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RESEARCH ARTICLE

EVALUATION OF ENHANCED EXTERNAL COUNTER PULSATION EFFECTIVENESS ON CLINICAL PROFILE AND HEALTH-RELATED QUALITY OF LIFE IN CORONARY HEART DISEASE PATIENTS

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ABSTRACT

Background: Enhanced External Counter Pulsation (EECP) is a non-invasive US FDA (United States Food and Drug Administration) approved outpatient treatment option for the complex problem of angina, a common symptom of coronary heart disease. A systematic review of the literature was done to assess the effect of EECP on the clinical profile that comprised physiological measurements, biochemical assessments, cardiac clinical symptoms, physical functional status, and Health-Related Quality of Life (HRQoL) in Coronary Heart Disease (CHD) patients.

Material and Methods: Total 258 EECP research articles from the early stage of EECP development till date were screened. Out of 258 EECP articles, total 60 articles (53 EECP articles for clinical profile and 7 articles for HRQoL matched the inclusion criteria and other (n=198) articles were excluded due to irrelevance to study objectives.

Results: All enrolled studies showed a significant improvement in angina pectoris and HRQoL with reduction of nitroglycerine use and exercise tolerance. Several gaps in research have been found for further research to evaluate the EECP effectiveness on Body Mass Index (BMI), Heart Rate, Cholesterol, Triglyceride, High Density Lipoprotein (HDL), Low Density Lipoprotein (LDL), HbA1C, SpO2, Vo2max levels with a comparative assessment of cardiac and non-cardiac metabolic markers including blood glucose.

Conclusions: There is further need of multi-centric randomized controlled trial studies to evaluate the effect of EECP on obese, diabetic, hypertensive and other metabolic disease patients and more research is required for further modifications in EECP equipment to treat chronic diseases by the non-invasive procedures.

Key words: Enhanced External Counter Pulsation, Angina pectoris, Health-Related Quality of Life, Coronary Heart Disease

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INTRODUCTION

Cardiovascular disease, especially Coronary Heart disease (CHD) is the number one killer and foremost cause of deaths around the world (Gupta, 2016). Angina pectoris, the prime symptom of coronary heart disease ranked first among causes of mortality (Pradhan, 2016). The current non-pharmacological and non-invasive therapy available for chronic stable angina (a typical symptom of coronary heart disease) and heart failure is Enhanced External Counter Pulsation (EECP). EECP is USA-FDA approved therapy for coronary heart disease patient (Prasad, 2010). EECP, an electro-mechanical system is a registered trademark of Vasomedical, Inc, New York, USA

and PSK (Chinese Company) is the exclusive distributor of Vasomedical'sdevices all over the world (Kantrowitz, 1953; Birtwell, 1965; Birtwell, 1968; Zheng, 1983 and Kumar, 2017). CHD patients usually undergo EECP treatment of 35 consecutive 1-hour sessions over 5–7 weeks. Treatment patient is continuously monitored for cardiac outputs, heart rate and spo2 using ECG and finger plethysmogram, which are connected to EECP device (Prasad, 2010; Sayami, 2010; Manchanda, 2017). This study designed to evaluate the effect of EECP in Clinical profile and HRQoL in CHD patients.

MATERIAL & METHODS

Searching Methods: A systemic review of literature of EECP on clinical profile and HRQoL in coronary heart disease patients was search through PubMed, Medline, Vasomedical

EECP manufacturer web-link, and Google scholar sources. Searching for the articles done as per inclusion and exclusion criteria of the study and the studies summarized in Table 1.

Table 1. Flow chart of screened and included studies



Inclusion Criteria: EECP article of Randomized Control Trial (RCT), case studies, prospective and retrospective studies on clinical profile and HRQoL in coronary heart disease patients were included.

Exclusion Criteria: Heart Failure studies, Non-cardiac EECP studies with RCT, Case studies, Prospective & Retrospective and reviews of EECP papers excluded from the study.

