Clinical effects of enhanced external counterpulsation treatment in patients with ischemic heart failure

Güçlendirilmiş dışardan kontrpulsasyon tedavisinin iskemik kalp yetersizliği olan hastalarda klinik etkileri

Güliz Kozdağ, Gökhan Ertaş[1], Fatih Aygün, Ender Emre, Ahu Kırbaş, Dilek Ural, Özlem Soran[2]

Department of Cardiology, Faculty of Medicine, Kocaeli University, Kocaeli-*Turkey*
[1]Clinic of Cardiology, Gümüşhane State Hospital, Gümüşhane-*Turkey*
[2]University of Pittsburgh, Cardiovascular Institute, Pittsburgh, PA-*USA*

ABSTRACT

Objective: Enhanced external counterpulsation (EECP) is a noninvasive treatment that is proven safe and effective in patients with coronary artery disease (CAD) and heart failure (HF). The aims of this study are to investigate the clinical effects of EECP therapy in patients with symptomatic CAD and chronic HF, and to find out an answer to the question: Does EECP therapy have any effect on the prognostic markers of HF?
Methods: This study was designed as a prospective cohort study. A total of 68 consecutive patients with symptomatic CAD and chronic HF referred to EECP therapy were enrolled in this study between November 2007 and December 2010; 47 patients (39 males and 8 females, 65±7, years), have undergone EECP treatment, and 21 patients (20 males and 1 female, 62±10 years), who did not want to participate in the EECP program comprised the control group. Statistical analysis was performed using t tests for dependent and independent samples, Mann-Whitney U test, Chi-square and Fischer exact tests.
Results: EECP therapy resulted in significant improvement in post-intervention New York Heart Association functional class ($p<0.001$), left ventricular ejection fraction ($p<0.001$), B-type natriuretic peptide levels ($p<0.003$), uric acid levels ($p<0.05$), free-T3/free-T4 ratio ($p<0.034$) and mitral annular E ($p<0.05$) velocity, compared with baseline, a finding not evident in the control group.
Conclusion: EECP treatment significantly improved clinical and some biochemical parameters, which are mostly prognostic markers in patients with symptomatic CAD and chronic HF. *(Anadolu Kardiyol Derg 2012; 12: 214-21)*
Key words: Enhanced external counter pulsation, chronic heart failure, coronary heart disease, functional class

ÖZET

Amaç: Güçlendirilmiş dışardan kontrpulsasyon (EECP), koroner arter hastalığı (KAH) ve kalp yetersizliği (KY) olan hastalarda güvenli ve efektif olduğu kanıtlanmış invaziv olmayan bir tedavi yöntemidir. Bu çalışmanın amacı EECP tedavisinin semptomatik KAH ve KY olan hastalardaki klinik etkilerini araştırmak ve EECP tedavisinin KY'nin prognostik faktörleri üzerine herhangi bir etkisi var mı? Sorusuna cevap bulmak.
Yöntemler: Bu çalışma prospektif kohort çalışma olarak dizayn edildi. Kasım 2007 ve Aralık 2010 arasında EECP tedavisi için başvuran 68 semptomatik KAH ve kronik KY olan hasta çalışmaya dahil edildi. 47 hasta (39 erkek ve 8 kadın, 65±7, yaş) EECP tedavisine alındı. EECP programına katılmak istemeyen 21 hasta (20 erkek ve 1 kadın, 62±10 yaş) kontrol grubunu oluşturdu. Sürekli değişkenler 2-tailed t test ve Mann-Whitney U testi ile analiz edildi. Kategorik veriler ve oranlar χ^2 veya Fisher exact test ile analiz edildi.
Bulgular: EECP tedavisi sonrası New York Kalp Cemiyeti'nin fonksiyonel sınıflaması ($p<0.001$), sol ventrikül ejeksiyon fraksiyonu ($p<0.001$), B-tip natriüretik peptid düzeyleri ($p<0.003$), ürik asit düzeyleri ($p<0.05$), serbest-T3/serbest-T4 oranı ($p<0.034$) and mitral anüler E ($p<0.05$) hızlarında anlamlı düzelme saptandı. Kontrol grubunda aşikar bir değişiklik izlenmedi.
Sonuç: EECP tedavisi, semptomatik KAH ve kronik KY olan hastalardaki prognostik biyokimyasal ve klinik parametreleri anlamlı olarak düzeltti. *(Anadolu Kardiyol Derg 2012; 12: 214-21)*
Anahtar kelimeler: Geliştirilmiş dış ters nabız, kalp yetersizliği, koroner arter hastalığı, fonksiyonel sınıflama

