The Effect of Enhanced External Counterpulsation on the Vascular State, Indicators of Glycemic Control and Quality of Life in Patients with Coronary Artery Disease and Type 2 Diabetes Mellitus

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Aim. To study the effect of enhanced external counterpulsation (EECP) on the functional status, quality of life, structural and functional state of the vascular bed, and markers of glycemic control in patients with coronary artery disease (CAD) and type 2 diabetes mellitus (DM).

Material and methods. A pilot prospective randomized study included 30 patients with CAD and DM. Using a random number generator, patients were randomized into 2 groups: EECP (n=15) and a comparison group (n=15). All patients (n=30) received optimal medical therapy (OMT) during 3 months of follow-up. Patients in the EECP group underwent a course of EECP (35 hours, cuff pressure: 220-280 mmHg) during the first 7 weeks of the study. At baseline and after 3 months of follow-up, patients in both groups underwent an assessment of clinical status, quality of life (based on the SF-36 questionnaire), as well as a 6-minute walk test to assess exercise tolerance. The dynamics of fasting glucose, postprandial glucose, insulin resistance index (HOMA-IR) and glycated hemoglobin were assessed. Photoplethysmography and applanation tonometry were performed to assess the state of the vascular bed.

Results. In the EECP group, after 3 months, there was a decrease in the frequency of angina attacks and an improvement in the functional class of angina according to the Canadian Cardiovascular Society (CCS) classification. A significant improvement in exercise tolerance was revealed [an increase in the 6-minute walking distance by 51 (35; 65) m, $p<0.05$], as well as an improvement in the physical and mental components of health according to the SF-36 questionnaire. A positive dynamics was shown in relation to the indicators of the state of both large vessels and the microvasculature ($p>0.05$), with the exception of the reflection index and the stiffness index ($p<0.05$). There was also a significant decrease in the HOMA-IR [-9.9% (-26.5; -4.0) vs 7.7% (-7.9; 13.8), p=0.004], as well as in the levels of fasting glucose [-10.5% (-15.8; -4.0) vs -2.7 (-8.3; 5.9), p=0.012] in the EECP group, compared with the OMT group.

Conclusion. EECP course therapy in addition to OMT has a positive effect on the functional status and quality of life of patients with CAD and DM. After 3 months of observation, there was noted a positive dynamics of the vascular state, as well as markers of glycemic control, and these changes were more pronounced in the EECP group. The results obtained may indicate the effectiveness of EECP as an add-on treatment for this group of patients.

Key words: enhanced external counterpulsation, coronary artery disease, diabetes mellitus, vascular bed, markers of glycemic control, quality of life.

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Introduction

Enhanced external counterpulsation (EECP) is a non-invasive and safe method for the treatment of stable coronary artery disease (CAD), including in the presence of changes in the coronary bed that do not allow for revascularization. [1]. In recent years, we have a tendency to expand the range of indications for the application of this method. The positive impact of EECP on quality of life, exercise tolerance, frequency of angina attacks, the need for nitroglycerin preparations and the number of hospitalizations, as well as on the structural and functional state of the cardiovascular system, is being actively studied [2-6].

The study of EECP in the treatment of patients with CAD and type 2 diabetes mellitus (DM) deserves special attention. DM is a risk factor for the development and progression of CAD, and also significantly worsens the prognosis of patients after surgery [7-11]. According to the ISCHEMIA studies, patients with chronic CAD and DM had a worse prognosis for myocardial infarction (MI) and cardiovascular death compared with patients without DM [12]. The use of non-invasive adjunctive therapies could greatly facilitate the treatment of patients with CAD in combination with DM, as well as improve their quality of life. According to available data, the use of EECP helps to reduce the frequency of angina attacks in patients with CAD and DM and improve glycemic control [13,14]. Research by J.S. Martin et al. also showed a positive effect of EECP on peripheral vascular resistance and the functional state of the microvasculature in patients with impaired glucose tolerance [15].

We decided to investigate the results of this method in more detail, taking into account the effectiveness of EECP in this group of patients, including assessing its potential effect on markers of glycemic control. In Russia, a study of the use of EECP in the treatment of patients with CAD and DM has not been conducted, despite the wide possibilities of using this method. The question of the effectiveness of such treatment remains open and requires further consideration.

