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Research Article

Comparative Assessment of Treatment Outcomes of Various Myocardial Revascularization Strategies in Patients with Diffuse Coronary Artery Disease

Shevchenko Yu L, Ermakov D Yu*, Ulbashev DS, Katkov AA, Vakhrameeva A Yu

St. George Clinic of Thoracic and Cardiovascular Surgery, Pirogov National Medical and Surgical Center of the Russian Ministry of Health; 70 Nizhnyaya Pervomayskaya ul., 105203 Moscow, Russian Federation

***Corresponding author:** Ermakov Dmitriy Yuryevich, St. George Clinic of Thoracic and Cardiovascular Surgery, Pirogov National Medical and Surgical Center of the Russian Ministry of Health; 70 Nizhnyaya Pervomayskaya str., 105203 Moscow, Russian Federation.

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Abstract

Diffuse CAD may be associated with significantly worse surgical outcomes, as well as a higher risk of re-interventions and complications. This article provides a comparative analysis of treatment outcomes in patients with diffuse CAD who were treated with various revascularization strategies. **Objective:** To compare the efficacy and safety of conventional open surgical and endovascular repair of CAD, either alone or combined with extracardiac angiogenesis stimulation. **Materials and Methods:** The study enrolled 117 patients with CAD and diffuse coronary artery disease who were treated between 2011 and 2019 at the St. George Clinic of Thoracic and Cardiovascular Surgery. The study groups were as follows: Group I, CABG (n=30); Group II, PCI (n=30); Group III, CABG combined with extracardiac angiogenesis stimulation (n=30); Group IV, PCI combined with minimally invasive extracardiac angiogenesis stimulation (n=27). **Results:** The mean postoperative follow-up period was 40.6±25.8 months. The highest rate of repeat revascularization was reported in Group II, with 11 patients (36.6%), which was significantly higher than in Group IV, with 5 patients (18.5%) ($p<0.05$). The incidence of the MACE composite endpoint was significantly lower in Groups III and IV compared to Groups I and II ($p<0.05$), with the highest incidence observed in Group II. Survival rates in Groups III and IV were significantly higher compared to other groups. **Conclusion:** The extensive experience of the St. George Clinic suggests that combined myocardial revascularization is an effective and safe treatment option for patients with ischemic heart disease and diffuse coronary artery disease.

Keywords: Ischemic heart disease, diffuse coronary artery disease, myocardial revascularization, YurLeon technique.

Introduction

Coronary artery disease (CAD) patterns are a significant determinant of the optimal treatment strategy for patients with stable ischemic heart disease (IHD) [1]. Over recent decades, the prevalence of patients with diffuse multivessel CAD has increased [2,3]. These patients are typically elderly, polymorbid, and have high-grade angina refractory to drug therapy [3]. Diffuse CAD is a marker of poor prognosis for revascularization, with a limited range of available treatment options. It is one of the primary contributors to persistent or recurrent angina pectoris following coronary revascularization [4].

Complete revascularization by percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG) is not always viable for these patients and is associated with a significant risk of complications [5]. Significant calcification, small diameters

of the coronary arteries (CAs), tandem and diffuse CA lesions, and distal location of CA stenoses preclude both immediate and long-term favorable treatment outcomes [6,7]. Further investigations are required to determine the most appropriate treatment options for IHD patients with diffuse CAD, to facilitate optimal decision-making for revascularization strategies, and to evaluate the safety and efficacy of these interventions.

To improve treatment outcomes in these patients, Yuriy Shevchenko, a member of the Russian Academy of Sciences, developed the YurLeon technique of extracardiac angiogenesis stimulation, which was implemented into clinical practice as a supplement to direct revascularization (Patent RU No. 2758024C1; Application No. 2021105731) [8].

This article demonstrates the comparative results of combining CABG or PCI with the YurLeon technique in patients with diffuse CAD.

Material and Methods

A prospective, randomized study included 117 IHD patients admitted to the St. George Clinic of Thoracic and Cardiovascular Surgery (Pirogov National Medical and Surgical Center) between 2011 and 2019.