Address for Correspondence/Yazışma Adresi: Gökhan Ertaş M.D, Gümüşhane Devlet Hastanesi, Kardiyoloji Bölümü, 29000, Gümüşhane-*Türkiye*
Phone: +90 456 213 15 56 Fax: +90 456 213 43 46 E-mail: drgokhanertas@yahoo.com.tr

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Introduction

Coronary artery disease (CAD) is a leading cause of death and disability worldwide. Chronic myocardial ischemia resulting from CAD can cause stable angina and interfere with ordinary activities (1). As the incidence of angina and heart failure (HF) has increased, so has our understanding and treatment. Moreover, for the group of patients with underlying HF, substantial unmet needs remain. As a result, many patients are left to suffer their symptoms, restrict their activities and anticipate a reduced life expectancy (2). Treatment of CAD consists of medical, invasive surgical and non-surgical coronary interventions (3). Despite of those therapies, there are still many symptomatic patients who are not good candidates for coronary interventions (4, 5). Several non-pharmacological options for the treatment of patients with angina pectoris, with or without underlying HF, have been suggested. Of these modalities enhanced external counterpulsion (EECP) therapy represents the most effective non-invasive technique (6). Furthermore, the role of EECP therapy has been recently investigated for the treatment of HF (7-9).

However, effects of EECP therapy on prognostic markers of HF have not been determined in previous studies (10-16).

The aims of this study are: 1. To investigate the clinical effects of EECP therapy in patients with symptomatic CAD and chronic HF; 2. To find out an answer to the question: Does EECP therapy have any effect on the prognostic markers of HF such as the levels of brain natriuretic peptide (BNP), hemoglobin, high-sensitive C-reactive protein (hs-CRP), uric acid, Free-T_3 (fT3), creatinine and free-T_3/ free-T_4 (fT4) ratio?

Methods

Study design and population

This study was designed as a prospective cohort study. A total of 68 consecutive patients with symptomatic CAD and chronic HF referred to EECP therapy were enrolled in this study between November 2007 and December 2010. Forty-seven consecutive patients were recruited from a supervised EECP therapy program at the cardiology department and comprised the EECP group. Twenty-one age and gender matched consecutive patients with CAD and chronic HF who did not want to participate in the EECP program represented the control group. Study inclusion criteria included men and women (age >20 years) with documented CAD [prior myocardial infarction, coronary artery bypass surgery, documented CAD with angiography (at least one epicardial coronary artery having a luminal diameter narrowing of greater than 50%)] and chronic HF (based on history, functional capacity evaluation, physical examination, electrocardiography, chest radiology, echocardiography, left ventriculography and BNP levels). Exclusion criteria included unstable angina, decompensated HF, acute myocardial infarction, severe aortic regurgitation, systemic hypertension>180/110 mmHg, severe cardiac arrhythmia that would interfere with EECP triggering, deep vein thrombosis, phlebitis, hemorrhagic diathesis, use of anticoagulants with INR>3, pregnancy, abdominal aortic aneurysm> 5 cm, refusal to sign informed consent.

Data on demographics, medical history and current medication were collected (Table 1). All medications remained unchanged during the entire study period but could, if needed, be adjusted. Patients instructed to maintain their usual diet throughout the study.