RESULTS

Effect of eecp on clinical profile in coronary heart disease patients

Lawson et al.(1992) conducted a study on 18 patients with chronic angina treated with an improved system of enhanced external counter pulsation (EECP) and found that all patients improved in angina symptoms and generally decreased anti angina medications. A decrease in myocardial ischemia observed in 67 % patients and 89 % patients were symptom free. Sjukri et al.(1995) carried out a study on 201 coronary heart disease patients. The results of the study showed significant improvement in coronary perfusion by 86.8% and exercise tolerance by 94.2 %. Arora et al.(1999) performed a multi centric prospective randomized control study to assess safety and efficacy of enhanced external counter pulsation (EECP). A significant improvement in angina severity and exercise tolerance and timing was reported. EECP showed well tolerated and safe therapy for CHD patients. Lawson et al.(2000) carried out a study on 33 patients to evaluate the effect of EECP on long-term prognosis in CHD patients. The study suggests that particularly for the majority of patients demonstrating improvement by 64% in radionuclide stress perfusion post treatment and EECP may be an effective longterm therapy. Lawson et al.(2000) conducted a cohort study in 2,289 CHD patients to evaluate EECP safety and efficacy. EECP was found to be safe and well tolerated therapy with improvement in angina class by 74% with the significant pvalue (p<0.001) [16].Urano et al.(2001) performed a study on 512 CHD patients to examined EECP efficacy in myocardial ischemia, exercise tolerance and cardiac function. The result of the study reveals the improvement in exercise test parameters reduced myocardial ischemia by thallium scintigraphy in association with improved LV diastolic filling in patients with stable CAD. Stys et al.(2001) carried out a clinical registry of 37 centers with the enrollment of 395 chronic stable angina patients to examine the relation of the ER to post treatment improvement in Canadian Cardiovascular Society (CCS) angina class. After EECP, CCS improved by at least 1 class in 88% of patients, 87% of men and 92% of women. EECP is effective in improving CCS in chronic stable angina patients Barsness et al.(2001) performed a study on 1246 CHD patients to determine whether EECP is a safe and effective treatment for patients with angina pectoris. The results demonstrated significant improvement in angina and reduction in nitroglycerine anti-angina drugs by 61.7 %. Springer S et al.(2001) conducted a study on 28 CHD patients to assess psychological function and well-being status and observed significant improvement in psychological and well-being status Lakshmi et al.(2002) carried out a study on 2486 patients those were enrolled in the IEPR. The author revealed a significant improvement in angina class in patients whose DA ratio was increased and results sustained for 6 months. Stys et al.(2002) performed a study on 175 CHD patients and found the significant improvement in angina class in 85% of patients. This study results showed the EECP effectiveness in improving stress myocardial perfusion with exercise tolerance in CAD patients. Michaels et al., (2002) conducted a study on 10 CHD patients and found the significant improvement in diastolic and mean pressures with reduction of systolic pressure in the central aorta and the coronary artery of CAD patients. The study concludes that EECP may serve as a potential mechanical assistant device for CAD patients. Holubkov et al.. (2002) carried out a study on 771 CHD patients treated with EECP and results of this study conclude that EECP may be a safe treatment option for CAD patients Soran et al.(2002) performed a study on 1402 CHD patients and the results showed that angina decreased by at least one class in 67% of patients with LV dysfunction just after completion of EECP treatment. Fitzgerald et al., (2003) conducted a cohort study on 4669 CHD patients and found decreased angina episodes and nitroglycerin use and 74.8% reduction in Canadian Cardiovascular Society (CCS) functional class and improvement in angina sustained for 6 months. Bonetti et al. (2003) performed a study on 23 CHD patients to examine the effect of enhanced external counter pulsation (EECP) on endothelial function and found that 70 % patients get symptomatic relief by EECP treatment. The author revealed that significant improvement in endothelial function by EECP may benefit to the clinical status of CHD patients, Schecter et al., (2003) carried out a study of 20 CHD patients to investigate the influence of short-term external counterpulsation (ECP) therapy on flow-mediated dilation (FMD) in patients with coronary artery disease (CAD). The author revealed that external counterpulsation might improve vascular endothelial function and refractory angina pectoris in CHD patients. Tartaglia et al.., (2003) conducted a study on 25 CHD patients to determine the effect of EECP on exercise

Table 2. EECP Effectiveness on Clinical Profile in Coronary Heart Disease Patients