The aim of this pilot study is to study the effect of EECP therapy on the functional status of patients, exercise tolerance, quality of life, structural and functional state of the vascular bed, as well as markers of glycemic control in patients with CAD and concomitant DM.

Material and methods

A prospective randomized study was performed at the University Clinical Hospital No. 1 (Sechenov University).

Inclusion criteria: age from 30 to 80 years, signed informed voluntary consent to participate in the study, verified CAD, as well as a confirmed diagnosis of DM. Exclusion criteria: history of thrombophlebitis and/or phlebitis; aneurysm of the thoracic or abdominal aorta; severe pathology of the valvular apparatus of the heart; high pulmonary hypertension (grade 2-3); arrhythmias affecting the synchronization of EECP with ECG; decompensated heart failure; uncontrolled arterial hypertension (>180/110 mm Hg); coagulopathy; severe chronic lung disease; cardiac catheterization performed within 2-4 weeks before the study; treatment with anticoagulants with prothrombin time> 15 sec/INR> 3; pregnancy, breastfeeding; the presence of acute infectious diseases, or the patient's refusal to further participate in the study.

We examined 62 patients with stable CAD [class I-IV according to the classification of the Canadian Cardiovascular Society (CCS)] and DM (non-insulin-dependent), of which 30 patients were included in the study, meeting the inclusion/exclusion criteria. CAD was verified on the basis of coronary angiography (CAG) without coronary artery (CA) stenting (n=12), CAG with CA stenting (n=15), or CA bypass (n=3). 7 patients underwent myocardial infarction. All patients included in the study received optimal medical therapy (OMT) and were on an outpatient basis throughout the observation period. Hypoglycemic therapy in patients of both groups included biguanides, sulfonylurea derivatives, sodium-glucose cotransporter type 2 inhibitors, and dipeptidyl peptidase-4 inhibitors. The study protocol was approved by the local ethics committee of the Sechenov University.

Patients were randomized using a random number generator (Statistica 12; StatSoft Inc.) into two groups of 15 people. During the first 7 weeks of follow-up, patients of the first group underwent a course of EECP in addition to OMT (35 hourly procedures, 5 procedures per week) using the EECP® Therapy System Model TS3 cardiotherapeutic complex (Vasomedical Inc., USA). During the procedure, the pressure in the cuffs was in the range of 220-280 mm Hg. Control over the safety of treatment was carried out by monitoring adverse reactions during EECP procedures. Patients of the second group

received only OMT without the addition of EECP.

All patients (n=30) at baseline and after 3 months were measured fasting glycemia (FPG) and postprandial glycemia (PPG) to determine the dynamics of markers of glycemic control, as well as measured the level of glycated hemoglobin (HbA1c) and insulin resistance index (HOMA-IR). All patients underwent photoplethysmography (Angioscan-01, Angioscan, Russia) at baseline and after 3 months to assess the state of the vascular bed, as well as applanation tonometry (A-pulse CASPro, HealthSTATS, USA). Quality of life was determined using the SF-36 questionnaire. A 6-minute walk test (6MWT) was performed to assess exercise tolerance. The study design is shown in Figure 1.

Statistical analysis

Statistical data processing was carried out using the Statistica 12 program (StatSoft Inc, USA). Analysis of the type of distribution of quantitative and qualitative ordinal variables was not carried out taking into account the small sample size, so non-parametric statistical methods were used. Results are presented as median and interquartile range (25%; 75%). Groups were compared with each other using the Mann-Whitney's U-test for quantitative and qualitative ordinal variables and two-tailed Fisher's exact test for categorical variables. The Wilcoxon's test for quantitative and qualitative ordinal variables and McNemar's chi-square for categorical variables were used to assess changes in indicators from baseline (within each group). Delta-% was also determined to assess changes in quantitative and qualitative ordinal variables compared to the baseline, which was calculated by the formula: $\Delta\% = N1-N0/N0 \times 100\%$, where N0 is the value of the indicator initially, N1 is the value of the indicator in dynamics. Differences were considered statistically significant at a bilateral level of $p<0.05$. The size of each group was 15 people when calculating the sample size (calculator https://www.sealedenvelope.com/; alpha=5%, 1-beta=90%, non-inferiority limit=10%), taking into account the effect size (dynamics of angina pectoris FC in studies using EECP; 8% in the control group, 42% in the experimental group).

