Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Effect of enhanced external counterpulsation on saphenous vein graft patency in patients undergoing coronary artery bypass grafting

Jianbo Liao
The First Affiliated Hospital, Sun Yat-sen University
Chaoqun Wang
The First Affiliated Hospital, Sun Yat-sen University
Yi Zhang
The First Affiliated Hospital, Sun Yat-sen University
Hanri Xiao
The First Affiliated Hospital, Sun Yat-sen University
Hanlin Chen
The First Affiliated Hospital, Sun Yat-sen University
Qingyang Song
The First Affiliated Hospital, Sun Yat-sen University
Qiushi Ren
The First Affiliated Hospital, Sun Yat-sen University
Zhilin Miao
The First Affiliated Hospital, Sun Yat-sen University
Yizhong Zhang
The First Affiliated Hospital, Sun Yat-sen University
Zhuoming Zhou
The First Affiliated Hospital, Sun Yat-sen University
Zhongkai Wu
wuzhk@mail.sysu.edu.cn

The First Affiliated Hospital, Sun Yat-sen University
Mengya Liang
The First Affiliated Hospital, Sun Yat-sen University

Research Article

Keywords: External counterpulsation, coronary artery bypass grafting, saphenous vein graft, patency

Posted Date: October 30th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10800060/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Effect of enhanced external counterpulsation on saphenous vein graft patency in patients undergoing coronary artery bypass grafting

Jianbo Liao[1, 2*], Chaoqun Wang[1, 2*], Yi Zhang[1, 2*], Hanri Xiao[1, 2], Hanlin Chen[1, 2], Qingyang Song[1, 2], Qiushi Ren[1, 2], Zhilin Miao[1, 2], Yizhong Zhang[1, 2], Zhuoming Zhou[1, 2†], Zhongkai Wu[1, 2†], Mengya Liang[1, 2†]

[1] Department of Cardiac Surgery, First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.

[2] NHC Key Laboratory of Assisted Circulation, Sun Yat-sen University, China.

*Jianbo Liao, Chaoqun Wang and Yi Zhang contributed equally to this work.

†Mengya Liang, Zhongkai Wu and Zhuoming Zhou are corresponding authors.

Corresponding Authors:

Zhuoming Zhou, MD, Ph.D

E-Mail: zhouzhm8@mail.sysu.edu.cn

Zhongkai Wu, MD, Ph.D

E-Mail: wuzhk@mail.sysu.edu.cn

Mengya Liang, MD, Ph.D

E-Mail: liangmya@mail.sysu.edu.cn

Conflict of Interest Disclosure

All authors declare that they have no conflicts of interest relevant to this work.

Funding Statement

This study was supported by the Guangdong Provincial Basic and Applied Basic Research Foundation (Grant No. 2025A1515010776 to M.L.), National Natural Science Foundation of China (Grant No. 82600792 to Z.Z.), China Postdoctoral Science Foundation General Grant (Grant No. 2025M782346 to Z.Z.), and Postdoctoral Fellowship Program of China Postdoctoral Science Foundation (Grant No. GZB20250560 to Z.Z.).

Effect of enhanced external counterpulsation on saphenous vein graft patency in patients undergoing coronary artery bypass grafting

Abstract

Purpose: 10-20% of saphenous vein grafts (SVGs) occlude within the first year after coronary artery bypass grafting (CABG). Enhanced external counterpulsation (EECP) is a noninvasive therapy that improves coronary perfusion, reduces cardiac workload, and may attenuate neointimal hyperplasia and atherosclerosis. This study aimed to investigate the effect of EECP on SVG patency following CABG.

Methods: Patients undergoing isolated CABG between January 2017 and June 2023 were retrospectively enrolled. The EECP protocol included 35 one-hour sessions, initiated three months postoperatively. The primary outcome was SVG occlusion at one year, assessed by computed tomography angiography. Secondary outcomes included SVG occlusion at two years, stroke, heart failure, coronary revascularization, and recurrent angina. Propensity score matching (PSM), logistic regression, and Kaplan-Meier analysis were used to assess EECP's effects at both per-patient and per-graft levels.

Results: A total of 145 patients were included, with 39 patients undergoing EECP. After PSM, the EECP group showed a lower incidence of SVG occlusion than controls in per-patient (1-year OR 0.325, 95% CI 0.102–0.931; 2-year OR 0.296, 95% CI 0.088–0.916) and per-graft (1-year OR 0.336, 95% CI 0.137–0.768; 2-year OR 0.232, 95% CI 0.084–0.58). Kaplan-Meier analysis confirmed these results after PSM (per patient: hazard ratio [HR] 0.245, 95% CI 0.074–0.808; per graft: HR 0.384, 95% CI 0.176–0.839). No significant differences were observed in stroke, heart failure, coronary revascularization, or recurrent angina.

Conclusions: EECP was associated with a lower risk of SVG occlusion after CABG, suggesting it may be a valuable adjunct to optimize SVG patency and improve long-term outcomes.

Trial registration: ClinicalTrials.gov; NCT03235323. Registration date, 2017/09/05, "retrospectively registered".

Keywords: External counterpulsation, coronary artery bypass grafting, saphenous vein graft, patency.

Abbreviations and Acronyms

CABG = coronary artery bypass grafting

CAD = coronary artery disease

SVG = saphenous vein graft

EECP = enhanced external counterpulsation

PSM = propensity score matching

RCA = right coronary artery

LCX = left circumflex artery

BMI = body mass index

MI = myocardial infarction

LDL-C = low-density lipoprotein cholesterol

EVH = endoscopic vein harvesting

OR = odds ratio

HR = hazard ratio

CI = confidence interval

Introduction

Coronary artery disease (CAD) is the leading global cause of death and disability, disproportionately affecting low- and middle-income countries and accounting for millions of deaths and disability-adjusted life years annually[1-5]. According to both U.S. and European guidelines, coronary artery bypass grafting (CABG) continues to be the preferred and most effective treatment option for patients with multivessel coronary artery disease, left main coronary artery disease, diabetes, or impaired left ventricular function[6-8]. However, multiple arterial grafts are used in <10% of CABG operations currently performed in the United States due to their greater sensitivity to competitive flow and vasospasm, higher technical complexity, and increased perioperative complication risk limit routine use in clinical practice. By contrast, the great saphenous vein is the most commonly used autologous graft in CABG surgery due to its ease of harvest and sufficient length for distal anastomosis with approximately 95% of patients receiving at least one saphenous vein graft[9, 10]. However, high vein graft failure rate remains an inevitable challenge in the long-term graft patency. Approximately 10% of saphenous vein grafts (SVG) fail within one month after surgery owing to technical failure and thrombosis formation[11, 12]. An additional 15% of SVGs may fail within one year due to intimal hyperplasia[13]. Furthermore, due to accelerated atherosclerosis and plaque rupture, up to 40–50% of SVG may become occluded within 10 years following CABG[14]. Current measures for the prevention and treatment of SVG occlusion include refined surgical techniques such as the no-touch harvesting method and external vein support, optimized pharmacological regimens including dual antiplatelet therapy and statins, emerging nanotechnology- and gene-based approaches to locally modulate vascular remodeling, targeted anti-inflammatory treatments, and structured rehabilitation exercise programs which all failed to achieve consistent and clear clinical benefits [15].