Author	Study (Year)	Title of Study	Sample Size	Findings & Conclusion
Lawson et al [12]	1992	Efficacy of enhanced external counterpulsation in the treatment of angina	18	Myocardial ischemia 67% decrease, exercise duration increased, reduction in anti-
Siukri K et al[13]	1995	EECP in the treatment and rehabilitation of coronary patients in Indonesia	201	Exercise tolerance 94.2% improvement in CCS angina class
Arora et al [14]	1999	The multicenter study of enhanced external counterpulsation (MUST-EECP):	139	Exercise duration increase, angina severity reduced, extends times to exercise induced incharge Nitrochusering variantees
Lawson et al[15]	2000	Long-term prognosis of patients with angina treated with enhanced external	33	Improvement in stress perfusion after EECP, 64 % did not suffer any major adverse
Lawson et al[16]	2000	counterpulsation: five-year follow-up study Treatment benefit in the enhanced external counterpulsation consortium	2289	cardiovascular event due to effect of EECP at 5 year of study follow up. 74% angina pectoris patients improved in CCS angina class III & IV with significant p
				value (p<0.001)
Urano et al[17]	2001	Enhanced external counterpulsation improves exercise tolerance, reduces exercise-induced myocardial ischemia, and improves left ventricular diastolic filling in patients with coronary artery disease	512	Improvement in Exercise duration and tolerance with improvement in LV function. Improvement in diastolic filling and diastolic function.
Stys et al [18]	2001	Acute hemodynamic effects and angina improvement with enhanced external counterpulsation	395	CCS angina class improvement by at least 1 class in 88% of patients
Barsness et al [19]	2001	The International EECP Patient Registry (IEPR): design, methods, baseline	1246	Decrease in at least 1 anginal class by 81% and mean change decrease in anginal mission per work (6.4+12.6) with reduction of aitrachyspering we by 61.7%
Springer S et al[20]	2001	Psychosocial effects of EECP in the angina patient : A second study	28	Improvement in physical functioning and mental health with special reference to stress and OoL.
Lakshmi et al [21]	2002	Relation of the Pattern of Diastolic Augmentation During a Course of Enhanced External Counterpulsation (EECP) to Clinical	2486	At 6 months of follow up, the patients showed higher reduction in angina class who had the greatest increase in the DA ratio as compare to those who had decrease in the DA
Stys et al[22]	2002	Effects of enhanced external counter pulsation on stress radionuclide coronary	175	85% angina improvement, improvement in stress myocardial perfusion and maximize
Michaels et al[23]	2002	perfusion and exercise capacity in chronic stable angina pectoris. Left ventricular systolic unloading and augmentation of intracoronary pressure	10	exercise functions Diastolic BP increase, Systolic B.P decrease and increment in coronary flow by 28%
Holubkov et al[24]	2002	and Doppler flow during enhanced external counterpulsation. Comparison of patients undergoing enhanced external counterpulsation and	771	during EECP treatment Angina improvement in CCS class higher who received EECP therapy as compare to
		percutaneous coronary intervention for stable angina pectoris.		PCI group.
Soran et al[25]	2002	Enhanced external counterpulsation as treatment for chronic angina in patients with left ventricular dysfunction: a report from the International EECP Patient Registry (IEPR)	1402	Improvement in angina at least one class in 67% of patients with LV dysfunction 70.6% after 6 month of follow up.
Fitzgerald et al[26]	2003	Enhanced external counterpulsation as initial revascularization treatment for anging refractory to medical therapy	4,669	Decrease in anginal episode per week with significant value $p<0.001$, reduced nitrodycerine uses and CCS angina class reduction in 74.8 nations
Bonetti et al[27]	2003	Enhanced external counterpulsation improves endothelial function in patients with symptomatic CAD	23	Enhanced peripheral endothelial function immediately after EECP treatment with contribution to clinical benefit of EECP
Schecter et al [28]	2003	External counterpulsation therapy improves endothelial function in patients with refractory anging pectoris	20	Significant improvement in angina class (p<0.001), nitrate consumption decrease $(p<0.001)$ with improvement in andothelial functions
Tartaglia et al[29]	2003	Exercise capability and myocardial perfusion in chronic angina patients tracted with anhanced arternal counterpulsation	25	96% patients improved by at least one functional angina class and exercise duration increased in traducting increased in traductional angina class and exercise total duration in increased in traductional matrix and reduction in increased in traductional matrix and reductional
Werner et al[30]	2003	Practicability and limitations of enhanced external counterpulsation as an	48	Anginal episode reduced by 48%, Nitroglycerine reduction by 51 % and work capacity
Lawson et al[31]	2003	Analysis of baseline factors associated with reduction in chest pain in patients	4592	Significant improvement in angina by 73% in at least 1 class and 2 classes by 35.2 %
		with angina pectoris treated by enhanced external counterpulsation.		and 3 classes by 17.3%. Mean angina episodes per week decrease to 2.5 per week after EECP treatment and nitroglycerine uses per week after EECP was 2.5 times per week and improvement in functional status also observed.
Linnemeier et al [32]	2003	Enhanced external counterpulsation in the management of angina in the elderly.	3037	Angina improvement in 81% at 6 months with reduction in nitroglycerine use and improvement in well-being status with decrease rate of cardiac hospitalization has been
Linnemeier et al [33]	2003	Enhanced External Counterpulsation for the relief of angina in patients with diabetes: safety, efficacy and 1- year clinical outcomes.	1532	Significant improvement in CCS angina class by 69% in diabetes mellitus immediately after EECP and 86% at 1 year follow up, reduction in nitroglycerine use and improvement in well-being status has been observed and confirm that EECP is safe, effective and well tolerable treatment