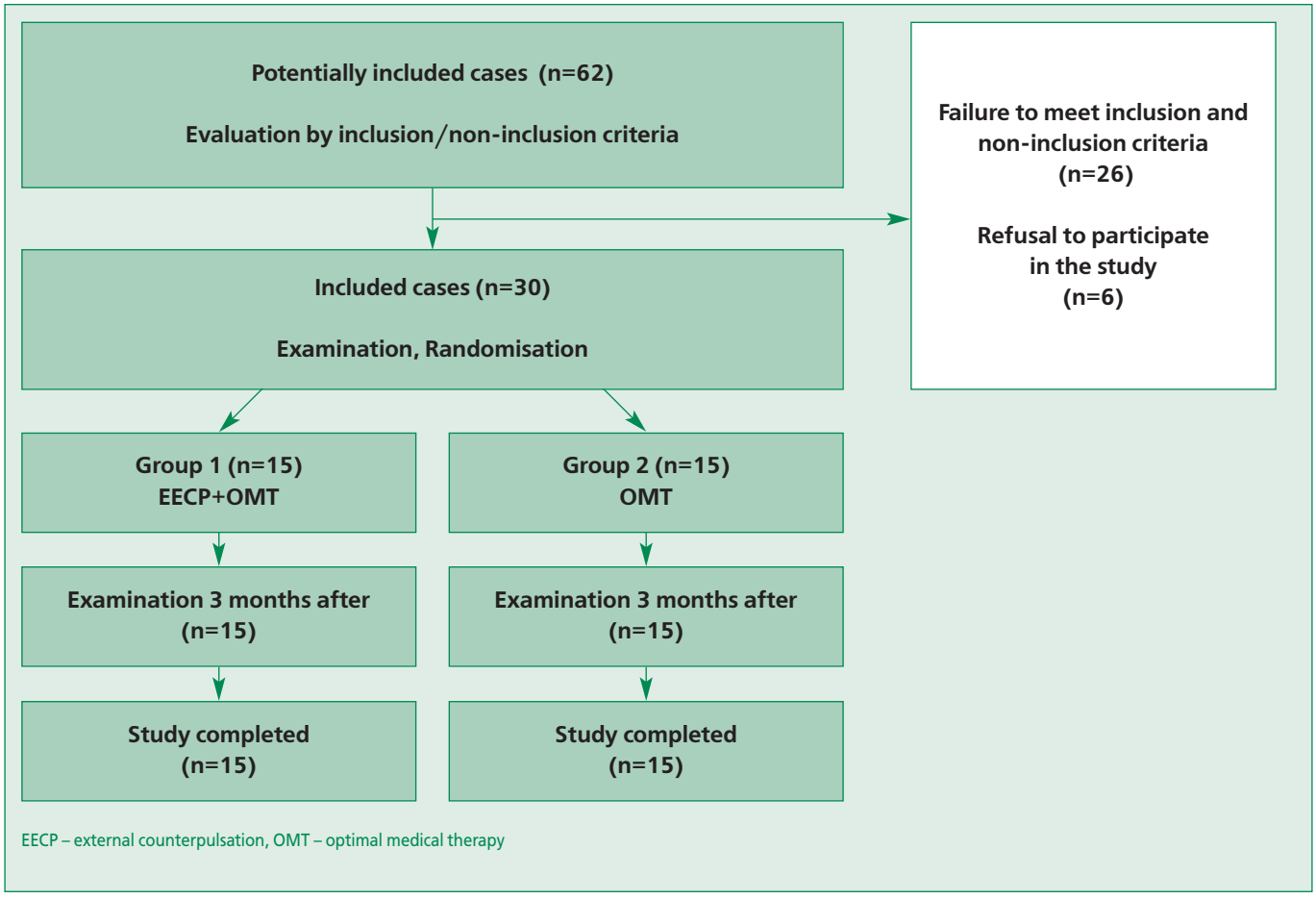

Figure 1. Flow chart of the study design

Table 1. Baseline Characteristics of the Study Groups

Parameter	Group 1 (n=15)	Group 2 (n=15)	p
Age, years	67.0 (61.0; 72.0)	65.0 (60.0; 73.0)	0.709
Men, n	8	10	0.710
BMI, kg/m²	31.0 (28.7; 35.0)	31.7 (29.4; 37.2)	0.678
Smoking, n	1	1	1.0
Disease characteristics			
CAD duration, years	7.0 (5.0; 10.0)	8.0 (7.0; 10.0)	0.320
Multivessel lesion, n	11	10	1.0
History of myocardial infarction, n	4	3	1.0
CA stenting, n	5	6	1.0
CABG, n	1	2	1.0
DM duration, years	8.0 (7.0; 11.0)	8.0 (5.0; 12.0)	0.787
CHF, n	9	8	1.0
Hypertension	13	13	1.0
Medical therapy			
Beta-blockers, n (%)	15	14	1.0
CCB, n	6	8	0.715
Nitrates, n	2	1	1.0
ACEIs/ARBs, n	10	11	1.0
Diuretics, n	5	5	1.0
Myocardial cytoprotectors, n	5	6	1.0
Hypoglycemic therapy, n	15	15	1.0

BMI – body mass index, CABG – coronary artery bypass grafting, CCB – calcium channel blockers, ACEIs – angiotensin-converting enzyme inhibitors, ARBs – angiotensin II receptor blockers

Results

Characteristics of the examined groups

The studied groups were comparable in terms of the main clinical and demographic indicators (Table 1).

Quality of life and exercise tolerance

During the follow-up period, patients in the EECP group didn't report side effects. In both study groups, we didn't observe cases of myocardial infarction, acute cerebrovascular accident and deaths. We noted an improvement in the angina pectoris FC according to the CCS classification in 8 patients (Table 2) on the background of ongoing therapy (EECP+OMT and only OMT).

We noted a significant increase in walking distance according to the 6MWT data when assessing the dynamics of exercise tolerance and quality of life in patients in the EECP group, as well as an increase in the physical and mental health components (Table 3).

Structural and functional state of the vascular bed