Enhanced external counterpulsation (EECP) is a noninvasive therapy that improves coronary perfusion and endothelial function by sequential inflation and deflation of pneumatic cuffs on the lower limbs during the cardiac cycle, thereby alleviating ischemic symptoms and improving functional capacity in patients with coronary artery disease. 2023

AHA/ACC/ACCP/ASPC/NLA/PCNA Guideline recommend EECP to treat patients with coronary artery disease and refractory angina pectoris who do not respond to conventional revascularization methods or intensive medical therapy[16]. In addition to alleviating angina symptoms, EECP also exhibits anti-inflammatory effects, improves endothelial function, promotes vasodilation, and has anti-atherosclerotic properties, as evidenced by experimental data showing significant attenuation of intimal hyperplasia and vascular remodeling in a hypercholesterolemic swine model[17-20]. Therefore, we hypothesize that EECP may improve postoperative graft patency through the aforementioned mechanisms. Here, we aim to perform a respective cohort study analysis to evaluate SVG patency in patients after alone CABG between EECP and medical therapy alone, and to identify a certain subgroup of patients who are likely to have a greater benefit from EECP compared with medical therapy alone.

METHODS

The present research was a retrospective cohort study. Patients undergoing isolated CABG between January 2017 and June 2023 were identified, and the association between postoperative EECP and SVG patency and clinical outcomes was evaluated using propensity score matching (PSM) and time-to-event analyses. To reduce time-related bias, cohort entry (time zero) was defined as 3 months after CABG, corresponding to the earliest clinically eligible time for EECP initiation. Only patients who survived and remained eligible for follow-up imaging at this landmark were included in the analysis. PSM was performed within the landmark-defined cohort. EECP exposure was analyzed using an as-treated framework. Patients were classified as exposed if they initiated EECP after the 3-month postoperative landmark. Patients who did not initiate EECP were assigned to the control group. Patients who were eligible for EECP but did not initiate treatment or have not completed all treatment courses were included in the control group. This study received approval from the Institutional Review Boards of the First Affiliated Hospital of Sun Yat-sen University (approval No. [2017] 144). Written informed consent was obtained from patients in the EECP group,

whereas the requirement for informed consent was waived for patients in the control group. The study was registered at the National Institutes of Health (ClinicalTrials.gov; NCT03235323).

Population

This was a single-institution, retrospective, observational cohort study focusing on graft patency in CABG patients after EECP or medical therapy alone. The study cohort was initially identified by searching the Inpatient Medical Record System at the First Affiliated Hospital of Sun Yat-sen University (Guangzhou, China) for all patients who underwent isolated CABG between January 2017 and June 2023. Clinical data, including cardiovascular risk factors, imaging and angiographic examinations, medical history, and treatment regimens, were extracted from HIS electronic medical record system. The patients were categorized into an EECP group and a control group according to EECP initiation status after the 3-month landmark. The standard EECP treatment protocol involves one-hour sessions, five days per week, over a period of seven weeks. Patients in the EECP group received a total of 35 EECP sessions starting three months after CABG surgery. A completed-treatment framework was applied, whereby only patients who completed the full EECP protocol were considered exposed. Both groups received dual antiplatelet therapy and lipid-lowering therapy for one year postoperatively. The control group received only pharmacological treatment and did not undergo EECP therapy. Follow-up coronary computed tomography angiography or invasive coronary angiography was performed within predefined time windows at approximately 1 year (9–15 months) and 2 years (21–27 months) after CABG. If multiple imaging studies were available within a given time window, the examination closest to the target time point was used for analysis. All post-CABG angiographic data from January 2017 to September 2025 at the First Affiliated Hospital of Sun Yat-sen University were reviewed. Data collection included patient demographics, bypass graft configurations, and angiographic assessment details. Inclusion criteria include patients who underwent CABG and have the computed tomography angiography or invasive angiography. Exclusion criteria were as follows: 1. Concomitant cardiac procedures in addition to CABG. 2. Age less than 18 years. 3. History of stroke, malignancy, peripheral artery disease, rheumatic or

autoimmune diseases, or active infection. 4. Total arterial revascularization. 5. Postoperative intra-aortic balloon pump support. A detailed flowchart is shown in **Figure 1**. The operation report was considered essential for accurately determining graft type and configuration. Each patient had only one postoperative angiogram analyzed.

Outcome Measures

The survival status of participants was obtained through electronic medical records or telephone interviews. The primary endpoint was SVG occlusion evaluated by coronary computed tomography angiography in one-year and two-year follow-up. The secondary endpoints included nonfatal stroke, heart failure, coronary revascularization, recurrent angina, and bleeding events including reoperation to control bleeding and non-CABG-related bleeding in skin, nose, and mouth at one year after CABG. The patency of SVG was assessed using computed tomography angiography and coronary angiography, with grading defined as occlusion (Fitzgibbon grade O)[21]. The classifications for target coronary territory were as follows: Right coronary artery (RCA) territory included distal coronary anastomoses at the right coronary, posterior descending artery, left ventricular branch, or acute marginal branch of the RCA; Left circumflex artery (LCX) territory included anastomotic sites at marginal branches and intermediate artery.

Statistical Analysis

Statistical analyses were conducted according to a predefined analysis plan. Continuous variables were expressed as median with interquartile range (IQR), while categorical variables were presented as counts and percentages. PSM was applied to minimize potential confounding and selection bias between the EECP and control groups. Propensity scores were estimated using a multivariable logistic regression model incorporating clinically relevant baseline covariates, including age, sex, body mass index (BMI), preoperative myocardial infarction, serum creatinine level, smoking status, diabetes mellitus, hypertension, low-density lipoprotein cholesterol (LDL-C), and endoscopic vein harvesting (EVH). A 1:1 nearest-neighbor matching algorithm without replacement

was used to generate matched cohorts. Comparisons of continuous variables were performed using the independent-samples *t*-test for normally distributed data, while categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. Multivariable logistic regression and Cox proportional hazards models were constructed to evaluate the association between EECP and study outcomes. Model 1 was adjusted for basic demographic variables (age, sex, and BMI), and Model 2 was further adjusted for preoperative myocardial infarction, creatinine, smoking status, diabetes, hypertension, LDL-C, and EVH. For per-graft analyses, generalized estimating equations were employed to account for within-patient correlations arising from multiple grafts per individual, with adjustment for the same covariates used in the per-patient analyses. Time-to-event outcomes were analyzed using Kaplan–Meier survival curves and compared by the log-rank test, with hazard ratios (HRs) and 95% confidence intervals (CIs) estimated using Cox proportional hazards regression. The proportional hazards assumption was assessed and confirmed prior to model interpretation. All statistical tests were two-sided, and a P value < 0.05 was considered statistically significant. All analyses were performed using R software (version 4.5.1).

Results

Basic characteristics

A total of 145 patients who underwent CABG were enrolled in this study, with 39 patients (26.9%) receiving EECP and 106 patients (73.1%) receiving control treatment (**Figure 1**). Baseline characteristics before and after PSM are summarized in **Table 1**, while operative characteristics of all patients are presented in **Table 2**. PSM identified 78 patients (39 in the EECP group and 39 in the control group), with comparable propensity score distributions between the matched groups (**Figure 2**), and all preoperative baseline characteristics were balanced with a standardized mean difference of less than 0.1.