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Bagger et al[3/]	2004	Effect of Enhanced External Counternulsation on	23	Deduction in dobutaming induced wall motion abnormalities observed after EECD
Bagger et al[34]	2004	Dobutomine Induced Lieft Ventricular Wall Motion	23	treatment
		Abnormalities in Severe Chronic Angina Pectoris		ireatinent
Michaels et al[35]	2004	Two year outcomes after Enhanced External Counternulsation for stable anging	1007	Significant improvement by 73 % anging improvement 50% improvement in well
whenaels et al[55]	2004	nectoris (from the International EECP national registry [IEPP])	1097	being of CAD patients at 2 years of follow up
Lawson at al [26]	2004	Effectiveness of enhanced external counternulsation in patients with left main	2861	Significant improvement in angine posteric and reduction in nitrochastring use and
Lawson et al [50]	2004	disease and anging	2801	significant improvement in angina pectoris and reduction in introgrycerine use and
Maguda at al[27]	2004	uiscase and anglina.	10	Significant improvement in evening appoints and evenes metabolism of CUD notions.
Masuda et al[37]	2004	improvement of oxygen metabolism in ischemic myocardium as a result of	10	Significant improvement in exercise capacity and oxygen inetabolism of CHD patients
		enhanced external counterpulsation with negatin pretreatment for patients		treated with EECP and intravenous neparin infusion comolined therapy was observed.
XX 11 . 15003	2004	with stable angina	•	
Henrikson et al [38]	2004	Enhanced external counterpulsation therapy: significant clinical	28	Significant improvement in angina by 82% and effective treatment for CAD patients
		improvement without electrophysiologic remodeling.		
Taguchi et al [39]	2004	Effects of Enhanced External Counterpulsation	24	Study conclude that increments in ANP without enhancement in BNP was an important
		on Hemodynamics and Its Mechanism		mechanism for EECP effectiveness
		Relation to Neurohumoral Factors		
Lawson et al [40]	2005	Predictors of benefit in angina patients one year after completing enhanced	2,007	Angina reduced by at least 83 % immediately, and improvement in weekly anginal
		external		episodes, frequency of nitroglycerine use decreased and well-being status improved by
		counterpulsation: initial responders to treatment versus non responders.		63%.
Michaels et al [41]	2005	Frequency and efficacy of repeat enhanced external counterpulsation for stable	1192	After EECP treatment, 86 % reported decrease in angina CCS class by at least one and
		angina pectoris (from the International EECP Patient Registry)		57 % patients discontinued nitroglycerine use.
				After 2 years 70% patients reported significant decrease in angina and nitroglycerine
				consumption
Arora et al [42]	2005	Effects of enhanced counterpulsation on vascular cell release of coagulation	30	Study suggests that EECP may not play a vital role in controlling coagulation factors in
		factors		coronary heart disease patients, further research required
McCullough et al [43]	2006	Impact of body mass index on outcomes of enhanced external counterpulsation	2730	Changes in angina and duke activity status have been observed in all BMI patients.
		therapy		Greater reduction of angina is directly proportional to BMI value
Soran et al [44]	2006	Two-year outcomes after enhanced external counterpulsation	363	At 2 years of follow up 55% patients showed improvement in angina and prove that
		(EECP) therapy in patients with refractory angina pectoris and left ventricular		EECP is effective and durable therapy approach for CAD patients and 52% CHD
		dysfunction (report from the International EECP Patient Registry)		patients discontinued nitroglycerin use
Akhtar et al [45]	2006	Effect of External Counterpulsation on Plasma Nitric Oxide and Endothelin-1	13	EECP increases nitric oxide and decrease endothelial -1 level and changes sustained for
		Levels		3 months in CHD patients
Nichols et al[46]	2006	Enhanced External Counterpulsation	20	Study suggest that EECP can reduce arterial stiffness and may improve wave reflection
		Treatment Improves Arterial Wall Properties and Wave		characteristics in CHD patients and these changes decrease left ventricular afterload,
		Reflection Characteristics in Patients With Refractory Angina		myocardial oxygen demand and can reduce anginal episodes
Lawson et al [47]	2006	Two-year outcomes in patients with mild refractory angina treated with	1458	Improvement in angina by 70-74 % with reduction of nitroglycerine use by 52% with
		enhanced external counterpulsation.		better well-being persist till 2 years of follow up
Novo et al [48]	2006	Enhanced external counterpulsation for treatment of refractory angina pectoris.	25	Significant improvement in angina by 84% and reduced inducible ischemia and maximal
				benefits observed in patients with worst systolic failure
Loh et al [49]	2006	The immediate and long-term outcome of enhanced external counterpulsation	58	At least one class CCS angina improvement by 78% after 1 year and increase exercise
		in		capacity with reduction in nitroglycerine use
		treatment of chronic stable refractory angina.		
Arora et al[50]	2007	Effect of enhanced external counterpulsation on	11	No significant effect on myocardial perfusion has been observed due to very less number
		myocardial perfusion in patients with stable angina: A		of sample size and highly variable clinical responses and study suggest for further
		multicenter radionuclide study		research to assess EECP effectiveness on myocardial perfusion
Michaels et al [51]	2007	The effects of enhanced external counterpulsation on time- and frequency-	27	Improvement in heart rate variability in diabetic CHD patients and associated with
		domain measures of heart rate variability.		reduced with reduced mortality rate
McCullough[52]	2007	Residual high-grade angina after enhanced external	902	Researcher observed high residual grade angina after EECP in those patients who had
		Counterpulsation therapy		severe angina and multivessel diseases