According to photoplethysmography and applanation tonometry, in the EECP group we observed the dynamics of such functional indicators of the state of large vessels as phase shift (PS) and central aortic systolic pressure (CASP) ($p<0.05$), as well as the radial augmentation index (rAI) ($p<0.05$) associated with the structural state of the aorta. We also noted an increase in the occlusion index (IO) ($p<0.001$) and the functional index of the microvasculature (Table 4). We noted a tendency to improve the structural parameters of large vessels (stiffness index [SI], $p=0.069$) and microvasculature (reflection index [RI], $p=0.054$). The dynamics of the studied parameters in the comparison group was insignificant.

Glycemic control markers

Positive dynamics in the EECP+OMT group was established in relation to FPG, PPG and HOMA-IR ($p<0.05$) (Table 5). During treatment, we didn't

Table 2. Changes in CCS functional class

FC according to CCS	Group 1 (n=15)			Group 2 (n=15)			p*	p†
	Initially	After 3 months	$p_{0\text{-}3\ months}$	Group 1 (n=15)	Group 2 (n=15)	$p_{0\text{-}3\ months}$		
I, %	20,0	53,3	<0,001	26,7	40,0	<0,001	0,317	0,089
II, %	53,4	33,3	0,004	40,0	33,3	0,180	0,089	1
III, %	20,0	13,4	0,180	26,7	26,7	0,782	0,317	0,021
IV, %	6,6	0	0,009	6,6	0	0,009	1	1

p* - intergroup comparison of baseline indicators, p† - intergroup comparison after 3 months

CCS – Canadian Cardiovascular Society

Table 3. Changes in quality of life and exercise tolerance.

Indicator	Group 1 (n=15)	Group 2 (n=15)	p
PH (scores)			
Initially	45.7 (40.6; 50.7)	49.9 (44.2; 55.4)	0.187
After 3 months	50.2 (45.4; 52.0)	50.3 (44.2; 55.6)	0.539
Dynamics of the indicator for 3 months, Δ%	5.3 (0.2; 11.4)	0.4(0; 5.5)	0.041
$p_{0\text{-}3\ months}$	0.002	0.158	
MH (scores)			
Initially	47.9 (46.3; 56.3)	52.1 (45.9; 56.8)	0.713
After 3 months	52.1 (47.8; 60.0)	52.1 (46.7; 56.8)	0.902
Dynamics of the indicator for 3 months, Δ%	3.8 (1.9; 6.7)	1.3 (-0.4; 3.0)	0.026
$p_{0\text{-}3\ months}$	0.003	0.170	
6-minute walking distance (m)			
Initially	325 (235; 422)	376 (326; 450)	0.174
After 3 months	401 (290; 465)	385 (340; 465)	0.838
Dynamics of the indicator for 3 months, Δ%	18.2 (8.8; 23.4)	2.7 (-1.3; 5.3)	<0.001
$p_{0\text{-}3\ months}$	<0.001	0.074	