Primary outcomes

The SVG occlusion rates in the EECP and control groups are presented in **Table 3-5**. In the per-patient analysis, the EECP group demonstrated significantly lower SVG occlusion rates compared with the control group (1-year odds ratio [OR] 0.354, 95% confidence interval [CI] 0.124–0.870; 2-year OR 0.296, 95% CI 0.100–0.768). Similarly, in the per-graft analysis, the EECP group also showed superior outcomes (1-year OR 0.398, 95% CI 0.162–0.979; 2-year OR 0.288, 95% CI 0.109–0.759). After PSM, the EECP group continued to exhibit significantly lower SVG occlusion rates than the control group in the per-patient analysis (1-year OR 0.325, 95% CI 0.102–0.931; 2-year OR 0.296, 95% CI 0.088–0.916). Consistent findings were observed in the per-graft analysis, where the EECP group outperformed the control group (1-year OR 0.336, 95% CI 0.137–0.768; 2-year OR 0.232, 95% CI 0.084–0.580). In line with the unadjusted models, the adjusted models likewise indicated that the EECP group achieved significantly lower SVG occlusion rates than the control group, confirming the robustness of the findings. Kaplan-Meier event curves and multivariable-adjusted models, shown in **Figure 3-4** and **Table 6**, indicated a significant trend toward lower SVG occlusion rates in the EECP group in per-patient and per-graft analysis after PSM (Per patient: hazard ratio [HR] 0.245, 95% CI 0.074–0.808; per graft: HR 0.384, 95% CI 0.176–0.839). There was no significant difference in the target vessel SVG occlusion rate between the two groups before and after PSM, shown in **Table S1**.

Secondary outcomes

Regarding long-term follow-up, no significant differences were observed between the EECP and control groups for nonfatal stroke, heart failure, coronary revascularization or bleeding events, as shown in **Table S2**. However, the control group had a higher incidence of recurrent angina, though the differences were not statistically significant.

Subgroup analyses

Subgroup treatment effect interactions, shown in **Figure 5** and **Figures S1**, revealed that the EECP group had a lower rate of SVG occlusion in patients over 65 years of age, without a history of

myocardial infarction, without a history of smoking, without a history of hypertension, and with a creatinine level below 81 μmol/L. Due to the small sample size of the subgroup analyses, these results should be considered descriptive and hypothesis-generating only.

Discussion

In our current retrospective cohort analysis, the major findings can be summarized as follows. First, in patients undergoing isolated CABG, EECP therapy after surgery was associated with a significantly lower SVG occlusion rate at patient-level and graft-level compared with the control group. Second, during the two-year follow-up, the EECP group demonstrated comparable long-term outcomes with respect to nonfatal stroke, heart failure, coronary revascularization, recurrent angina and bleeding events compared with the control group. Third, subgroup analyses revealed that the benefit of a lower SVG occlusion rate with EECP remain robust among patients over 65 years of age, without prior myocardial infarction, without a history of smoking or hypertension, and with baseline creatinine levels below 81 μmol/L, with no significant interaction effects identified.

Despite advances in SVG harvesting and handling techniques, intraoperative quality assessment using transit-time flow measurement, and the application of guideline-directed medical therapy, up to 40–50% of SVG may become occluded within 10 years after CABG[14]. Notably, EECP has been demonstrated as a noninvasive intervention capable of improving endothelial function primarily through sustained increases in diastolic shear stress, leading to activation of endothelial-protective signaling pathways, enhanced nitric oxide production, and inhibition of inflammation and intimal hyperplasia, suggesting a potential role in preserving vascular graft integrity[22]. Currently, EECP is primarily recommended for the relief of refractory angina in patients with stable ischemic heart disease (Level of Evidence: B)[23]. Supporting evidence derives from a randomized controlled trial that enrolled 42 symptomatic CAD patients randomized in a 2:1 ratio to EECP (n = 28) versus sham EECP (n = 14). Over the 7-week study period, EECP significantly improved the mean

Canadian Cardiovascular Society angina class compared with controls ($P < 0.001$)[24]. Furthermore, a meta-analysis of 13 observational studies including 949 patients reported that 86% of EECP-treated patients experienced at least a one-class improvement in Canadian Cardiovascular Society angina[25]. Another meta-analysis of 240 CAD patients (EECP, n = 120; control, n = 120) showed that EECP improved endothelial dysfunction and enhanced long-term exercise tolerance[22]. Of note, findings from our center have demonstrated that EECP improved endothelial function by increasing arterial wall shear stress, attenuating lipid-lowering–related endothelial injury, inhibiting vascular smooth muscle cell proliferation and migration, and consequently suppressing neointimal hyperplasia and the progression of atherosclerosis[26, 27]. Therefore, we hypothesize that EECP may improve postoperative graft patency through the aforementioned mechanisms and this study aimed to evaluate the long-term effect of EECP on SVG patency.

Our results demonstrated that EECP therapy was associated with a lower risk of SVG occlusion rates compared with the control group. We observed significant differences between the EECP group and the control group, particularly in terms of SVG occlusion. The unadjusted models showed that the EECP treatment group had significantly better 1-year and 2-year SVG occlusion rates at both the patient and graft levels, with HR consistently below 1. These results suggest that, without any adjustments, EECP appears to be associated with a lower risk of SVG occlusion. Furthermore, after PSM and adjustment in the Cox regression model, EECP was associated with a 61–76% relative reduction in the risk of SVG occlusion, at both the patient and graft levels. This indicates that after controlling for several confounding factors, such as age, sex, and comorbidities, the benefit of EECP persists, but the statistical significance of the results was somewhat consistent due to sample size limitations and the potential effects of adjustment. This change may reflect heterogeneity in treatment effects, meaning that EECP may have varying impacts across different patient populations.

Based on existing evidence, we hypothesize three potential mechanisms by which EECP was associated with a lower risk of SVG occlusion. First, EECP improves endothelial function. Liang et

al. demonstrated that EECP enhanced the proliferation, migration, adhesion, and tube formation of endothelial progenitor cells in hypertensive patients, thereby promoting sustained endothelial repair[28]. Similarly, Wang et al. found that EECP significantly reduced arachidonic acid–induced platelet aggregation, thereby improving endothelial function by reducing platelet activity[29]. Second, EECP suppresses vascular inflammation. Several studies have reported that EECP-induced shear stress enhances chronic nitric oxide production, thereby upregulating endothelial nitric oxide synthase or nitric oxide signaling, exerting anti-inflammatory and anti-atherosclerotic effects[19, 30-34]. EECP has also been shown to significantly reduce proinflammatory biomarkers such as tumor necrosis factor-α and monocyte chemoattractant protein-1[19, 24, 35, 36]. Third, EECP inhibits vascular smooth muscle cell proliferation and migration, thereby reducing intimal hyperplasia and modulating apoptosis-related genes. In a porcine hypercholesterolemia model, Zhang et al. observed that despite a two-fold increase in peak arterial wall shear stress, intimal area, wall thickness, and vascular smooth muscle cell content were significantly higher in the cholesterol group compared with the EECP + cholesterol group and controls, confirming the inhibitory effect of EECP on vascular smooth muscle cell proliferation and neointimal hyperplasia[26]. Moreover, Xiong et al. reported that EECP downregulated the pro-apoptotic gene Apaf-1 and upregulated the anti-apoptotic gene BIRC2, thereby protecting endothelial cells from apoptosis, reducing necrotic cell formation, and delaying atherosclerotic progression[37]. This explanation underscores the role of EECP in our study, where it exerts its effect during the neointimal hyperplasia phase, which was associated with a lower risk of occlusion rate of SVG.