Inclusion criteria:

- Symptomatic III-IV IHD;
- CAD refractory to optimal drug therapy;
- Absence of hemodynamically significant cardiac valve disease;
- Diffuse CAD (with two or more segments of one main artery affected, involving more than 50% of the entire length of the vessel, hemodynamically significant luminal narrowing, and a smallest distal diameter of less than 2 mm);
- Left ventricular ejection fraction (LVEF) of less than 40%.

Non-inclusion criteria:

- Left ventricular (LV) aneurysm;
- Need for cardiac resynchronization therapy;
- Renal and hepatic failure;
- LV or atrial thrombosis;
- Hemodynamically significant cardiac valve disease;
- Malignancies.

Upon admission, the patients were randomized into four groups using a random number generator: Group I for CABG (n=30); Group II for PCI (n=30); Group III for CABG combined with extracardiac angiogenesis stimulation (n=30); and Group IV for PCI combined with a minimally invasive procedure of extracardiac vascularization induction (n=27). All study groups were well-balanced for clinical and angiographic characteristics (p=NS) (Tables 1 and 2).

Parameter		Group I (n=30)	Group II (n=30)	Group III (n=30)	Group IV (n=27)	p
Age, years (M±SD)		59.2±5.3	61.1±6.1	58.3±4.9	62.2±3.8	NS
Male, n (%)		22 (73.3)	22 (73.3)	20 (66.7)	19 (70.4)	NS
Chronic obstructive pulmonary disease (COPD), n (%)		8 (26.7)	7 (23.4)	9 (30.0)	7 (25.9)	NS
Smoking, n (%)		19 (63.4)	18 (60.0)	20 (66.7)	17 (63.0)	NS
Type 2 diabetes mellitus, n (%)		20 (66.7)	23 (76.7)	21 (70.0)	19 (70.4)	NS
LVEF (M±SD, %)		33.5±4.8	36.8±5.1	35.5±5.3	34.7±6.1	NS
Arterial hypertension, n (%)		23 (76.7)	24 (80.0)	22 (73.3)	20 (74.1)	NS
History of acute cerebrovascular accident (ACVA), n (%)		2 (6.6)	3 (10.0)	2 (6.6)	2 (7.4)	NS
History of acute myocardial infarction (AMI), n (%)		29 (96.7)	28 (93.3)	30 (100)	25 (92.6)	NS
Angina pectoris classification	III, n (%)	23 (76.7)	21 (70.0)	22 (73.4)	19 (70.4)	NS
	IV, n (%)	7 (23.3)	9 (30.0)	8 (26.6)	8 (29.6)	NS

NYHA CHF classification	I, n (%)	3 (10.0)	4 (13.3)	2 (6.7)	3 (11.1)	NS
	II, n (%)	17 (56.7)	15 (50.0)	16 (53.3)	15 (55.6)	NS
	III, n (%)	9 (30.0)	10 (33.3)	11 (36.7)	8 (29.6)	NS
	IV, n (%)	1 (3.3)	1 (3.3)	2 (6.7)	1 (3.7)	NS
NS: Non-significant						

Table 1: Clinical Characteristics

The mean age of the patients was 59.5±7.5 years. The majority of the patients were male (70.1±4.1%) and were diagnosed with NYHA III angina pectoris and NYHA II chronic heart failure (CHF).

Initial coronary angiography showed an average of 95.5±10.4 significant stenoses in Groups I–IV. On average, 59% of the patients presented with triple vessel CAD. All patients had significant atherosclerotic involvement of the left anterior descending artery or the left main trunk. Most patients (75.1%) were right-dominant (Table 2).