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Yavari et al [53]	2007	Effects of enhanced external counterpulsation on anginal symptoms and improvements in objective	67	Study conclude that EECP is a safe, well tolerated and effective non-invasive therapy for CHD patients
Loh et al[54]	2008	measures of myocardial ischemia Enhanced external counterpulsation in the treatment of chronic refractory angina: a long-term follow-up outcome from the International Enhanced External Counterpulsation Patient Registry	1477	After 1 year EECP treatment 78% patients reported reduction in CCS angina class and 74 % of patients sustained improvement at 3-years follow
Erdling et al[55]	2008	Enhanced external counter pulsation in treatment of refractory angina pectoris: two year outcome and baseline factors associated with treatment failure	86	After EECP treatment 79% of patients showed improvement in CCS class immediately and 61.5% of patients sustained these benefits till 12 months and 29% at 2 years follow up and study conclude that EECP is safe & effective for CAD with angina pectoris patients and patients with CCS angina class III & IV reported maximum improvement
Buschmann et al[56]	2009	Improvement of fractional flow reserve and collateral flow by treatment with external counterpulsation.	23	Improvement in CCS and NYHA class in CAD patients with significant improvement in pressure derived collateral flow index and fractional flow also increased
Esmaeilzadeh et al[57]	2009	Evaluation of left ventricular systolic and diastolic regional function after enhanced external counter pulsation therapy using strain rate imaging.	20	Reduction in NYHA angina class & improvement in LV systolic and diastolic function in patients with chronic angina with increment in LVEF from 40.25 % -46.25% with significant p value ($p < 0.001$)
Soran et al [58]	2012	Comparison of long term clinical outcomes, event free survival rates of patients undergoing enhanced external counterpulsation for coronary artery disease in the united states and turkey.	2072	Significant reduction in the severity of angina in CAD patients at 1 years of follow up
Eslamian et al[59]	2013	Therapeutic effects of enhanced external counterpulsation on clinical sumptoms, echocardiographic measurements, perfusion scan parameters and exercise tolerance test in CAD patients with refractory angina.	50	Significant improvement in angina severity ($p<0.001$), wellbeing status and ischemia severity ($p=0.044$) and demonstrated useful safe and effective treatment method for angina pectoris in CHD patients
Bozorgi et al [60]	2014	Effect of enhanced external counterpulsation (eecp) on exercise time duration and functional capacity in patients with refractory angina pectoris	20	Significant reduction in the severity of angina and physical functioning sustained for 6 months
Beck et al [61]	2014	Enhanced external counterpulsation improves endothelial function and exercise capacity in patients with ischaemic left ventricular dysfunction	24	Significant improvement in plasma level of nitrates and improved peak VO2 and reduce LV function with significant improvement in peripheral vascular function and functional canacity
Tabary et al [62]	2015	Assessment the clinical and paraclinical effects of enhanced external counter pulsation therapy in patients with coronary artery disease.	48	Improvement in Hemoglobin, LVEF, Diastolic and systolic B.P, Chest pain, dyspnea and improve clinical conditions
Subramanian et al [63]	2016	Effect of Enhanced External Counter Pulsation Treatment on Aortic Blood Pressure, Arterial Stiffness and Ejection Fraction in Patients with Coronary Artery Disease	72	Central B.P significantly decrease with improvement in LV function in CAD patients
Darren T Beck et al [64]	2016	Enhanced External Counter Pulsation Reduces Indices of Central Blood Pressure And Myocardial Oxygen Demand in Patients with Left Ventricular Dysfunction	17	EECP worked as adjuvant therapy and improvement in functional status, central B.P and myocardial oxygen demand in CAD patients