PH – physical health summary score, MH – mental health summary score

observe a decrease in the level of glycated hemoglobin. In the comparison group, no statistically significant results were demonstrated, although we observed a moderate decrease in PPG levels ($p>0.05$).

Discussion

According to the selection results, only 30 patients met all the necessary criteria and successfully completed the full course of EECP (35 hours). In total, 525 hours of counterpulsation were performed in the main study group.

The presence of diuretics among the drugs taken is due to the presence of chronic heart failure with congestion in the systemic circulation in 60% of the studied patients. The low need for drugs of the nitroglycerin group is probably due to the selection of OMT and a decrease in the frequency and intensity of angina pectoris, as well as its equivalents, against this background. Only three of the 30 patients included in the study were taking short-acting nitrates, so we couldn't assess the change in the need for drugs in this group during EECP therapy.

Table 4. Dynamics of indicators of the state of the vascular wall

Indicator	Group 1 (n=15)	Group 2 (n=15)	p
Stiffness Index (SI)			
Initially	8.0 (7.4; 8.8)	8.0 (7.1; 8.4)	8.0 (7.4; 8.8)
After 3 months	7.8 (7.2; 8.5)	8.0 (7.1; 8.4)	7.8 (7.2; 8.5)
Dynamics of the indicator for 3 months, Δ%	-2.7 (-4.5; 2.5)	1.2 (-4.8; 4.5)	-2.7 (-4.5; 2.5)
$p_{0\text{-}3\ months}$	0.069	0.932	
Reflection Index (RI)			
Initially	32.5 (28.3; 40.2)	30.2 (27.0; 39.2)	0.683
After 3 months	30.8 (27.8; 36.8)	32.2 (25.6; 36.9)	0.512
Dynamics of the indicator for 3 months, Δ%	-4.9 (-16.4; 1.1)	-2.9 (-8.0; 6.3)	0.267
$p_{0\text{-}3\ months}$	0.053	0.496	
Phase Shift (PS)			
Initially	6.8 (4.5; 7.4)	6.7 (4.1; 8.2)	0.595
After 3 months	7.0 (5.4; 8.1)	6.7 (5.0; 8.5)	0.806
Dynamics of the indicator for 3 months, Δ%	11.0 (1.4; 36.1)	0.0 (-4.3; 9.0)	0.045
$p_{0\text{-}3\ months}$	0.012	0.660	
Occlusion Index (IO)			
Initially	1.52 (1.40;1.72)	1.56 (1.40; 1.80)	0.744
After 3 months	1.63 (1.47;1.82)	1.56 (1.40; 1.70)	0.202
Dynamics of the indicator for 3 months, Δ%	7.3 (4.2; 10.3)	-1.3 (-4.8; 5.8)	0.007
$p_{0\text{-}3\ months}$	<0.001	0.733	
Radial Augmentation Index (rAI)			
Initially	0.744	0.744	0.870
After 3 months	0.202	0.202	0.148
Dynamics of the indicator for 3 months, Δ%	0.007	0.007	0.045
$p_{0\text{-}3\ months}$	0.744	0.744	
Central Aortic Systolic Pressure (CASP), mm Hg.			
Initially	128 (122; 137)	128 (124;132)	0.595
After 3 months	121 (114;126)	125 (122.0;135)	0.023
Dynamics of the indicator for 3 months, Δ%	-5.8 (-8.1; -5.1)	-1.6 (-4.7; 2.5)	0.001
$p_{0\text{-}3\ months}$	0.007	0.016	

Table 5. Changes in glycemic control indicators.