The study was conducted in accordance with the declaration of Helsinki and approved by local institutional Ethics Committee. All patients signed the informed consent form.

Study protocol

All patients were seen in clinic by the study physician and nurse coordinator during their baseline and post EECP visit (within 1-3 days) after the last day of their EECP treatment for the EECP group. Control group's first evaluation was accepted as the beginning day of the treatment period which was 7 weeks for the control group as EECP therapy group. Both group had clinical evaluation, physical examination and echocardiographic measurements at the first and last evaluation (after 7 weeks). Fasting blood samples were drawn for the determination of biochemical and hemostatic values at first and the last study day. Canadian Cardiovascular Society classification (CCS) was used to assess angina status and New York Heart Association (NYHA) classification was used to assess HF status.

EECP technique

EECP (EECP TS4, by Vasomedical Inc, New York, USA) is a therapeutic system that consists of an air compressor, a treatment table, a control console and an integrated set of air cuffs. These compressive cuffs are designed to be wrapped around the patient's lower extremities and buttocks. A cardiologist and the EECP therapist, a specialized technician, sets cuff inflation and deflation to the cardiac cycle guided by the electrocardiogram (ECG); systolic and diastolic pressure augmentation during EECP is monitored using finger plethysmography (17). Cuffs are timed to inflate sequentially from the calf to the lower thigh to the upper thigh and buttock just after the onset of diastole, and then deflate simultaneously prior to the beginning of systole. Pressures applied to the cuffs range from 220 to 300 mmHg. Pressure applied in this study was 280-300 mmHg. A typical course of EECP therapy consists of 35 hours of treatment, 1 hour per day, 5 days per week, over a 7-week period. We followed the same EECP therapy protocol. Pulse oximetry was monitored continuously during the treatment session, and the subject's clinical status was re-evaluated if the oxygen saturation dropped by 4%.

Pharmacological therapy

The standard treatment for patients with chronic stable angina pectoris and HF included beta-blockers, angiotensin-converting enzyme inhibitor, and/or an angiotensin-receptor blocker (ACE-I/ARB), aspirin, digoxin, diuretics, long acting nitrate and other medications were given at the physician's discretion.

Table 1. Baseline characteristics of study patients

Variables	EECP group (n=47)	Control group (n=21)	*p
Age, years	65±7	62±10	NS
Gender, male/female	39/8	20/1	NS
NYHA Class	2.6±0.7	2.1±0.6	0.043
CCS Class	2.5±0.9	1.6±0.7	0.001
Systolic BP, mmHg	114±23	125±16	NS
Diastolic BP, mmHg	76±8	71±9	0.039
Diabetes, %	57	48	NS
Hypertension, %	68	57	NS
Dyslipidemia, %	68	81	NS
Medical treatment			
Beta-blocker, %	85	95	NS
Calcium channel blocker, %	34	33	NS
Nitrate, %	60	52	NS
Aspirin, %	91	95	NS
Clopidogrel, %	26	14	NS
ACE-I/ARB, %	89	81	NS
Spironolactone, %	36	14	NS
Loop diuretic, %	68	52	NS
Statin, %	62	76	NS
LVEF, %	33±17	27±7	NS
TSH, mg/dL	1.95±0.78	1.01±0.78	0.002
Free-T_3, mg/dL	2.74±0.59	2.82±0.57	NS
Free-T_4, mg/dL	1.40±0.26	1.36±0.58	NS
Uric Acid, mg/dL	6.73±2.76	6.73±2.34	NS
Creatinine, mg/dL	1.17±0.47	1.23±0.47	NS

Continuous variables are given as mean±SD and categorical variables are presented as percentage values
*2-tailed t test, Mann-Whitney U test and Chi-square test
ACE-I/ARB- angiotensin-converting enzyme-inhibitors/angiotensin-II receptor blockers, BNP - brain natriuretic peptide, BP - blood pressure, CCS - Canadian Cardiovascular Society, EECP -enhanced external counter pulsation, LVEF - left ventricular ejection fraction, NS - not significant, NYHA-New York Heart Association, T_3 - triiodothyronine, T_4 - thyroxine, TSH-thyroid-stimulating hormone