Limitation

First, this study is a retrospective analysis. Although potential confounding biases were controlled through PSM, information bias and selection bias could not be fully avoided. Despite PSM, unmeasured confounders, such as patient motivation or rehabilitation adherence, may still influence treatment allocation and outcomes. Important surgery- and graft-level factors, such as target vessel

quality, degree of native coronary stenosis, and detailed graft configuration, were not consistently available and could not be fully adjusted for, which may result in residual confounding. Further prospective randomized clinical trials are needed for a more robust analysis. Our center has established a related RCT study and is currently recruiting participants (ClinicalTrials.gov ID: NCT03235323). Secondly, this is a study with a small sample size. Although we successfully balanced baseline characteristics between the groups through PSM, there may still be unmeasured confounders, or the small sample size may have led to statistical instability, which could affect the adjusted HR values. And although the generalized estimating equation model was used to correct for cluster effects and avoid statistical bias due to data correlation in the analysis of coronary vessel levels, the sample size (295 venous grafts) may be insufficient to detect small effect differences. Larger-scale population studies are needed to strengthen these findings. Third, the study did not analyze the data based on the location of coronary vessels (e.g., sequential grafts or single-vessel grafts) or stratify by target vessel quality. Future research should explore the heterogeneity of effects. Fourth, the study did not comprehensively examine hemodynamic and hematological indicators, including inflammatory biomarkers and endothelial function indicators, so it could not verify the direct effects of EECP in slowing the degeneration of venous grafts. Fifth, this study only evaluated the short-term patency rate of SVG; however, the long-term effects of EECP on clinical outcomes require further evaluation through extended follow-up.

Conclusion

In this study, we found that the SVG occlusion rate in the EECP group was lower than that in the control group (Per patient: HR 0.245; per graft: HR 0.384). This study provides preliminary evidence that EECP is associated with a reduced risk of venous graft occlusion at the patient level, suggesting a potential role for EECP as an adjunctive strategy to improve venous graft patency after CABG. Future studies in larger, prospective cohorts are warranted to confirm these findings and to identify patient subgroups that may derive the greatest benefit from EECP therapy.

Acknowledgements

The presentation of the manuscript in Abstracts from 106th AATS Annual Meeting. Part of the abstract and data presented in this manuscript have been previously published at https://www.jtcvs.org/article/S0022-5223(26)00435-6/fulltext. This study was supported by the Guangdong Provincial Basic and Applied Basic Research Foundation (Grant No. 2025A1515010776 to M.L.), National Natural Science Foundation of China (Grant No. 82600792 to Z.Z.), China Postdoctoral Science Foundation General Grant (Grant No. 2025M782346 to Z.Z.), and Postdoctoral Fellowship Program of China Postdoctoral Science Foundation (Grant No. GZB20250560 to Z.Z.).

Conflict of Interest

The authors declare that they have no conflicts of interest.

Data Availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Code availability

Not applicable.

Authors' contributions

• **Jianbo Liao**: Writing original draft, supervision, methodology, investigation, formal analysis, conceptualization.

• **Chaoqun Wang**: Writing original draft, data curation, formal analysis, investigation, methodology.

• **Yi Zhang**: Investigation, data curation, methodology, writing original draft

• **Hanri Xiao**: Writing- review & editing.

• **Hanlin Chen:** Visualization, writing-original draft.

• **Qingyang Song**: Writing- review & editing.

• **Qiushi Ren**: Writing- review & editing.

• **Zhilin Miao**: Writing original draft, visualization.

• **Yizhong Zhang**: Writing original draft, visualization.

• **Zhuoming Zhou**: Data curation, writing-original draft.

• **Mengya Liang**: Writing- review & editing.

• **Zhongkai Wu**: Writing- review & editing.

Declarations

Ethics Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the Ethics Committee of First Affiliated Hospital of Sun Yat-sen University (approval No. [2017] 144). Informed consent was obtained from all individual participants included in the study.

Consent to Participate

Informed consent was obtained from all patients for the study.

Consent for Publication

The manuscript was approved by all authors for publication.

380 Table 1. Baseline characteristics of patients before and after propensity score matching.

Characteristics	Before PSM				After PSM			
	Total	Control	EECP	P	Total	Control	EECP	P
N	145	106	39		78	39	39	
Age (median [IQR])	65.00 [58.00, 70.00]	64.50 [58.00, 70.00]	65.00 [58.50, 69.50]	0.690	64.00 [58.00, 69.00]	63.00 [58.00, 68.50]	65.00 [58.50, 69.50]	0.984
Male (%)	128 (88.3)	95 (89.6)	33 (84.6)	0.589	68 (87.2)	35 (89.7)	33 (84.6)	0.735
BMI (median [IQR])	25.00 [23.32, 26.93]	24.87 [23.20, 27.08]	25.90 [23.77, 26.74]	0.621	25.65 [23.75, 26.92]	25.39 [23.74, 27.06]	25.90 [23.77, 26.74]	0.838
Smoking (%)	79 (54.5)	60 (56.6)	19 (48.7)	0.511	40 (51.3)	21 (53.8)	19 (48.7)	0.821
Alcohol (%)	36 (24.8)	26 (24.5)	10 (25.6)	1.000	21 (26.9)	11 (28.2)	10 (25.6)	1.000
Medical history								
Hypertension (%)	74 (51.0)	55 (51.9)	19 (48.7)	0.880	40 (51.3)	21 (53.8)	19 (48.7)	0.821
Diabetes (%)	41 (28.3)	29 (27.4)	12 (30.8)	0.844	24 (30.8)	12 (30.8)	12 (30.8)	1.000
Chronic Pulmonary disease (%)	4 (2.8)	2 (1.9)	2 (5.1)	0.628	3 (3.8)	1 (2.6)	2 (5.1)	1.000
Atrial fibrillation (%)	1 (0.7)	1 (0.9)	0 (0.0)	1.000	0 (0)	0 (0)	0 (0)	NA
Peripheral artery disease (%)	2 (1.4)	2 (1.9)	0 (0.0)	0.951	0 (0)	0 (0)	0 (0)	NA
Preoperative PCI (%)	25 (17.2)	19 (17.9)	6 (15.4)	0.912	14 (17.9)	8 (20.5)	6 (15.4)	0.768
Preoperative MI (%)	47 (32.4)	30 (28.3)	17 (43.6)	0.123	36 (46.2)	19 (48.7)	17 (43.6)	0.820
Creatinine (median [IQR])	81.00 [72.00, 96.00]	82.00 [72.25, 97.00]	80.00 [70.50, 91.50]	0.354	83.00 [71.50, 97.00]	89.00 [76.50, 98.50]	80.00 [70.50, 91.50]	0.115

LVEF (median [IQR])	66.00 [59.00, 72.00]	66.00 [59.00, 72.00]	65.00 [59.50, 70.00]	0.716	66.50 [58.25, 72.50]	68.00 [55.50, 74.50]	65.00 [59.50, 70.00]	0.545
Brain Natriuretic Peptide (median [IQR])	174.10 [62.50, 663.30]	220.25 [63.55, 716.32]	115.00 [48.85, 494.00]	0.287	160.05 [55.83, 813.07]	294.30 [79.80, 1231.50]	115.00 [48.85, 494.00]	0.160
LDL-C (median [IQR])	2.68 [2.15, 3.33]	2.64 [2.10, 3.34]	2.69 [2.26, 3.21]	0.772	2.77 [2.26, 3.31]	2.81 [2.22, 3.38]	2.69 [2.26, 3.21]	0.660

EECP, enhanced external counterpulsation, BMI, body mass index; MI, myocardial infarction; LVEF; left ventricular ejection fraction; LDL-C, low-density lipoprotein cholesterol; PSM, propensity score matching; IQR, interquartile range; PCI, percutaneous coronary intervention.