capacity and myocardial perfusion by comparing results of maximal exercise radionuclide testing pre- and post-EECP treatment. A significant improvement in treadmill times has been reported and radionuclide perfusion scores showed a significant reduction in ischemic segments [29]. Werner et al. (2003) performed a study on 48 CHD patients and weekly angina episodes were reduced by 48%, nitroglycerin puffs were reduced by 51%, work capacity was improved by 22%. Study validates the reduction of angina with significant improvement of work capacity after EECP [30].Lawson et al., (2003) carried out a study on 4592 CHD patients and his collected data from international enhanced external counter pulsation (EECP) patient registry showed significant improvement in angina by 73% in at least 1 class and 2 classes by 35.2 % and 3 classes by 17.3%. The mean angina episodes per week decrease to 2.5 per week after EECP treatment and nitroglycerine uses per week after EECP was 2.5 times per week and improvement in functional status also observed in the study., [31]. Linnemeier et al., (2003) conducted a study on 3037 CHD patients to determine whether enhanced external counterpulsation is a safe and effective treatment for angina in octogenarians. At 6-month follow-up, 81% patients sustained angina improvement. This study concludes that enhanced external counterpulsation is effective and well tolerable noninvasive treatment [32]. Linnemeier et al., (2003) performed another study on 1532 IEPR patients. The author demonstrated that after 1 year, maintenance of angina rate was reduced in 86% of patients with diabetes. The author concludes that EECP is a safe, well-tolerated and effective treatment option for the relief of angina in diabetes patients. Bagger et al., (2004) carried out a study on 23 patients with angina pectoris and positive dobutamine stress echocardiogram. This study was done to evaluate EECP effectiveness on dobutaminestressinduced wall motion score among angina patients. The reduction in dobutamine-induced wall motion abnormalities after EECP therapy was reported. Michaels et al.(2004) conducted the long-term outcomes of enhanced external counter pulsation in 1097 CHD patients to relieve angina and improving the quality of life in a large cohort of patients with chronic angina pectoris. 73 % patients had a reduction by at least 1 angina class at the end of treatment, and 50% reported an improvement in the quality-of-life assessment after enhanced external counter pulsation; these results were sustained at 2-year follow-up. Lawson et al.(2004) performed a study on 2861 CHD patients to examine the safety and effectiveness of EECP therapy. Post-EECP, patients had improved their CCS angina by at least one class. At 6-month follow-up, the CCS class improved reduction in angina episodes and nitroglycerin use. Enhanced external counterpulsation was proven an effective therapy in relieving angina in patient's angina patients. Masuda et al., (2004) carried out a study on total 18 CHD patients. Out of 18 patients, 11 were treated with EECP and 7 were treated 5000 IU heparin pretreatment along with EECP. The study was done to evaluate EECP and intravenous heparin injection therapy effectiveness in angina pectoris patients and the results of the study showed significant improvement in exercise capacity and oxygen metabolism of coronary heart disease patients treated with combination therapy of EECP and heparin. Henrikson et al.(2004) conducted a study on 28 CHD patients and found that Post EECP, most patients (82%) had at least a one full class improvement in their angina pattern. EECP remains an effective treatment for severe CAD. Taguchi et al., (2004) performed a study on 24 patients with myocardial infarction. This study was done to assess haemodynamic effects of EECP and its mechanism with special reference to neurohumoral factors. This finding of this study suggests that an increase in ANP without an increase in BNP is an important mechanism for the effects of EECP therapy. Lawson et al.(2005) carried out a study on 2007 CHD patients and demonstrated the angina reduction by 83% at least one CCS angina class and improvement in weekly angina episodes and their frequency of nitroglycerine use decreased with improvement in well-being status by 63% [40]. Michaels et al., (2005) conducted a study on 1192 CHD patients to assess the frequency, efficacy, predictors, and long-term success of repeat enhanced external counter pulsation (EECP) therapy in relieving angina in a large cohort of angina patients. After 2 years of EECP therapy, 70% patients reported the significant decrease in angina and nitroglycerine consumption. Arora et al.(2005) performed a study on 30 patients with stable angina pectoris having class II-IV. This study was done to assess the effect of EECP on vascular cell release of coagulation factors. The author reveals that EECP may not play the significant role in controlling coagulation factors in CHD patients. McCullough et al.(2006) carried out a study on 2730 obese heart patients to evaluate the association of baseline body mass index (BMI) on the outcomes of enhanced external counter pulsation (EECP) therapy for chronic stable angina.

A greater reduction in weekly angina episodes from baseline to follow up observed and study conclude that reduction of angina is directly proportional to BMI value. Akhtar et al., (2006) conducted a study on 13 CHD patients to evaluate the effect of EECP treatment on plasma nitric oxide and endothelin-1 level. This study concludes that EECP may increase nitric oxide and decreases endothelin-1 levels. Soran et al., (2006) carried out a cohort study on 363 CHD patients and post EECP treatment, there was a significant decrease in severity of angina class (p <0.001), and 72% patients were improved from severe angina and 52 % of patients discontinued nitroglycerin use. At 2 years of follow up 55%, patients showed improvement in angina and prove that EECP is effective and durable therapy approach for CAD patients and 52% CHD patients discontinued nitroglycerin use. Nichols et al.., (2006) performed a study on 20 angina patients to prove the hypothesis of arterial properties and wave reflection characteristics favorably altered after EECP. The study revealed that EECP treatment may reduce arterial stiffness and can improve wave reflection characteristics in patients with angina. Lawson et al., (2006) conducted a study on 1458 CHD patients and found that EECP significantly reduced angina frequency, nitroglycerin use. Significant improvements in angina by 70-74 % with reduction of nitroglycerine use by 52% with better well-being persist until 2 years of follow up.