Echocardiographic assessment

All participants underwent transthoracic echocardiography by means of an echocardiograph equipped with a broadband transducer (Vivid 7®, GE VingMed Ultrasound AS; Horten, Norway). Measurements of the left atrium, left ventricle (LV), and right ventricle (RV) were obtained from the parasternal long-axis and apical 4-chamber views, in accordance with standard criteria. Left ventricular ejection fraction (LVEF) was calculated using the modified Simpson rule in the apical 2- and 4-chamber views. Mitral flow was measured from the apical 4-chamber view with pulsed-wave Doppler, by placing the sample volume at the tips of the mitral leaflets. The following Doppler indexes of mitral flow were analysed: mitral flow velocity during early (E) and late (A) filling, their ratio (E/a ratio), deceleration time E and deceleration time E/mitral E velocity ratio.

Blood samples

Before the first treatment day, each patient had fasting blood samples drawn from a large antecubital vein for the determination of biochemical and hemostatic values. The BNP levels were analyzed by means of the Triage® BNP test (Biosite Incorporated; San Diego, Calif) within 24 hour after hospitalization. The normal value for the Triage® BNP test was <100 pg/mL. The samples were centrifuged for 10 min and serum free-t3 (fT3), free-t4 (fT4) and thyroid-stimulating hormone (TSH) levels were measured by means of an Immulite® 2000 advanced immunoassay system (Siemens Medical Solutions USA, Inc.; Malvern, Pa). The refer-

ence intervals of our laboratory were as follows: TSH, 0.4 to4 µIU/ml; fT3, 1.57 to 4.71 pg/mL; and fT4, 0.8 to 1.9 ng/dl. Uric acid levels were evaluated by automated biochemistry analyzer (Aeroset, Abbot, Minnesota, USA). Serum hs-CRP, was measured by a sensitive nephelometric assay (Image 800 Immunochemistry System, Beckman Coulter, LA, USA). Fasting blood samples were repeated at the end of the 7 weeks period for every patient. Serum albumin, glucose and lipid levels were measured by standard methods.

Statistical analysis

The SPSS 13.0 (SPSS Inc., an IBM company; Chicago, Ill, USA) package was used for statistical analyses. Results are presented as mean±SD, as median and interquartile ranges, or as percentages and numbers for categorical data. Normality tests were used for all variables. Continuous variables that were normally distributed were analyzed with the 2-tailed *t* test, and unequally distributed variables were analyzed with the Mann-Whitney test and Wilcoxon test. The unpaired, or "independent samples" t-test is used when two separate sets of independent and identically distributed samples are obtained, one from each of the two populations being compared. It was used to paired t-tests to make comparison within groups. Dependent samples (or "paired") t-tests typically consist of a sample of matched pairs of similar units, or one group of units that has been tested twice (a "repeated measures" *t*-test). Categorical data and proportions were analyzed using the Chi-square or Fisher exact test where appropriate. A p value less than 0.05 was considered as statistically significant.

Results

Basal characteristics

Our study population was comprised of 68 patients with documented CAD and chronic HF, 47 patients in the EECP group and 21 in the age-gender matched control group. Baseline characteristics between the groups were almost similar. All patients had angina pectoris and HF symptoms (fatigue and shortness of breath). CCS class and NYHA class was higher in EECP treatment group compared to control group at baseline characteristics. Diastolic blood pressure was higher in EECP group than control group (Table 1). Patients underwent a mean of 34 hours of EECP, with 94% completing a 35-hour course of therapy.

The effects of EECP therapy

There were no significant change in concomitant medication use and no serious adverse effects throughout the study. There were no myocardial infarctions, coronary artery bypass surgery, percutaneous coronary intervention or death occurring during the course of EECP therapy.

