72)	1 (0.55)	
III	2 (1.10)	0 (0)	
No	66 (36.46)	108 (59.67)	
DOE class, n (%)			0.0416*
Yes			
I	12 (6.63)	61 (33.70)	
II	59 (32.60)	2 (1.10)	
III	11 (6.08)	0 (0)	
No	99 (54.70)	118 (65.19)	

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LVEF (%), mean ± SD	44.53 ± 14.45	49.14 ± 12.02	<0.0001#
TMT time (s), mean ± SD	7.07 ± 3.93	9.44 ± 3.76	<0.0001#
VO2max (mL/kg/min), mean ± SD	19.05 ± 9.92	24.59 ± 10.71	<0.0001#
MET value, mean ± SD	5.44 ± 2.83	7.03 ± 3.05	<0.0001#
*Calculated using the chi-square test. P<0.05 considered statistically significant. #Calculated using the student's paired t-test. P<0.05 considered statistically significant.			

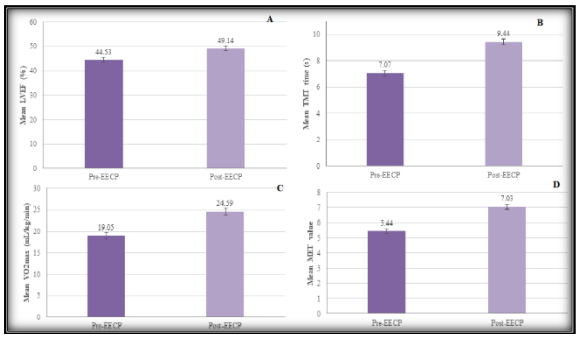

Figure 1: compares the mean (A) LVEF (B) TMT time (C) VO2max and (D) MET value.

DISCUSSION

EECP therapy is the only mechanical therapy that has proven its effectiveness in improving both myocardial supply in angina patients, and endothelial function, and reducing myocardial demand.[11] A number of studies have demonstrated positive clinical responses to EECP, and comprise of increase in exercise tolerance, reductions in angina and nitrate use, and enhanced quality of life. Considering the advantages of EECP, that are not limited to its non-invasive nature, proven positive clinical outcomes, relative low cost compared to surgical cardiac treatments, EECP might possibly be considered as first-line treatment option with invasive revascularization reserved for EECP failures.[12] This cross-sectional, retrospective, registry-based study was conducted to examine the efficacy of EECP in patients with CAD or HF, in whom CABG or PCI were not an option. Previous studies across the world have demonstrated similar findings over the last few decades.

The landmark Multi-center study of Enhanced External Counter Pulsation (MUST-EECP) trial was a multicentre, blinded study which randomly assigned 139 patients to either full-dose EECP or a sham method with minimal pressures. There was no significant difference in the distribution of patients with inactive or active CP for the different Canadian Cardiovascular Society (CCS) classes (I, 25.8% vs 26.8%; II, 51.5% vs 49.3%; III, 22.7% vs 23.9%; p>0.9). A statistically significant difference was noted in the mean exercise duration in both patients with inactive CP (432 ± 22 s, pre-EECP vs. 464 ± 22 s post-EECP; p<0.03) and with active CP (426 ± 20 s vs 470 ± 20 s respectively; p<0.001). Furthermore, after one month of EECP treatment, a significant increase in time to ST segment depression on stress testing and significant decreases in angina frequency was observed. The MUST-EECP trial proved its effectiveness against exercise-induced ischemia in patients with symptomatic CAD.[13]

Eslamian F et al performed a prospective interventional study to assess the therapeutic effects of EECP on clinical symptoms, echocardiographic measurements, perfusion scan parameters and exercise tolerance test in CAD patients with refractory angina. Compared with baseline (43.55 ± 11.60 %), they found a significant difference in EF at one-month (45.35 ± 11.30 %; p=0.016) and after one-year (45.74 ± 11.52 %; p=0.038) of EECP treatment. In addition, treatment with EECP resulted in significant reduction in angina severity (p<0.001), and increase in the mean exercise test duration (344.86 ± 150.84 s, at baseline vs 387.23 ± 148.47 s, after one-month; p<0.001).[14] Lawson WE and colleagues assessed the long-term prognosis of 33 patients with angina treated with EECP. Of these, 79% responded to the treatment while the remaining 21% were non-responders. Over the 5-year follow-up period, subsequent major adverse cardiovascular events (MACE) included four deaths and eight patients with cardiovascular events. Non-responders showed a statistically significant increase in MACE than responders (86% vs 23%; p<0.01). Five years post treatment with EECP, 64% patients survived without MACE or the need for revascularization.[9]