Novo *et al..*, (2006) carried out a study on 25 CHD patients to evaluate the efficacy of EECP on clinical symptoms, myocardial ischemia and cardiac performed in intractable angina patients. 84 percent of patients showed an increment in at least one functional angina class and reduced inducible ischemia and maximal benefits observed in patients with worst systolic failure had been observed. Loh *et al.*(2006) did a study on 58 CHD patients to assess EECP immediate and long term effectiveness in chronic stable refractory angina patients. This study results showed that angina improved at least one class CCS angina improvement by 78% after 1 year and increase exercise capacity with the reduction in nitroglycerine use. Arora *et al..*, (2007) conducted a study on 11 CHD patients to assess the effect of EECP on myocardial perfusion.

Table 3.	EECP	Effectiveness	on Health-	Related Q	uality o	of Life in	Coronary	Heart	Disease	Patients
					•/		•/			

Author	Study (Year)	Title of Study	Sample Size	Conclusion
Arora et al	2002	Effects of enhanced external counterpulsation on Health- Related Quality of Life continue 12 months after treatment: a substudy of the Multicenter Study of Enhanced External Counterpulsation	139	Significant improvement in Health-related QoL in patients who had active EECP as compare to those having inactive EECP in all HR-QoL parameters (p<0.05)
Kumar et al	2009	Effect of Enhanced External Counterpulsation on Clinical Symptoms, Quality of Life, 6-Minute Walking Distance, and Echocardiographic Measurements of Left Ventricular Systolic and Diastolic Function After 35 Days of Treatment and at 1-Year Follow Up in 47 Patients With	47	Significant improvement in QoL and walking capacity
Wu et al	2012	Chronic Refractory Angina Pectoris Enhanced external counterpulsation in patients with refractory angina pectoris: a pilot study with six months follow-up regarding physical capacity and health-related quality of life.	34	Improvement in physical and functional capacity with HR-QoL improvement
Ziaeirad et al	2012	The effects of enhanced external counterpulsation on health- related quality of life in patients with angina pectoris	64	Angina &QoL improvement
Jorgensen et al	2013	Improvement of angina, quality of life, and working capacity after enhanced external counterpulsation	One special case	QoL& Angina improvement
May O et al	2015	Enhanced external counterpulsation – Effect on angina pectoris, QoL and exercise capacity after 1 year	50	Improvement in exercise capacity with generic and disease specific QoL improvement
Shakouri S Kazem	2015	Effect of Enhanced External Counterpulsation and Cardiac Rehabilitation on Quality of Life, Plasma Nitric Oxide, Endothelin and High Sensitive CRP in Patients With Coronary Artery Disease: A Pilot Study	42	Mean change in Quality of life and endothelial functioning has been observed in CAD patients

In this study no significant effect on myocardial perfusion seen due to very less sample size and highly variable clinical responses [50]. Michaels et al., (2007) performed a study on 27 patients and significant improvement in in heart rate variability in diabetic CHD patients and associated with reduced with reduced mortality rate had been reported [51]. McCullough et al.(2007) did a study on 902 patients from the IEPR. This study was done to evaluate the degree of residual angina on the clinical outcomes of EECP and conclude that residual high grade angina pectoris occurs after post EECP in those patients who had the history of severe angina and multivessel disease. Yavari et al.(2007) conducted a study on 67 CHD patients to assess EECP efficacy in relieving angina and improving myocardial ischemia. The results of this study conclude that EECP is safe, effective and well tolerated therapy for angina pectoris treatment. Loh et al.(2008) did a study on 1477 CHD patients to evaluate EECP effectiveness. Immediately after EECP, angina reduction has been seen with p<0.001. The improvement in CCS class was improved by at least 1 class in 78% of the patients and by at least 2 classes in 38% and sustained in 74% of the patients during follow-up for 3 years. Erdling et al.(2008) carried out a study on 86 CHD patients and conclude that after EECP treatment 79% of patients showed improvement in CCS class immediately and 61.5 % of patients sustained these benefits till 12 months and 29 % at 2 years follow up. The author concludes that EECP is safe & effective for CAD with angina pectoris patients and patients with CCS angina class III & IV reported maximum improvement. Buschmann et al.(2009) conducted a study on 23 CHD patients and found improvement in CCS and NYHA class in CAD patients with significant improvement in pressure derived collateral flow index and fractional flow, which also increased. Esmaeilzadeh et al.(2009) performed a study on 20 CHD patients to assess the effects of EECP on cardiac functions and found the reduction in NYHA angina class. Significant improvement was observed in LV systolic, diastolic function in angina patient. Soran et al.(2012) conducted a study on 2072 patients and treated with EECP. Significant reduction by 76-84 % in the severity of angina in CAD patients at 1 years of follow up was reported and both US