After treatment period NYHA functional classification (2.60±0.75.vs 1.72±0.68, p<0.001) and CCS functional classification of angina (2.47±0.88, vs 1.57±0.74, p<0.001) were significantly improved in the EECP group. LVEF and fT3/fT4 ratio significantly increased (p<0.001, p=0.034) in patients with EECP therapy. There was a significant reduction on uric acid (p<0.03,) and BNP (p<0.001, p=0.003) levels with EECP (Table 2). Mitral annular E velocity, deceleration time/E velocity significantly improved in the EECP group (Table 3). These findings, except improvement seen in the CCS class, were not evident in the control group. It was determined that TSH levels were higher after treatment compared to baseline level but TSH level was in normal ranges (Table 2). It was not determined any meaningful change of serum albumin, glucose and lipid levels in both groups (data are not shown).

Discussion

This study demonstrates that EECP therapy compared with controls resulted in significant improvement of functional capacity assessed by NYHA classification; significant increase in LVEF, fT3/fT4 levels and deceleration time/E velocity and significant decrease in BNP and uric acid levels in patients with CAD and chronic HF. EECP group had greater angina status improvement compared to controls and EECP therapy resulted in a significant improvement in NYHA class compared with baseline, a finding not evident in the control group.

Previous studies showed that patients with higher NYHA class had worse prognosis. NYHA class can be improved by medical treatments such as beta blockers, ACE-I/ARB, aldosterone antagonists and bi-ventricular pacemaker (cardiac resynchronization). In our study, patients were on optimal tolerated CAD and HF regime but continue to have severe symptoms with low functional capacity. EECP is a noninvasive, pneumatic technique that utilizes electrocardiogram gated diastolic inflation of a series of lower-extremity cuffs to effectively increase diastolic and mean intracoronary pressures as well as coronary flow while reducing systolic pressure in the central aorta and the coronary artery (18). In addition, EECP improves diastolic filling, decreases left ventricular end-diastolic pressure, and improves LV peak filling rate, end-diastolic volume, and time to peak filling rate (19). The hemodynamic effects produced by EECP are similar to intra-aortic balloon pump (IABP). Sequential inflation of the cuffs, at the onset of diastole, produces aortic counterpulsation and an increase in diastolic pressure while rapid deflation of the cuffs, at the onset of systole, decreases systolic pressure in the vascular system (2). Unlike intraaortic balloon counterpulsation, EECP also increases venous return further, enhancing thus cardiac output (20, 21). Furthermore, as diastolic inflation pressure is increased, the preload is increased, afterload is decreased, contractility is increased and mechanical efficiency is neutral (17). It could be easier to understand why EECP therapy resulted in a significant improvement in functional capacity if it would be given attention of its effect on the circulation. Previous studies showed that improvement in NYHA class has been associated with a favorable prognosis (22, 23). It has been

Table 2. Comparison of clinical and laboratory parameters among patients with or without EECP treatment

Variables	EECP group (n=47)	*p	Control group (n=21)	*p
NYHA Class				
Before treatment	2.60±0.75	<0.001	2.13±0.62	NS
After treatment period	1.72±0.68		2.00±0.40	
CCS Class				
Before treatment	2.47±0.88	<0.001	1.63±0.72	0.023
After treatment period	1.57±0.74		1.20±0.51	
BNP, pg/mL				
Before treatment	782±959	0.003	702±606	NS
After treatment period	463±683		565±563	
Hemoglobin, mg/dL				
Before treatment	13.17±1.88	NS	13.33±1.83	NS
After treatment period	13.28±1.66		13.29±1.80	
hs-CRP, mg/dL				
Before treatment	0.68±0.75	NS	0.78±0.54	NS
After treatment period	0.65±0.85		0.95±0.73	
Uric acid, mg/dL				
Before treatment	6.70±2.74	0.032	6.68±2.40	NS
After treatment period	5.71±2.32		6.16±1.90	
TSH, mg/dL				
Before treatment	1.97±1.52	NS	1.01±0.78	0.035
After treatment period	1.93±2.10		1.33±0.80	
Free-T_3, mg/dL				
Before treatment	2.74±0.60	NS	2.82±0.57	NS
After treatment period	2.89±0.35		3.01±0.38	
Free-T_4, mg/dL				
Before treatment	1.41±0.27	NS	1.36±0.58	NS
After treatment period	1.33±0.30		1.20±0.16	
Free-T_3/Free-T_4 ratio				
Before treatment	2.05±0.55	0.034	2.78±2.74	NS
After treatment period	2.24±0.45		2.56±0.50	
Creatinine, mg/dL				
Before treatment	1.17±0.47	NS	1.24±0.48	NS
After treatment period	1.16±0.48		1.24±0.65	