Table 2. Surgical and graft characteristics of patients undergoing CABG

Characteristics		Total (N=145)	Control (N=106)	EECP (N=39)	P
Cardiopulmonary bypass		145	106	39	1.000
Cardiopulmonary bypass time (median [IQR])		125.95 [111.00, 152.00]	129.50 [113.50, 162.50]	125.00 [94.33, 141.00]	0.029
Total number of grafts		439	317	122	0.387
Graft type	Internal mammary artery, n (%)	142 (32.3)	103 (32.5)	39 (32.0)	0.686
	Radial artery, n (%)	2 (0.5)	2 (0.6)	0 (0)	1.000
	Saphenous vein, n (%)	295 (67.2)	212 (66.9)	83 (68.0)	0.223
Mean number of grafts per patient		3.03	2.99	3.13	0.387
Mean number of SVGs per patient		2.03	2	2.13	0.223
Endoscopic vein harvesting, n (%)		22 (15.2)	16 (15.1)	6 (15.4)	1.000

EECP, enhanced external counterpulsation; SVG, saphenous vein grafts.

Table 3. Multivariable logistic regression analyses of vein graft occlusion at 1 and 2 years after CABG before PSM.

Outcome		Occlusion events before PSM				
		Control	EECP	Model	OR (95% CI)	P
One year	Per patient	36/106 (44%)	6/39 (15.4%)	Unadjusted	0.354 (0.124–0.870)	0.033
				1	0.346 (0.120–0.861)	0.032
				2	0.296 (0.095– 0.793)	0.022
	Per graft	50/212 (23.6%)	9/83 (10.8%)	Unadjusted	0.398 (0.162–0.979)	0.045
				1	0.400 (0.162–0.989)	0.047
				2	0.339 (0.121–0.951)	0.04
Two years	Per patient	30/70 (42.9%)	6/33 (18.2%)	Unadjusted	0.296 (0.100–0.768)	0.017
				1	0.258 (0.083–0.698)	0.011
				2	0.145 (0.029– 0.524)	0.008
	Per graft	42/143 (29.4%)	7/69 (10.1%)	Unadjusted	0.288 (0.109–0.759)	0.012
				1	0.243 (0.094–0.626)	0.003
				2	0.176 (0.052–0.589)	0.005

Odds ratios (ORs) and 95% confidence intervals (CIs) were derived from logistic regression models comparing the EECP and control groups. Unadjusted models present crude estimates. Model 1 was adjusted for age, sex, and BMI. Model 2 was further adjusted for preoperative myocardial infarction, creatinine, smoking status, diabetes, hypertension, LDL-C, and EVH.

EECP, enhanced external counterpulsation; PSM, propensity score matching; OR, odds ratio; CI, confidence interval.

Table 4. Multivariable logistic regression analyses of vein graft occlusion at 1 and 2 years after CABG after PSM.

Outcome		Occlusion events after PSM				
		Control	EECP	Model	OR (95% CI)	P
One year	Per patient	14/39 (35.9%)	6/39 (15.4%)	Unadjusted	0.325 (0.102–0.931)	0.043
				1	0.353 (0.109–1.039)	0.067
				2	0.260 (0.061–0.937)	0.049
	Per graft	21/79 (26.6%)	9/83 (10.8%)	Unadjusted	0.336 (0.137–0.768)	0.012
				1	0.315 (0.126–0.731)	0.009
				2	0.300 (0.108–0.771)	0.015
Two years	Per patient	12/28 (42.9%)		Unadjusted	0.296 (0.088–0.916)	0.04

		6/33 (18.2%)	1	0.294 (0.081–0.967)	0.05	
			2	0.127 (0.015–0.684)	0.029	
			Unadjusted	0.232 (0.084–0.580)	0.003	
	Per graft 19/58 (32.8%)	7/69 (10.1%)	1	0.208 (0.072–0.537)	0.002	
			2	0.148 (0.036–0.486)	0.003	

Odds ratios (ORs) and 95% confidence intervals (CIs) were derived from logistic regression models comparing the EECP and control groups. Unadjusted models present crude estimates. Model 1 was adjusted for age, sex, and BMI. Model 2 was further adjusted for preoperative myocardial infarction, creatinine, smoking status, diabetes, hypertension, LDL-C, and EVH.

EECP, enhanced external counterpulsation; PSM, propensity score matching; OR, odds ratio; CI, confidence interval.

Table 5. One- and two-year saphenous vein graft occlusion before and after PSM.

Outcome			Before PSM				After PSM			
			Total	Control	EECP	P	Total	Control	EECP	P
Occlusion	One year	Per patient	42/145 (29.0%)	36/106 (44.0%)	6/39 (15.4%)	0.048	20/78 (25.6%)	14/39 (35.9%)	6/39 (15.4%)	0.070
		Per graft	59/295 (20.0%)	50/212 (23.6%)	9/83 (10.8%)	0.022	30/162 (18.5%)	21/79 (26.6%)	9/83 (10.8%)	0.018
	Two years	Per patient	36/103 (35.0%)	30/70 (42.9%)	6/33 (18.2%)	0.026	18/61 (29.5%)	12/28 (42.9%)	6/33 (18.2%)	0.068
		Per graft	49/212 (23.1%)	42/143 (29.4%)	7/69 (10.1%)	0.003	26/127 (20.5%)	19/58 (32.8%)	7/69 (10.1%)	0.003

EECP, enhanced external counterpulsation. PSM, propensity score matching.

Table 6. Cox proportional hazards analyses of vein graft occlusion before and after PSM.

Outcome	Model	Occlusion (before PSM)		Occlusion (after PSM)	
		HR (95% CI)	P	HR (95% CI)	P
Per patient	Unadjusted	0.245 (0.074–0.808)	0.012	0.245 (0.074–0.808)	0.012
	1	0.223 (0.067–0.742)	0.014	0.311 (0.085–1.135)	0.077
	2	0.229 (0.068–0.770)	0.017	0.283 (0.072–1.104)	0.069
Per graft	Unadjusted	0.403 (0.198–0.821)	0.010	0.384 (0.176–0.839)	0.013
	1	0.402 (0.197–0.820)	0.012	0.399 (0.182–0.872)	0.021
	2	0.404 (0.196–0.831)	0.014	0.439 (0.191–1.008)	0.052

Hazard ratios (HRs) and 95% confidence intervals (CIs) were derived from cox regression models comparing the EECP and control groups. Unadjusted models present crude estimates. Model 1 was adjusted for age, sex, and BMI. Model 2 was further adjusted for preoperative myocardial infarction, creatinine, smoking status, diabetes, hypertension, LDL-C, and EVH.