and turkey group got good results [58]. Eslamian et al. (2013) performed a study on 50 CHD patients to assess Enhanced External Counter Pulsation (EECP) effectiveness on clinical symptoms, echocardiographic measurements, and perfusion scan parameters and exercise tolerancetest. A significant improvement was observed in angina severity and wellbeing status. Bozorgi et al.(2014) did a study on 20 CHD patients with refractory angina. A significant reduction in angina classes III and IV was reported with sustained results for 6 months. The author concludes that EECP decreased symptoms and increased total exercise time and sustained these results for 6 months. Beck et al.(2014) conducted a study on 24 CHD patients and significant improvement in plasma level of nitrates, improved peak VO2, and reduced LV function with significant improvement in peripheral vascular function and functional capacity had been reported. Tabary et al.(2015) performed a study on 48 CHD patients to assess clinical and para-clinical effects of enhanced external counter pulsation (EECP) effectiveness. Significant improvement in hemoglobin, LVEF, diastolic and systolic B.P, Chest pain, dyspnea and improvement in clinical conditions had been reported [62].Subramanian et al. (2016) did a study on 72 CHD patients and found significant improvement in central systolic pressure, brachial systolic pressure, aortic pulse pressure, and augmentation pressure and augmentation index. Darren T Beck et al. (2016) conducted the study on 17 CHD patients. The author concludes that EECP may be useful as an adjuvant therapy for improving functional classification and improve central blood pressure, aortic pulse pressure, wasted left ventricular energy, andmyocardial oxygen demand in CHD patients.

Effect of eecp on hr-qol in coronary heart disease patients

Arora *et al.*(2002) conducted a study to assess EECP effectiveness on HRQoL. A significant improvement in HRQoL was observed at 12 months of follow up. The result shows improvements in HRQoL changes after EECP treatment Kumar *et al.*(2009) did a prospective study and found that EECP significantly improved angina symptoms, dyspnea on

exertion, and quality of life after 35 days of treatment and at1 year follow up. EECP also improved the 6-minute walking capacity. Wu et al.(2012) performed a study to evaluate EECP after six months regarding physical capacity and HRQoL in patients with refractory AP. Patients enhanced walking distance on average by 29 m after EECP. CCS class also improved and persisted at six months follow-up. HRQoL improved significantly and the effects maintained at follow-up after the treatment. Ziaeirad et al.(2012) did a quasiexperimental study on 64 patients to evaluate the QoL of patients with angina pectoris after treatment with enhanced external counterpulsation. The author reveals that EECP is an effective noninvasive method in treating patients with angina pectoris and in developing their HRQoL. Jorgensen et al.(2013) conducted a special case study of the 43-year-old woman who had 15 hospital admissions in six years due to angina. The case study proves the EECP effectiveness towards angina recovery and significant improvement in HRQoL. May O et al.(2015) performed a study to assess the effect of EECP on QoL and exercise capacity in CAD patients. Author of this concludes that quality of life and exercise capacity was improved after EECP. Shakouri S Kazem et al.(2015) conducted a study to investigate the effect of EECP on plasma nitric oxide (NO) and HRQoL in CAD patients. The author revealed that HRQoLand NO level increased after EECP treatment in CHD patients. Summary of studies given in Table 2 & 3.

DISCUSSION

Above discussed EECP studies validates the significant improvement in CCS and NYHA angina classification, angina episodes, left ventricle ejection fraction functioning, exercise tolerance and HRQoL with reduction of nitroglycerine use & decrease hospitalization rate in coronary heart disease patients. EECP used for angina and heart failure for the past two decades, but still, more research required filling the gaps in research. There are very few or rare study conducted to assess EECP effectiveness on BMI, Heart Rate, Cholesterol, Triglyceride, High-Density Lipoprotein (HDL), Low-Density Lipoprotein (LDL), HbA1C, SpO2, Vo2max, 12-minute walk or run test and comparative prospective randomized trials on cardiac and non-cardiac metabolic markers.

Conclusion

Further clinical research is required to evaluate EECP effectiveness on obese, diabetic, hypertension and other metabolic disease patients with CHD and multi-centric randomized controlled trials are required for further modifications in EECP device to cure, prevent, and treat chronic diseases such as obesity, hypertension, diabetes, and neurological disorders by the non-invasive procedure.

Conflict of Interest

The authors have no conflicts of interest in this article.

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