Continuous variables are given as mean±SD
*paired t-test
BNP - brain natriuretic peptide, CCS - Canadian Cardiovascular Society, EECP - enhanced external counter pulsation, hs-CRP - high-sensitive C - reactive protein, LVEF - left ventricular ejection fraction, NS-not significant, NYHA-New York Heart Association, TSH-thyroid-stimulating hormone

shown that EECP treatment improved symptoms and functional capacity in patients with or without systolic HF (19-21). Lawson et al. (24) reported that beneficial effects seen after the EECP therapy were similar regardless of diastolic or systolic dysfunction in HF patients. The randomized controlled Prospective Evaluation of EECP in Congestive Heart failure (PEECH) trial results showed significant improvement in NYHA functional classification in patients with HF who have undergone EECP

Table 3. Comparison of echocardiographic parameters among patients with or without EECP treatment

Variables	EECP group (n=47)	*p	Control group (n=21)	*p
Ejection fraction, %				
Before treatment	32.26±16.29	<0.001	26.82±7.48	NS
After treatment period	35.65±15.13		27.08±7.27	
Deceleration time, s				
Before treatment	180±52	NS	212±46	NS
After treatment period	184±41		185±54	
Mitral peak E wave, cm/s				
Before treatment	85±19	0.049	64±26	NS
After treatment period	73±26		69±23	
Mitral E wave/Mitral A wave ratio				
Before treatment	1.2±0.6	NS	0.8±0.4	NS
After treatment period	1.0±0.6		0.9±0.4	
Deceleration time/ Mitral E velocity, msec/[cm/s]				
Before treatment	2.38±1.12	0.049	3.72±1.40	NS
After treatment period	2.87±1.16		3.08±1.63	

Continuous variables are given as mean±SD
*paired t-tests
EECP - enhanced external counter pulsation, NS - not significant

therapy (25). The results of our study supported previous studies findings because NYHA class was improved as above mentioned studies.

There were conflicting reports on the effects of EECP on systolic and diastolic functions in patients with EECP treatment in previous studies. While Yavari et al (26). reported that EECP had no significant effect on echocardiographic parameters, Estahbanaty et al. (27) determined that EECP reduced end-diastolic and end-systolic volumes and increased ejection fraction significantly in patients with baseline LVEF ≤ 50% (28). Recently, it was reported that EECP therapy improved global LV systolic and diastolic functions in patients with chronic angina pectoris. There was a significant increase in LVEF with EECP treatment in the above mentioned study (29). In our study, EECP therapy resulted in a significant increase in post-EECP LVEF levels, a finding not evident in the control group.

In the Strong Heart Study, Mishra et al. (30) compared the prognostic value of deceleration time, E-velocity, deceleration time/E-velocity, and deceleration slope in participants in the study, free of clinical cardiovascular disease, in predicting fatal and nonfatal cardiovascular events. It was showed that the deceleration time/E-velocity predicted cardiovascular events, whereas its components (deceleration time and E-velocity) did not. In our study, mitral in flow E velocity decreased and ratio of deceleration time/ E velocity increased after EECP treatment. This suggests an improvement in left ventricular diastolic functions after EECP therapy, a finding not evident in the control group.