EECP, enhanced external counterpulsation; PSM, propensity score matching; HR, hazard ratio; CI, confidence interval.

Figure Legends

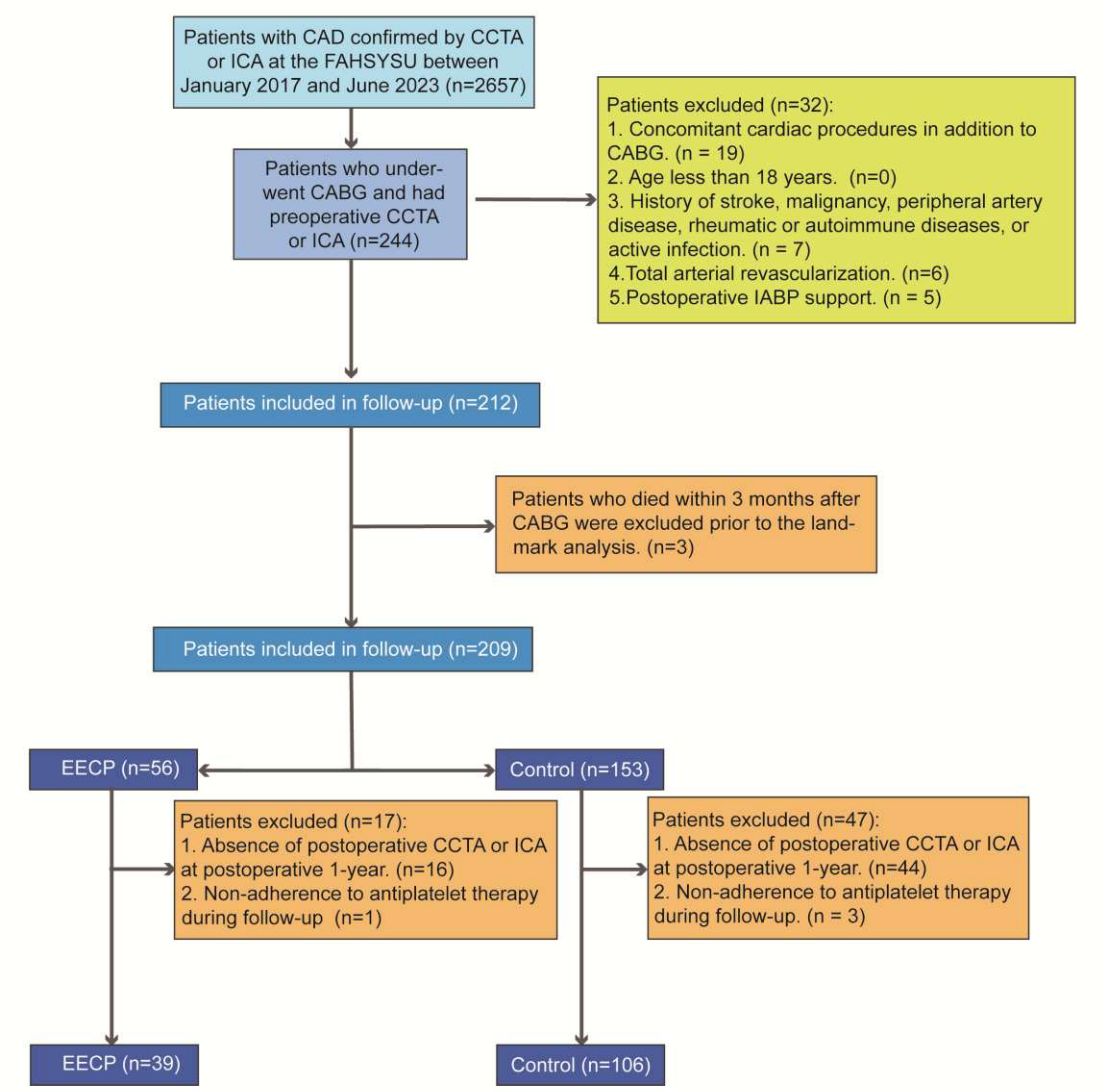
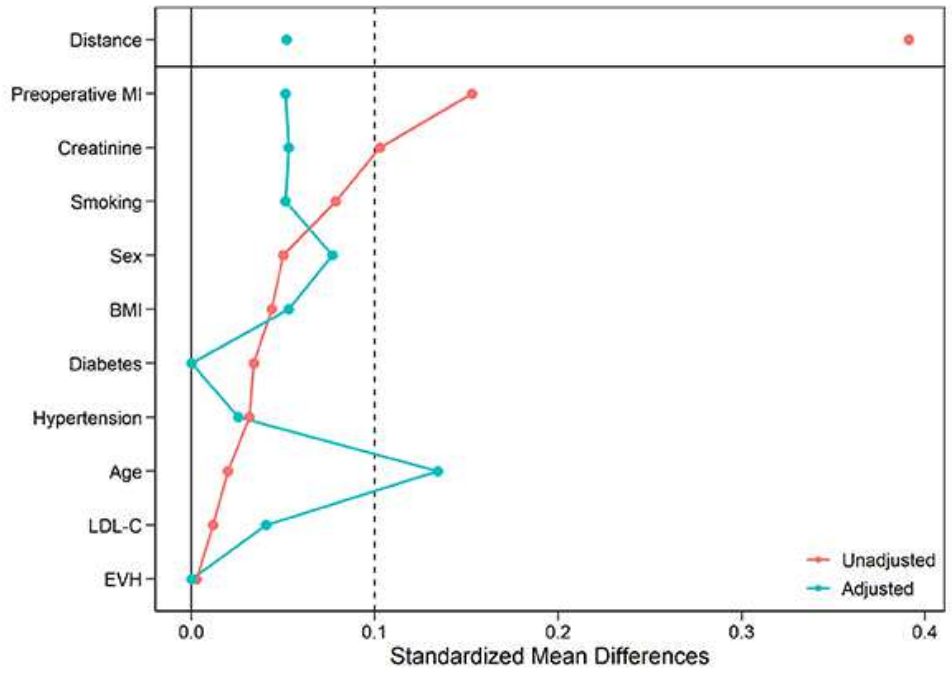


Figure 1. Flow diagram of patient selection for analysis.

CAD, coronary artery disease; CCTA, coronary computed tomography angiography; ICA, invasive coronary angiography; FAHSYSU, First Affiliation Hospital of Sun Yat-sen University, CABG, coronary artery bypass graft surgery; EECP, enhanced external counterpulsation, IABP, postoperative intra-aortic balloon pump.