Parameter	**Group I (n=30)**		**Group II (n=30)**	**Group III (n=30)**	**Group IV (n=27)**	**p**
CA lesions, total, n	99		96	103	84	NS
Number of coronary arteries (CAs) with significant stenoses	1, n (%)	1 (3.3)	4 (13.3)	1 (3.3)	3 (11.1)	NS
	2, n (%)	11 (36.6)	9 (30.0)	10 (33.3)	8 (29.6)	NS
	3, n (%)	18 (60.0)	17 (56.7)	19 (63.4)	15 (55.6)	NS
Location of CA stenoses						
Left main trunk, n (%)	2 (6.6)		2 (6.6)	3 (10.0)	1 (3.7)	NS
Left anterior descending artery, n (%)	30 (100)		30 (100)	30 (100)	27 (100)	NS
Circumflex artery, n (%)	21 (70.0)		21 (70.0)	22 (73.3)	23 (85.2)	NS
Right CA, n (%)	25 (83.3)		22 (73.3)	26 (86.6)	23 (85.2)	NS
Right CA dominance, n (%)	23 (76.7)		22 (73.3)	24 (80.0)	19 (70.4)	NS
NS: Non-Significant						

Table 2: Angiographic Characteristics

All patients consented to participate in the study, which was conducted in accordance with the ethical standards set forth in the Declaration of Helsinki by the World Medical Association. The study was approved by the Ethics Committee of Pirogov National Medical and Surgical Center of the Russian Ministry of Health.

The objective of this study was to compare the efficacy and safety of conventional open surgical and endovascular repair of CAD, either alone or combined with extracardiac vascularization stimulation.

Prior to the procedure, clinical data and echocardiography parameters were evaluated, and selective multi-projection coronary angiography was performed according to the established protocol. The results were then assessed by two independent observers.

The conventional CABG procedure was performed via sternotomy, with or without the use of cardiopulmonary bypass. In most cases, the internal mammary artery was used to bypass the left anterior descending artery, while the great or small saphenous vein was used to bypass lesions of the other coronary arteries CAs.

Invasive coronary imaging (intravascular ultrasound) was used during PCI to evaluate CAD severity, identify the optimal stent landing zone and dimensions, and monitor the associated outcomes. Endovascular repair was selected for cases deemed ineligible for CABG by the multidisciplinary team or for patients who declined open surgical revascularization.

In Group III, integrated myocardial revascularization entailed a combination of conventional CABG and YurLeon extracardiac myocardial vascularization stimulation. The procedure involved pericardium and epicardium desquamation using an abrasive glove, subtotal pericardiectomy, and wrapping of the heart with pericardial adipose tissue. Additionally, a postoperative introduction of sterile drainage discharge (50–80 mL) containing angiogenesis stimulation factors was conducted through an additional pericardial drain tube [9].

In Group IV, the first stage involved PCI to relieve the occlusion in a coronary artery. The second stage was the YurLeon technique, performed through a left mini-thoracotomy approach via a 7–10 cm skin incision located 6–8 cm laterally to the midline, typically within the 5th intercostal space. Following subtotal pericardectomy, pericardial adipose tissue was harvested by blunt and sharp dissection without electrocoagulation. After desquamation of the pericardium and epicardium, the heart was wrapped with the adipose tissue graft. A drain tube was then inserted into the remaining posterior portion of the pericardial cavity, followed by pleural cavity drainage and wound closure. On days 2–3, the pleural drain tube was removed, and a sterile drainage discharge containing high amounts of angiogenesis stimulation factors, prepared by the original technique, was introduced into the remaining pericardial cavity through a special drain tube [9].

Statistical Analysis

The statistical calculations were performed using Statistica 12 software (StatSoft, USA). The Shapiro-Wilk test and the Kolmogorov-Smirnov test were used to determine whether the data set followed a normal distribution. Descriptive statistics included the number of observations (n), mean (M), standard deviation (SD), and median (Me). For near-normal distributions, a one-way ANOVA test was used for comparisons across multiple groups. Non-normal data were analyzed using non-parametric tests, including the Kruskal-Wallis U-test for independent multiple samples and the Mann-Whitney U-test to compare differences between two samples. Differences were considered statistically significant at $p<0.05$. Major adverse cardiovascular events and survival rates were analyzed using Kaplan-Meier curves, plotted as step functions, with the function values between time points considered to be constants (Figure 1).