Indicator	Group 1 (n=15)	Group 2 (n=15)	p
FPG (mmol/l)			
Initially	7.0 (5.30; 7.80)	5.90 (5.60; 7.80)	0.713
After 3 months	6.1 (5.10; 6.80)	6.20 (5.70; 7.30)	0.345
Dynamics of the indicator for 3 months, Δ%	-10.5 (-15.8; -4.0)	-2.7 (-8.3; 5.9)	0.012
$p_{0\text{-}3\ months}$	0.005	0.477	
PPG (mmol/l)			
Initially	7.29 (6.30; 9.80)	8.24 (7.10;10.30)	0.267
After 3 months	6.90 (6.33;7.70)	8.10 (7.10; 9.98)	0.007
Dynamics of the indicator for 3 months, Δ%	-7.3 (-16.5; -0.7)	-1.3 (-4.9; 4.1)	0.116
$p_{0\text{-}3\ months}$	0.012	0.334	
HOMA-IR			
Initially	4.42 (2.53; 8.52)	5.69 (2.86; 8.10)	0.806
After 3 months	3.77 (2.11; 8.40)	5.95 (2.37; 7.46)	0.567
Dynamics of the indicator for 3 months, Δ%	-9.9 (-26.5; -4.0)	7.7 (-7.9; 13.8)	0.004
$p_{0\text{-}3\ months}$	<0.001	0.910	
HbA1c (%)			
Initially	7.20 (6.20; 8.50)	6.70 (6.20; 7.70)	0.486
After 3 months	7.0 (5.80; 8.10)	7.00 (6.20; 8.30)	0.935
Dynamics of the indicator for 3 months, Δ%	-3.3 (-7.8; 5.9)	-2.7 (-8.3; 5.9)	0.902
$p_{0\text{-}3\ months}$	0.363	0.490	

FPG – fasting plasma glucose, PPG – postprandial glycemia, HOMA-IR – insulin resistance index, HbA1c – glycated hemoglobin

The positive effect of EECP on the clinical status of patients and quality of life has been repeatedly confirmed in previous studies [1,2,16]. The results of our work suggest that the effectiveness of EECP in relation to the effect on quality of life is also applicable to the group of patients with coronary artery disease and type 2 diabetes mellitus. The most significant subjective assessment was an increase in exercise tolerance, which was accompanied by an improvement in angina pectoris class according to CCS within 1.5 months after completion of the course. We observed an increase in walking distance in both groups due to the influence of both EECP and OMT. The increase in distance along the 6MWT in the EECP group after 3 months averaged 51 m (35; 65) or 18.2%, which was significantly higher ($p<0.001$) than in the OMT group.

Many links in the physiology of changes induced by EECP still remain unexplored, despite ongoing studies. One of the main points of effect of EECP on the structure and functional ability of the endothelium may be the protection of vascular endothelial cells from apoptosis [17]. The second key link in this mechanism is the improvement of endothelial function by increasing the shear stress of the vascular wall, which entails a decrease in the proliferation and migration of smooth muscle cells, suppression of the formation of the extracellular matrix, and, as a result, this inhibits the development of atherosclerosis [18-20].

In this pilot study, such functional parameters of the vascular bed as PS and IO demonstrated statistically significant changes after 3 months of treatment only in the EECP group. Positive dynamics was observed in the analysis of the structural parameter of large vessels (rAI), and the functional parameter (CASP) ($p<0.05$). At the same time, no significant dynamics was shown in relation to such structural indicators as RI (microvasculature) and SI (large vessels) ($p>0.05$). The short duration of the study, as well as the severity of vascular changes in patients with coronary artery disease and type 2 diabetes mellitus, could lead to the result obtained.

One of the mechanisms by which EECP effects glycemic control may be shear stress. According to L.K. Walsh et al., the endothelium of arterioles subjected to intraluminal shear stress for 1 h becomes more insulin sensitive and an increase in insulin-induced dilatation of arterioles is observed [21]. This effect explains the decrease in the HOMA-IR insulin resistance index against the background of the EECP course, which was demonstrated, among other things, in our study.

P.D. Sardina et al reported in their study that EECP therapy reduced the concentration of advanced glycation end products and their receptors in this group of patients up to 6 months after treatment [22]. When assessing glycemic control indicators 48 hours and 2 weeks after the course, the authors found a decrease in FPG (-14.6 and -12.0%) and PPG (-14.6 and -13.5%), respectively [23]. In our study, the positive dynamics of glycemic control in the EECP group was 10.5% for FPG and 7.3% for PPG. The duration of the effect matters: 5 weeks after the

completion of the EECP course (3 months from inclusion in the study), the FPG and PPG values remained below the initial level. In the OMT group, a moderate, statistically insignificant decrease in PPG levels ($p>0.05$) was demonstrated, which is most likely due to the effectiveness of hypoglycemic therapy.