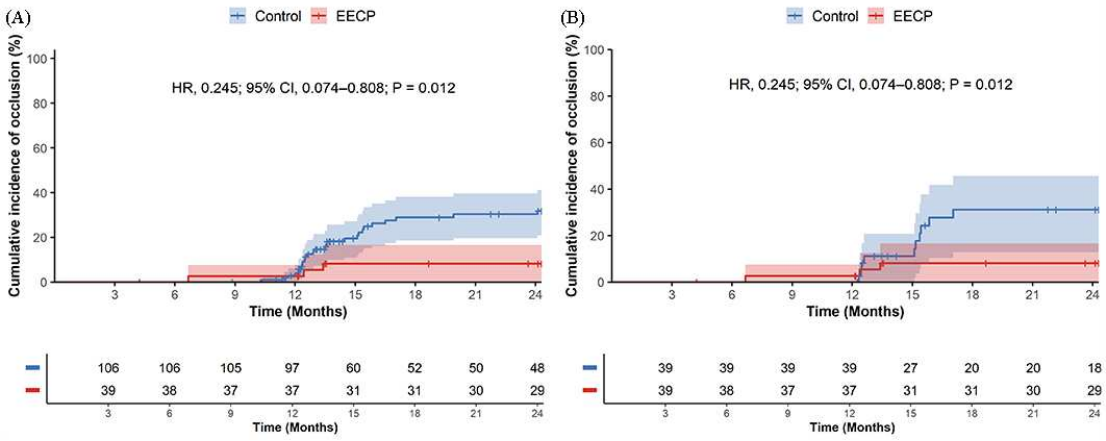


423

424 **Figure 2**. Love plot of standardized mean differences before and after propensity score matching. The dashed vertical
425 line indicates a standardized mean difference of 0.1, representing the threshold for adequate covariate balance.

426 MI, myocardial infarction; BMI, body mass index; LDL-C, low-density lipoprotein cholesterol; EVH, endoscopic vein
427 harvesting.

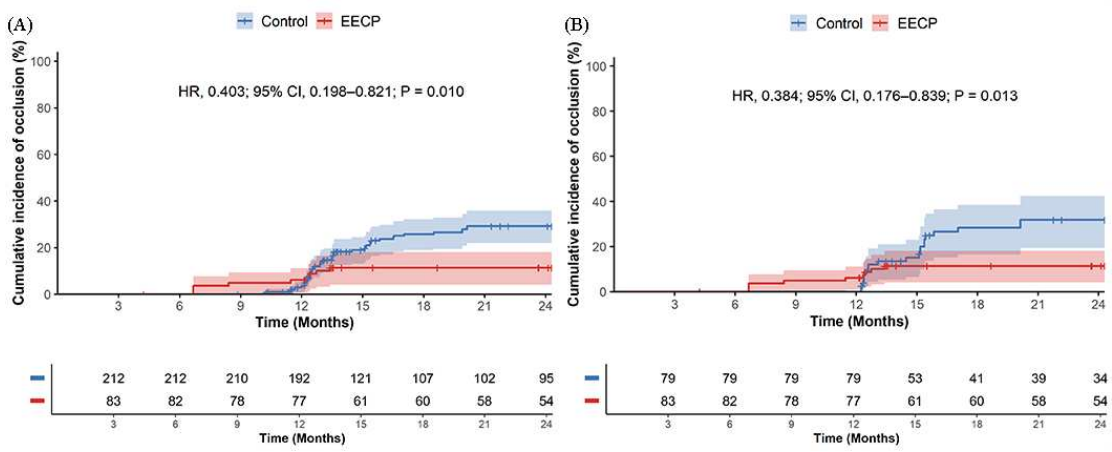
428



429

430 **Figure 3**. Kaplan-Meier-derived cumulative incidence of saphenous vein graft occlusion in a per-patient analysis
431 comparing the EECP and control groups. (A) Before propensity score matching, (B) After propensity score matching.
432 Hazard ratios were estimated using Cox proportional hazards models.

EECP, enhanced external counterpulsation; SVG, saphenous vein graft; PSM, propensity score matching.

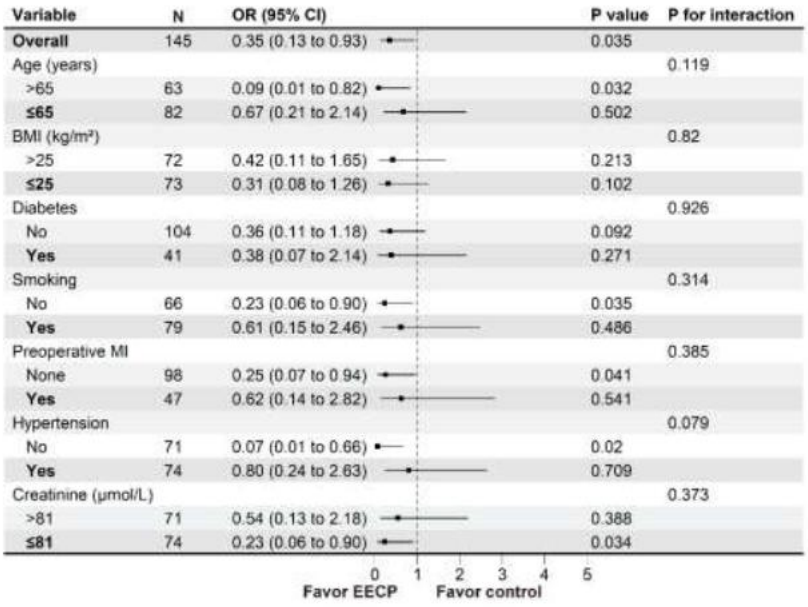


436

437 **Figure 4.** Kaplan-Meier-derived cumulative incidence of saphenous vein graft occlusion in a per-graft analysis
438 comparing the EECP and control groups. (A) Before propensity score matching, (B) After propensity score matching.
439 Hazard ratios were estimated using Cox proportional hazards models.

440 EECP, enhanced external counterpulsation; SVG, saphenous vein graft; PSM, propensity score matching.

441



442

443 **Figure 5.** Subgroup analyses of 1-year saphenous vein graft occlusion at the patient level comparing the EECP and
444 control groups before PSM. Odds ratios and 95% confidence intervals were derived from logistic regression models
445 across prespecified subgroups.

446 EECP, enhanced external counterpulsation; SVG, saphenous vein graft; PSM, propensity score matching; BMI, body
447 mass index; MI, myocardial infarction; OR, Odds ratios; CI, confidence interval.

448

449

Reference

1. Roth GA, Mensah GA, Johnson CO, et al. Global Burden of Cardiovascular Diseases and Risk Factors, 1990-2019: Update From the GBD 2019 Study. *J Am Coll Cardiol.* 2020;76 (25):2982-3021.

2. Nowbar AN, Howard JP, Finegold JA, Asaria P, Francis DP. 2014 global geographic analysis of mortality from ischaemic heart disease by country, age and income: statistics from World Health Organisation and United Nations. *Int J Cardiol.* 2014;174 (2):293-298.

3. Moran AE, Oliver JT, Mirzaie M, et al. Assessing the Global Burden of Ischemic Heart Disease: Part 1: Methods for a Systematic Review of the Global Epidemiology of Ischemic Heart Disease in 1990 and 2010. *Glob Heart.* 2012;7 (4):315-329.

4. Forouzanfar MH, Moran AE, Flaxman AD, et al. Assessing the global burden of ischemic heart disease, part 2: analytic methods and estimates of the global epidemiology of ischemic heart disease in 2010. *Glob Heart.* 2012;7 (4):331-342.