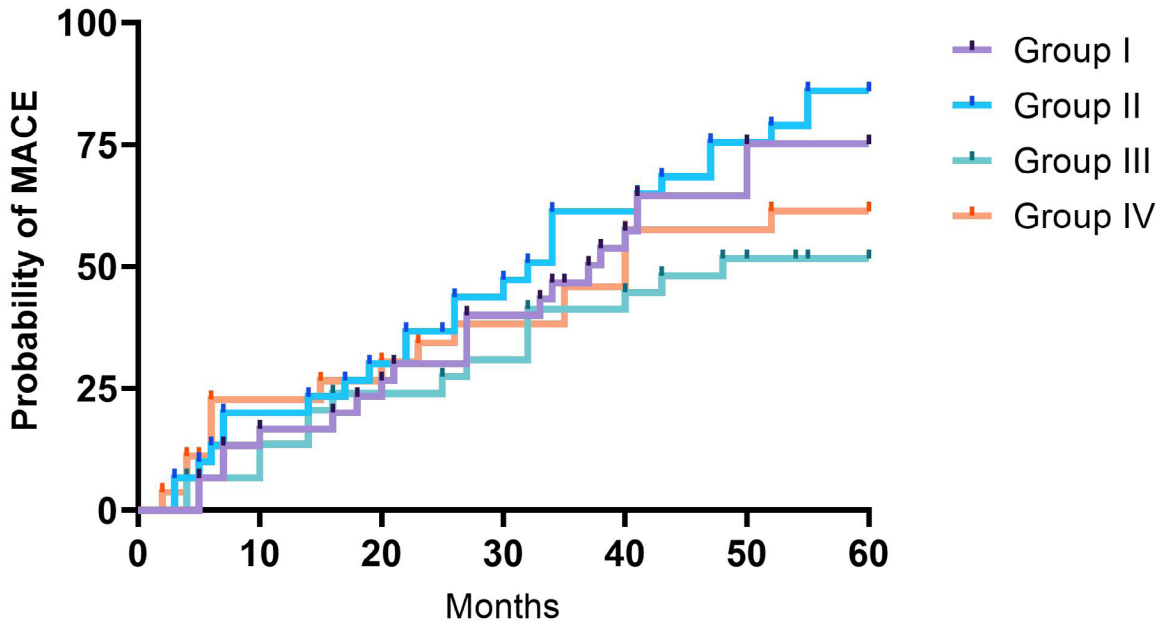

Figure 1: Cardiovascular adverse events (Kaplan-Meier curves)

Results

All patients in the CABG groups underwent left anterior descending artery grafting, with internal mammary artery conduits used in 28 (93.3%) patients from Group I and 29 (96.7%) patients from Group III. Autologous veins were used as bypass grafts for 54 of 82 stenoses in Group I and 56 of 85 stenoses in Group III (p=NS). Most patients had 3 distal anastomoses, with 19 (63.3%) in Group I and 18 (60.0%) in Group III (p=NS) (Figure 2). There were no significant differences between the study groups in primary procedural characteristics. One patient in Group I (3.3%) experienced postoperative bleeding, necessitating emergency re-exploration and hemostasis (Table 3).