The absence of statistically significant dynamics of HbA1c in our study may be due to both the lack of effect of EECP on the dynamics of the indicator, and be a consequence of the low power of the study. This work was carried out as a pilot, and we are currently planning to conduct similar work on a larger number of patients in order to further refute one of the two above hypotheses.

Study limitations

The main limiting factors in interpreting the results of this study were the small sample size and the absence of a control group that would receive sham counterpulsation to eliminate the placebo effect of EECP therapy. In addition, the measurement of vascular bed parameters and short-term markers of glycemic control, not only at the stage before and 3 months after inclusion in the study, but also immediately after the completion of the EECP course, can make it possible to more accurately assess the dynamics of the studied parameters.

Conclusion

In this pilot study, we demonstrated the positive effect of EECP on the state of the vascular bed, insulin resistance and glycemic control, as well as quality of life in such a difficult to treat group of patients as patients with coronary artery disease and diabetes mellitus. Currently, we continue to explore the possibilities of EECP, but many of the mechanisms and effects of this therapy remain unexplored. Thus, there remains a need to explore the possibilities of EECP in a large group of patients with coronary artery disease and concomitant type 2 diabetes mellitus.

Relationships and Activities. None.

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References

1. Jan R, Khan A, Zahid S, et al. The Effect of Enhanced External Counterpulsation (EECP) on Quality of life in Patient with Coronary Artery Disease not Amenable to PCI or CABG. Cureus. 2020;12(5):e7987. DOI:10.7759/cureus.7987.
2. Wu E, Desta L, Broström A, Mårtensson J. Effectiveness of Enhanced External Counterpulsation Treatment on Symptom Burden, Medication Profile, Physical Capacity, Cardiac Anxiety, and Health-Related Quality of Life in Patients With Refractory Angina Pectoris. J Cardiovasc Nurs. 2020;35(4):375-85. DOI:10.1097/JCN.0000000000000638.
3. Beck DT, Casey DP, Martin JS, et al. Enhanced external counterpulsation reduces indices of central blood pressure and myocardial oxygen demand in patients with left ventricular dysfunction. Clin Exp Pharmacol Physiol. 2015;42(4):315-20. DOI:10.1111/1440-1681.12367.
4. Sharma U, Ramsey HK, Tak T. The role of enhanced external counter pulsation therapy in clinical practice. Clin Med Res. 2013;11(4):226-32. DOI:10.3121/cmr.2013.1169.
5. Lawson WE, Hui JC, Kennard ED, Linnemeier G; IEPR-II Investigators. Enhanced External Counterpulsation Is Cost-Effective in Reducing Hospital Costs in Refractory Angina Patients. Clin Cardiol. 2015;38(6):344-9. DOI:10.1002/clc.22395.
6. Karaganov KS, Slepova OA, Lishuta AS, et al. Medium-term Effects of Enhanced External Counterpulsation in the Structural and Functional Parameters of Blood Vessels in Patients with Coronary Artery Disease. Rational Pharmacotherapy in Cardiology. 2021;17(4):557-63. DOI:10.20996/1819-6446-2021-08-03.
7. Sarwar N, Gao P, Seshasai SR, et al.; Emerging Risk Factors Collaboration. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. Lancet. 2010;375(9733):2215-22. DOI:10.1016/S0140-6736(10)60484-9.
8. Ram E, Sternik L, Klempfner R, et al. Type 2 diabetes mellitus increases the mortality risk after acute coronary syndrome treated with coronary artery bypass surgery. Cardiovasc Diabetol. 2020;19(1):86. DOI:10.1186/s12933-020-01069-6.
9. Kaze AD, Santhanam P, Musani SK, et al. Metabolic Dyslipidemia and Cardiovascular Outcomes in Type 2 Diabetes Mellitus: Findings From the Look AHEAD Study. J Am Heart Assoc. 2021;10(7):e016947. DOI:10.1161/JAHA.120.016947.