Holubkov R et al compared data of patients from the International EECP Patient Registry (IEPR) (n=323) treated with EECP and NHLBI Dynamic Registry (n=448) treated with elective PCI. Relative to those treated with PCI, recipients of EECP had a higher prevalence of various risk factors such as prior myocardial infarction (56.4% vs 27.8%; p <0.001), prior PCI (53.0% vs 33.3%; p <0.001), prior CABG (42.1% vs 18.6%; p <0.001), history of diabetes (37.9% vs 23.5%; p <0.001), and history of congestive heart failure (16.8% vs 9.2%; p <0.01). Patients treated with EECP had significantly lower mean LVEF levels (50.3% vs 59.2%; p <0.001). At 1 year, survival rates of EECP (98.7%), PCI (96.8%), and those of CABG during follow-up (4.5% EECP vs 5.7% PCI) in the two cohorts were comparable. Moreover, a significantly lower proportion of patients treated with EECP reported no anginal symptoms than those in the NHLBI Dynamic Registry (44% vs 73.4%; p <0.001). Higher rates of severe symptoms (CCS class III, IV, or unstable) were noted among IEPR patients (15.5%) than in the Dynamic Registry (9.5%; p=0.02).15 Soran O et al described the findings from the IEPR in a 2-year follow-up study of 363 patients treated with EECP for angina pectoris who had severe LV dysfunction. Post-treatment with EECP, a significant decrease in the severity of angina (p<0.001) was observed; in nearly 77% patients the severity decreased by ≥1 angina class, 18% patients had no angina, while in

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2% patients an increase in angina class was recorded. Overall, there was a statistically significant reduction in the mean number of weekly angina episodes by 8.2 ± 12.9 episodes (p<0.001).The researchers concluded EECP as a safe and effective treatment option in patients with angina pectoris and LV dysfunction.[16]

Qin X and colleagues performed a systematic review and meta-analysis to assess whether EECP significantly affects myocardial perfusion in CAD patients. They reported a significant increase in myocardial perfusion in patients with CAD (pooled weighted mean difference, -0.19; 95% CI, -0.38 to 0.00; p=0.049) with standard EECP therapy of 35–36 one-hour sessions in a seven-week period. To account for significant heterogeneity, they applied a random effects analysis (I2=89.1%; p=0.000), with no significant publication bias (Begg's p=0.091; Egger's p=0.282).3 Another recent systematic review and meta-analysis by Rayegani SM et al assessed the safety and effectiveness of EECP in patients with refractory angina. Two studies (n=96) showed a significant improvement in the overall inverse variance pooled mean difference for time to ST depression after EECP treatment (42.93; 95% CI, -48.65 to -37.21; p<0.00001), with no significant difference in the test for heterogeneity (I^2= 30%; p=0.23). Two studies (n=88) showed a significant improvement in the overall inverse variance pooled mean difference for exercise duration post-EECP (-44.60; 95% CI, -51.09 to 38.10; p<0.00001), with no significant difference in the test for heterogeneity (I^2=18%; p=0.27). Six studies (n=122) showed a significant improvement in the overall inverse variance pooled mean difference for CCS angina class post-EECP (2; 95% CI, 1.95 to 2.04; p<0.00001) with no significant difference in the test for heterogeneity (I^2=0%; p=0.97). Four studies (n=78) showed a significant improvement in the overall inverse variance pooled mean difference for daily angina episodes after EECP (1.30; 95% CI, 1.19 to 1.41; p<0.00001), with no significant difference in the test for heterogeneity (I^2=0%; p=0.99). Post-EECP, a significant improvement in the overall inverse variance pooled mean difference (7.33; 95% CI, 5.73 to 8.94; p<0.00001) for weekly angina episodes was noted in three studies (n=494), with no significant difference in the test for heterogeneity (I^2=11%; p=0.32).[17]

This study has some limitations. The generalizability of the findings of this study is limited as the registry included patients attending a single tertiary healthcare center in Western India. Considering its retrospective nature, the present study did not assess the safety outcomes in the population.

CONCLUSION

The findings of this registry-based study suggest that EECP therapy may be considered an effective non-invasive alternative therapy for patients with CAD or HF who are unfit or not willing to undergo CABG or PCI. Future studies with larger cohorts and longer follow-up periods should be considered to confirm the safety and efficacy of EECP in such patients.

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