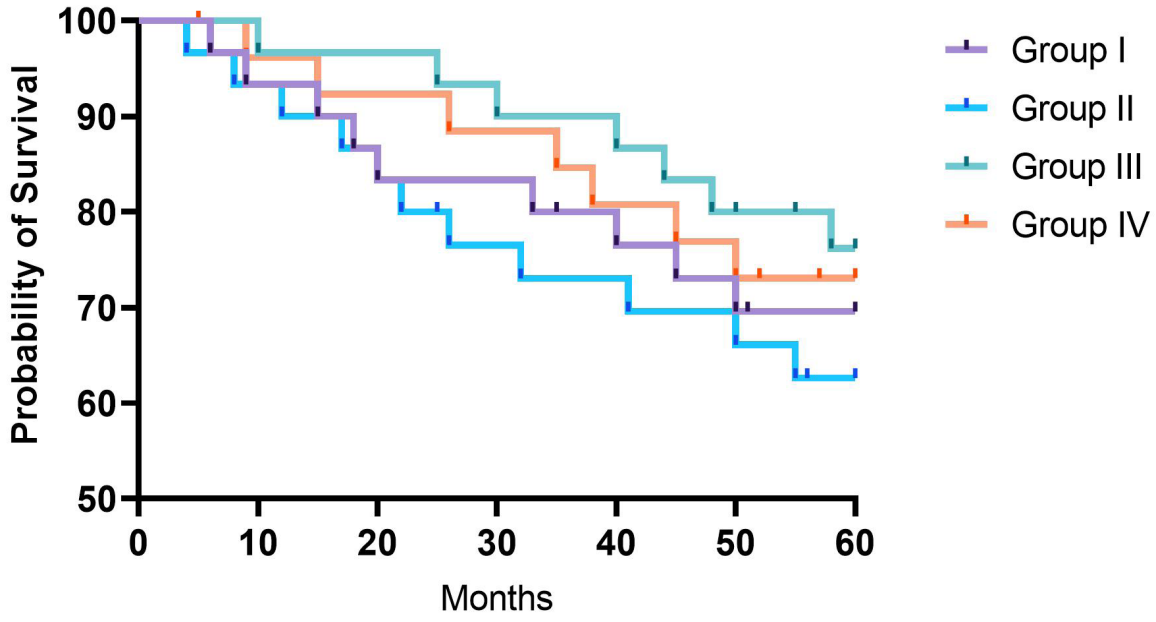

Figure 2: Patient survival (Kaplan-Meier curves)

Parameter	Group I (n=30)	Group III (n=30)	p
Total number of bypass grafts	82	85	NS
Number of autoarterial grafts, n (%)	28 of 82 (34.1)	29 of 85 (34.1)	NS
Number of autovenous grafts, n (%)	54 of 82 (65.9)	56 of 85 (65.9)	NS
Number of distal anastomoses			
1, n (%)	1 (3.3)	1 (3.3)	NS
2, n (%)	8 (26.7)	7 (23.3)	NS
3, n (%)	19 (63.3)	18 (60.0)	NS
4, n (%)	2 (6.7)	4 (13.3)	NS
Length of surgery, min (M±SD)	262.4±62.3	279.9±58.7	NS
Cardiopulmonary bypass, n (%)	9 (30.0)	10 (33.3)	NS
Inotrope support, n (%)	5 (16.7)	4 (13.3)	NS
Vasopressor support, n (%)	17 (56.7)	18 (60.0)	NS
Intraoperative blood loss, mL (M±SD)	362.9±58.7	359.1±55.9	NS
Complications			

Postoperative bleeding, n (%)	1 (3.3)	0	NS
Perioperative AMI, n (%)	0	1 (3.3)	NS
ACVA, n (%)	0	0	NS
Postoperative mortality, n (%)	0	0	NS
Postoperative hospital stay, bed days (M±SD)	9.8±4.52	9.2±4.31	NS
NS: Non-significant			

Table 3: Perioperative Characteristics of CABG Groups

In the PCI groups, 83 of 96 (86.5%) and 79 of 84 (88.1%) CAD lesions were successfully treated with the implantation of 152 stents in Group II and 135 in Group IV (p=NS). No significant differences were observed in the lengths of the stented segments or the average stent diameter between the groups. One patient in Group II experienced a PCI-associated AMI (Table 4).

Parameter	**Group II (n=30)**	**Group IV (n=27)**	**p**
Treated lesions, n (%)	83 (86.5)	74 (88.1)	NS
Number of stents implanted, n	152	135	NS
Length of the stented segment, mm (M±SD)	21.8±6.9	20.5±6.2	NS
Stent diameter, mm (M±SD)	2.74±0.65	2.78±0.72	NS
Number of PCI stages (M±SD)	1.5±0.6	1.5±0.5	NS
Complications			
PCI-associated AMI, n (%)	1 (3.3)	0	NS
ACVA, n (%)	0	0	NS
Postoperative mortality, n (%)	0	0	NS
NS: Non-significant			