10. Arnold SV, Bhatt DL, Barsness GW, et al.; American Heart Association Council on Lifestyle and Cardiometabolic Health and Council on Clinical Cardiology. Clinical Management of Stable Coronary Artery Disease in Patients With Type 2 Diabetes Mellitus: A Scientific Statement From the American Heart Association. Circulation. 2020;141(19):e779-e806. DOI:10.1161/CIR.0000000000000766.
11. Bundhun PK, Bhurtu A, Yuan J. Impact of type 2 diabetes mellitus on the long-term mortality in patients who were treated by coronary artery bypass surgery: A systematic review and meta-analysis. Medicine (Baltimore). 2017;96(22):e7022. DOI:10.1097/MD.0000000000007022.
12. Newman JD, Anthopolos R, Mancini GBJ, et al. Outcomes of Participants With Diabetes in the ISCHEMIA Trials. Circulation. 2021;144(17):1380-195. DOI:10.1161/CIRCULATIONAHA.121.054439.
13. Sahebjami F, Madani FR, Komasi S, et al. Refractory angina frequencies during 7 weeks treatment by enhanced external counterpulsation in coronary artery disease patients with and without diabetes. Ann Card Anaesth. 2019;22(3):278-82. DOI:10.4103/aca.ACA_86_18.
14. Martin JS, Beck DT, Aranda JM Jr, Braith RW. Enhanced external counterpulsation improves peripheral artery function and glucose tolerance in subjects with abnormal glucose tolerance. J Appl Physiol (1985). 2012;112(5):868-76. DOI:10.1152/japplphysiol.01336.2011.
15. Martin JS, Beck DT, Braith RW. Peripheral resistance artery blood flow in subjects with abnormal glucose tolerance is improved following enhanced external counterpulsation therapy. Appl Physiol Nutr Metab. 2014;39(5):596-9. DOI:10.1139/apnm-2013-0497.
16. Arora RR, Chou TM, Jain D, et al. The multicenter study of enhanced external counterpulsation (MUST-EECP): effect of EECP on exercise-induced myocardial ischemia and anginal episodes. J Am Coll Cardiol. 1999;33(7):1833-40. DOI:10.1016/s0735-1097(99)00140-0.
17. Xiong Y, Ren YF, Xu J, et al. Enhanced external counterpulsation inhibits endothelial apoptosis via modulation of BIRC2 and Apaf-1 genes in porcine hypercholesterolemia. Int J Cardiol. 2014;171(2):161-8. DOI:10.1016/j.ijcard.2013.11.033.
18. Xu L, Chen X, Cui M, et al. The improvement of the shear stress and oscillatory shear index of coronary arteries during Enhanced External Counterpulsation in patients with coronary heart disease. PLoS One. 2020;15(3):e0230144. DOI:10.1371/journal.pone.0230144.
19. Liu Y, Xiong Y, Liu D, et al. The effect of enhanced external counterpulsation on C-reactive protein and flow-mediated dilation in porcine model of hypercholesterolaemia. Clin Physiol Funct Imaging. 2012;32(4):262-7. DOI:10.1111/j.1475-097X.2012.01120.x.
20. Zhang Y, He X, Chen X, et al. Enhanced external counterpulsation inhibits intimal hyperplasia by modifying shear stress responsive gene expression in hypercholesterolemic pigs. Circulation. 2007;116(5):526-34. DOI:10.1161/CIRCULATIONAHA.
21. Walsh LK, Ghiarone T, Olver TD, et al. Increased endothelial shear stress improves insulin-stimulated vasodilatation in skeletal muscle. J Physiol. 2019;597(1):57-69. DOI:10.1113/JP277050.
22. Sardina PD, Martin JS, Dzieza WK, Braith RW. Enhanced external counterpulsation (EECP) decreases advanced glycation end products and proinflammatory cytokines in patients with non-insulin-dependent type II diabetes mellitus for up to 6 months following treatment. Acta Diabetol. 2016;53(5):753-60. DOI:10.1007/s00592-016-0869-6.
23. Sardina PD, Martin JS, Avery JC, Braith RW. Enhanced external counterpulsation (EECP) improves biomarkers of glycemic control in patients with non-insulin-dependent type II diabetes mellitus for up to 3 months following treatment. Acta Diabetol. 2016;53(5):745-52. DOI:10.1007/s00592-016-0866-9.

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