Higher uric acid levels were shown to be a strong predictor for worse prognosis in systolic HF patients and in patients at high risk of cardiovascular disease (31-33). Jankowska et al. (32) reported that serum uric acid level increased in parallel to chronic HF severity expressed as NYHA class and hyperuricemia defined as serum uric acid level ≥ 6.5 mg/dl was strongly and independently related to poor prognosis. Before EECP treatment, the uric acid levels were higher than 6.5 mg/dl in both groups. Although after 7 weeks both groups had lower uric acid level compared to baseline levels, reduction of uric acid levels reached statistical significance in patients with EECP therapy. In this study, EECP treatment resulted in a significant reduction in post-EECP uric acid levels, a finding not evident in control group.

The plasma renin concentration decreased, renal plasma flow and glomerular filtration rate increased as well as of the sodium and chloride excretion rates of healthy volunteers without any known cardiovascular, renal, hepatic, pulmonary or endocrine disease (34). Creatinine levels were not evaluated in the above- mentioned study. We could not find any statistical difference between creatinine levels, which were measured at the baseline and after 7 weeks in both groups in this study. Renal plasma flow, glomerular filtration rate and sodium excretion rates was not evaluated in this presented study but we observed that the patients usually needed to urinate approximately in 15 to 20 minutes after beginning EECP therapy. We might speculate that this observation might support to increase renal plasma flow with EECP. It was reported that while serum creatinine and

uric acid had statistically significant positive correlation, glomerular filtration rate and uric acid had negative correlation in patients with CAD (35). However, creatinine level did not change in patients with EECP. In this study, reduced uric acid levels might be a predictor for better renal function after 7 weeks therapy with EECP but this theory needs to be clarified in the future.

High BNP levels have been shown to be independent predictors of mortality and other cardiac composite endpoints for populations with risk of CAD, diagnosed CAD, and diagnosed HF (36, 37). Decreased level of BNP has been inversely related to maximal performance and VO2 max (38). In our study, EECP therapy resulted in a significant decrease in post-EECP BNP levels, a finding not evident in the control group. Reduced BNP levels associated with improvement in CCS class and NYHA class in study patients. Augmentation of renal plasma flow and the sodium excretion rates and increment of ejection fraction may help to reduce BNP levels with EECP therapy.

Thyroid function abnormalities may predict poor prognosis as high BNP levels (39-41). Previously, we have shown that decreased fT3/fT4 ratio might predict worse outcome in patients with dilated cardiomyopathy (41). It was recently shown that cardiac resynchronization therapy (CRT) which is a major treatment option for patients with advanced chronic HF improved fT3/fT4 ratio in patients with reverse remodeling but not patients without reverse remodeling. Authors concluded that improvement of thyroid functional status may play an important role in reverse remodeling of patients with CRT (42). Improvement of fT3/fT4 ratio could be a parameter, which shows recovery of cardiac functions in the above mentioned study. In the presented study, EECP therapy resulted in a significant improvement in post-EECP fT3/fT4 ratio, a finding not evident in the control group. Improvement of fT3/fT4 ratio after EECP treatment might be a sign for recovery of cardiac functions like decreased BNP levels.

Study limitations

Our study included several limitations. The sample size of this study was small and included patients neither with a diagnosis of decompensated HF nor with acute myocardial infarction. These groups may have had a different response to EECP therapy. Therefore, we cannot generalize our results. Another limitation of the study was the quality of life could not be evaluated in this study. Perhaps the major limitation of this study is the lack of a long-term follow- up.

Conclusion

NYHA class, increased BNP and uric acid levels, decreased fT3/fT4 ratio and decreased LVEF are one of the predictors of poor outcomes in patients with HF. In our study, EECP therapy resulted in a significant improvement in post- EECP NYHA class, significant decrease in BNP and uric acid levels and a significant increase in fT3/fT4 ratio and LVEF in patients with EECP. These results suggest EECP therapy might reverse some characteristics of poor prognosis of chronic HF with CAD.

Conflict of interest: None declared.

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