Table 4: Perioperative Characteristics of PCI Groups

The mean postoperative follow-up period was 40.6±25.8 months. The highest rate of repeat revascularization (PCI, with no repeat CABG allowed) was observed in Group II, with 11 patients (36.6%), significantly higher than in Group IV, with 5 patients (18.5%) ($p<0.05$). There were no significant differences in the incidence of acute myocardial infarctions, acute cerebrovascular accidents, and cardiovascular mortality between the groups. However, a lower proportion of these complications was reported for Groups III and IV. The incidence of the MACE composite endpoint was significantly lower in Groups III and IV compared to Groups I and II ($p<0.05$), with the highest incidence observed in Group II. There were no significant differences between Groups III and IV. Survival rates in Groups III and IV were significantly higher compared to Groups I and II (Table 5).

Parameter	**Group I (n=30)**	**Group II (n=30)**	**Group III (n=30)**	**Group IV (n=27)**	**p**
Repeat revascularization, n (%)	9 (30.0)*	11 (36.6)*	6 (20.0)*	5 (18.5)*	<0.05
AMI, n (%)	5 (16.7)	4 (13.3)	3 (10.0)	4 (14.8)	NS
ACVA, n (%)	1 (3.3)	2 (6.7)	1 (3.3)	1 (3.7)	NS
Cardiovascular deaths, n (%)	7 (23.3)	8 (26.7)	5 (16.7)	6 (22.2)	NS
MACE, n (%)	22 (73.3)*	25 (83.3)*	15 (50.0)*	16 (59.3)*	<0.05
All-cause deaths, n (%)	9 (30.0)	11 (36.6)*	7 (23.3)*	7 (25.9)*	<0.05
*: statistically significant differences, p<0.05; NS: Non-significant					

Table 5: Five-Year Surgical Outcomes

Discussion

The selection of the most appropriate revascularization strategy for patients with diffuse multivessel CAD has remained a significant clinical challenge over the past few decades [10]. The available treatment options have both advantages and disadvantages. Coronary endarterectomy offers an option to achieve complete surgical revascularization for patients who are not eligible for CABG [11]. However, this technique is associated with a high risk of perioperative myocardial infarction, which has been identified as a key factor limiting its widespread adoption [12]. Transmyocardial laser revascularization has been subject to significant controversy, with low-quality evidence for the efficacy of the technique [13–15]. Incomplete revascularization using minimally invasive CABG in diffuse multivessel CAD avoids major surgical invasion, but it is associated with a high rate of re-interventions and significant cardiovascular complications [16]. Similarly, endovascular treatment in this group was associated with a high frequency of repeat PCI performed for recurrent myocardial ischemia, as reported during the long-term follow-up [17].

In their meta-analysis of 12 studies involving a total of 6,529 patients, Meier et al. concluded that coronary collateralization exerted a considerable protective effect, reducing mortality risk. Patients with high intracardiac and extracardiac collateralization had a 36% reduced mortality risk [18].

The implementation of surgical stimulation of extracardiac myocardial vascularization into clinical practice has considerably expanded the range of treatment options available to patients with diffuse multivessel CAD [19,20].

In this study, the combination of CABG or PCI with the YurLeon technique yielded the most favorable long-term outcomes, including clinical improvement, a notable reduction in the incidence of MACEs, and an enhanced long-term survival rate compared to the control groups. It was observed that the risk of repeat revascularization in the PCI+YurLeon group was lower than that reported in the group of endovascular treatment alone. These findings demonstrate the efficacy of extracardiac myocardial vascularization.

The present study was limited by the small number of patients included and the evaluation of treatment outcomes at different long-term intervals post-surgery.

Conclusion

The extensive experience of the St. George Clinic suggests that combined myocardial revascularization is an effective and safe treatment option for IHD patients with diffuse CAD. The current state of medical technology allows surgeons to combine CABG and extracardiac myocardial vascularization stimulation seamlessly. This novel hybrid approach, which integrates intravascular imaging-guided PCI with the minimally invasive YurLeon technique, expands the range of therapeutic options for patients who were previously considered terminally ill.

Conflict of interest: The authors declare no conflict of interest.

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