5. Ounpuu S, Yusuf S. Singapore and coronary heart disease: a population laboratory to explore ethnic variations in the epidemiologic transition. *Eur Heart J.* 2003;24 (2):127-129.

6. Lawton JS, Tamis-Holland JE, Bangalore S, et al. 2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *J Am Coll Cardiol.* 2022;145 (3):e18-e114.

7. Neumann FJ, Sousa-Uva M, Ahlsson A, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. *Eur Heart J.* 2019;40 (2):87-165.

8. Zhou Z, Jian B, Chen X, et al. Heterogeneous treatment effects of coronary artery bypass grafting in ischemic cardiomyopathy: A machine learning causal forest analysis. *The Journal of Thoracic and Cardiovascular Surgery.* 2024;168 (5):1462-1471.e1467.

9. Caliskan E, de Souza DR, Böning A, et al. Saphenous vein grafts in contemporary coronary artery bypass graft surgery. *Nat Rev Cardiol.* 2020;17 (3):155-169.

10. Zhou Z, Fu G, Feng K, et al. Randomized evidence on graft patency after off-pump versus on-pump coronary artery bypass grafting: An updated meta-analysis. *International Journal of Surgery.* 2022;98:106212.

11. Hess CN, Lopes RD, Gibson CM, et al. Saphenous vein graft failure after coronary artery bypass surgery: insights from PREVENT IV. *Circulation*. 2014;130 (17):1445-1451.

12. Zhou Z, Liang M, Zhuang X, et al. Long-term Outcomes After On-Pump vs Off-Pump Coronary Artery Bypass Grafting for Ischemic Cardiomyopathy. *Annals of Thoracic Surgery*. 2023;115 (6):1421-1428.

13. Motwani JG, Topol EJ. Aortocoronary saphenous vein graft disease: pathogenesis, predisposition, and prevention. *Circulation*. 1998;97 (9):916-931.

14. Goldman S, Zadina K, Moritz T, et al. Long-term patency of saphenous vein and left internal mammary artery grafts after coronary artery bypass surgery: results from a Department of Veterans Affairs Cooperative Study. *J Am Coll Cardiol*. 2004;44 (11):2149-2156.

15. Zhou Z, Chen W, Cao Y, Abdi R, Tao W. Nanomedicine-based strategies for the treatment of vein graft disease. *Nature Reviews Cardiology*. 2025;22 (4):255-272.

16. Virani SS, Newby LK, Arnold SV, et al. 2023 AHA/ACC/ACCP/ASPC/NLA/PCNA Guideline for the Management of Patients With Chronic Coronary Disease: A Report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. *Circulation*. 2023;148 (9):e9–e119.

17. Gurovich AN, Braith RW. Enhanced external counterpulsation creates acute blood flow patterns responsible for improved flow-mediated dilation in humans. *Hypertension Research*. 2013;36 (4):297-305.

18. Zhang Y, He X, Liu D, et al. Enhanced External Counterpulsation Attenuates Atherosclerosis Progression Through Modulation of Proinflammatory Signal Pathway. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 2010;30 (4):773-780.

19. Barsness GW. Enhanced External Counterpulsation in Unrevascularizable Patients. *Current interventional cardiology reports*. 2001;3 (1):37-43.

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):526-534.

21. FitzGibbon GM, Burton JR, Leach AJ. Coronary bypass graft fate: angiographic grading of 1400 consecutive grafts early after operation and of 1132 after one year. *Circulation*. 1978;57 (6):1070-1074.

22. Yang H, Song L, Ning X, et al. Enhanced external counterpulsation ameliorates endothelial dysfunction and elevates exercise tolerance in patients with coronary artery disease. *Frontiers in Cardiovascular Medicine.* 2022;9:997109.

23. 2014 ACC/AHA/AATS/PCNA/SCAI/STS Focused Update of the Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, and the American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. 2014;64 (18):1929-1949.

24. Braith RW, Conti CR, Nichols WW, et al. Enhanced External Counterpulsation Improves Peripheral Artery Flow-Mediated Dilation in Patients With Chronic Angina: A Randomized Sham-Controlled Study. *Circulation.* 2010;122 (16):1612-1620.

25. Shah SA, Shapiro RJ, Mehta R, Snyder JA. Impact of enhanced external counterpulsation on Canadian Cardiovascular Society angina class in patients with chronic stable angina: a meta-analysis. *Pharmacotherapy.* 2010;30 (7):639-645.

26. 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):526-534.

27. Zhou Z, Jian B, Fu G, et al. Evolution, coronary artery bypass surgery and outcomes of right ventricular dysfunction in ischaemic cardiomyopathy. *European Journal of Cardio-Thoracic Surgery.* 2023;63 (4):ezad136.

28. Liang J, Shi J, Wei W, Wu G. External Counterpulsation Attenuates Hypertensive Vascular Injury Through Enhancing the Function of Endothelial Progenitor Cells. *Frontiers in Physiology.* 2021;11:590585.

29. Wang Y, Xu D. The Effect of Enhanced External Counterpulsation on Platelet Aggregation in Patients with Coronary Heart Disease. *Cardiovascular Drugs and Therapy.* 2022;36 (2):263-269.

30. Harrison DG, Widder J, Grumbach I, Chen W, Weber M, Searles C. Endothelial mechanotransduction, nitric oxide and vascular inflammation. *Journal of internal medicine.* 2006;259 (4):351-363.

31. Masuda D, Nohara R, Hirai T, et al. Enhanced external counterpulsation improved myocardial perfusion and coronary flow reserve in patients with chronic stable angina;

evaluation by(13)N-ammonia positron emission tomography. *Eur Heart J*. 2001;22 (16):1451-1458.

32. Akhtar M, Wu GF, Du ZM, Zheng ZS, Michaels AD. Effect of external counterpulsation on plasma nitric oxide and endothelin-1 levels. *Am J Cardiol*. 2006;98 (1):28-30.

33. Levenson J, Pernollet MG, Iliou MC, Devynck MA, Simon A. Cyclic GMP release by acute enhanced external counterpulsation. *American journal of hypertension*. 2006;19 (8):867-872.

34. Green DJ, Hopman MT, Padilla J, Laughlin MH, Thijssen DH. Vascular Adaptation to Exercise in Humans: Role of Hemodynamic Stimuli. *Physiological reviews*. 2017;97 (2):495-528.

35. Casey DP, Conti CR, Nichols WW, Choi CY, Khuddus MA, Braith RW. Effect of Enhanced External Counterpulsation on Inflammatory Cytokines and Adhesion Molecules in Patients With Angina Pectoris and Angiographic Coronary Artery Disease. *The American Journal of Cardiology*. 2008;101 (3):300-302.

36. Braith RW, Conti CR, Nichols WW, et al. Enhanced external counterpulsation improves peripheral artery flow-mediated dilation in patients with chronic angina: a randomized sham-controlled study. *Circulation*. 2010;122 (16):1612-1620.

37. Xiong Y, Ren Y-f, Xu J, et al. Enhanced external counterpulsation inhibits endothelial apoptosis via modulation of BIRC2 and Apaf-1 genes in porcine hypercholesterolemia. *International Journal of Cardiology*. 2014;171 (2):161-168.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryMaterials.docx