Long-term outcomes of microsurgical vs standard coronary artery bypass grafting in patients with concomitant diabetes mellitus

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Abstract

Introduction. CABG outcomes are particularly complicated in patients with diabetes mellitus due to diffuse coronary disease and smaller target artery diameters, increasing the risk of graft occlusion. The quality of the distal anastomosis, enhanced by microsurgical technique, may be critical for long-term results in this group.

Objective. To compare the long-term outcomes of microsurgical versus standard coronary artery bypass grafting (CABG) in patients with concomitant diabetes mellitus.

Methods. A retrospective analysis included 478 diabetic patients who underwent isolated CABG between 2012 and 2022. Patients were stratified into two groups: those undergoing standard CABG (OPT, $n = 186$) and those undergoing microsurgical CABG (MICRO, $n = 292$). To mitigate selection bias, 1:1 propensity score matching was performed, yielding 167 matched pairs ($n = 167$ per group). The primary endpoint for long-term outcomes was freedom from major adverse cardiac and cerebrovascular events (MACCE). Secondary endpoints included overall survival and the individual components of MACCE.

Results. The microsurgical technique was associated with a statistically significant increase in freedom from MACCE compared to the standard technique (10-year freedom: 59.4 % vs 44.3 %, $p = 0.012$). Multivariate Cox regression identified duration of inotropic support ($p = 0.006$), female sex ($p = 0.012$), number of grafts ($p = 0.003$), and left ventricular end-diastolic volume (LVEDV; $p = 0.007$) as independent predictors of MACCE.
No statistically significant difference in overall survival was observed between groups (10-year survival: 82.0 % vs 65.8 %; $p = 0.060$). Multivariate analysis identified female sex ($p = 0.037$) and number of grafts ($p = 0.021$) as independent factors influencing survival.
Cardiac mortality was significantly lower in the MICRO group ($p = 0.003$). Independent predictors of cardiac mortality included female sex ($p = 0.025$), patient age ($p = 0.034$), and number of grafts ($p = 0.026$).
While a trend towards improved freedom from repeat revascularization was noted in the MICRO group, the difference was not statistically significant ($p = 0.17$). No independent predictors for repeat revascularization were identified.
The incidence of myocardial infarction was significantly reduced in the MICRO group ($p < 0.001$). On multivariate analysis, the microsurgical technique ($p = 0.001$), female sex ($p = 0.011$), cardiopulmonary bypass duration ($p = 0.043$), aortic cross-clamp time ($p = 0.046$), inotropic support duration ($p = 0.001$), and number of grafts ($p = 0.028$) were independent factors associated with myocardial infarction risk.

Conclusion. In patients with diabetes mellitus, microsurgical CABG is associated with superior long-term outcomes, evidenced by significantly greater freedom from MACCE, reduced cardiac mortality, and a lower incidence of myocardial infarction compared to the standard technique.

Keywords: cardiopulmonary bypass; coronary artery bypass grafting; diabetes mellitus; long-term results; microsurgical technique; surgical microscope

Отдаленные результаты сравнения микрохирургической и стандартной техники коронарного шунтирования у пациентов с сопутствующим сахарным диабетом

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Аннотация

Актуальность. Проблема реваскуляризации миокарда путем коронарного шунтирования осложняется у пациентов с сахарным диабетом из-за диффузного поражения коронарного русла и малого диаметра целевых артерий, что повышает риск окклюзии шунтов. Качество дистального анастомоза, обеспечиваемое микрохирургической техникой, может быть критически важным для долгосрочных исходов у этой группы.

Цель. Сравнить отдаленные результаты микрохирургической и стандартной техник коронарного шунтирования у пациентов с сопутствующим сахарным диабетом.

Методы. Проведен ретроспективный анализ данных 478 пациентов с сахарным диабетом, перенесших изолированное коронарное шунтирование в период с 2012 по 2022 г. Пациенты были разделены на две группы: группа стандартной техники (OPT, $n = 186$) и группа микрохирургической техники (MICRO, $n = 292$). Для выравнивания групп по базовым характеристикам применялась псевдорандомизация (propensity score matching), где после сопоставления размер каждой группы составил 167 пациентов. При оценке долгосрочных результатов лечения первичной конечной точкой была свобода от больших неблагоприятных сердечно-сосудистых и цереброваскулярных событий (англ. Major Adverse Cardiac and Cerebrovascular Events, MACCE), в которую входили кардиальная смерть (смерть, возникшая из-за заболевания сердца), инфаркт миокарда, инсульт, повторная реваскуляризация. В качестве вторичных конечных точек оценивали выживаемость и отдельные компоненты MACCE.

Результаты. Микрохирургическая техника демонстрировала статистически значимое преимущество в плане отсутствия MACCE ($p = 0{,}012$). Десятилетняя свобода от MACCE составила 44,3 % в группе OPT и 59,4 % в группе MICRO. Многофакторный регрессионный анализ выявил продолжительность инотропной поддержки ($p = 0{,}006$), женский пол ($p = 0{,}012$), количество шунтов ($p = 0{,}003$) и конечный диастолический объем левого желудочка ($p = 0{,}007$) как независимые предикторы MACCE.

Статистически значимых различий в общей выживаемости между группами OPT и MICRO выявлено не было ($p = 0{,}060$). Десятилетняя выживаемость составила 65,8 и 82 % соответственно. Многофакторный регрессионный анализ выявил женский пол ($p = 0{,}037$) и количество шунтов ($p = 0{,}021$) как независимые факторы, влияющие на выживаемость.

Микрохирургическая техника демонстрировала статистически значимое преимущество в плане кардиальной летальности ($p = 0{,}003$). Многофакторный регрессионный анализ указал на женский пол ($p = 0{,}025$), возраст пациентов ($p = 0{,}034$) и количество шунтов ($p = 0{,}026$) как на значимые независимые предикторы кардиальной летальности.

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Анализ свободы от повторной реваскуляризации выявил тенденцию к улучшению в группе MICRO, но различия не достигли статистической значимости ($p = 0{,}17$). Статистически значимых предикторов повторной реваскуляризации выявлено не было.
Микрохирургическая техника была связана со статистически значимым снижением риска инфаркта миокарда ($p < 0{,}001$). Многофакторный регрессионный анализ выявил микрохирургическую технику ($p = 0{,}001$), женский пол пациента ($p = 0{,}011$), продолжительность искусственного кровообращения ($p = 0{,}043$), время пережатия аорты ($p = 0{,}046$), продолжительность инотропной поддержки ($p = 0{,}001$) и количество шунтов ($p = 0{,}028$) как независимые факторы, связанные с риском развития инфаркта миокарда.

Заключение. Микрохирургическая техника коронарного шунтирования у пациентов с сахарным диабетом связана с улучшением долгосрочных результатов, проявляющимся в более низкой частоте MACCE, кардиальной летальности и увеличении частоты случаев без инфаркта миокарда.

Ключевые слова: искусственное кровообращение; коронарное шунтирование; микрохирургическая техника; операционный микроскоп; отдаленные результаты; сахарный диабет

Introduction

Microsurgical coronary artery bypass grafting (CABG) using an operating microscope is a highly precise technique for direct myocardial revascularization. Its main advantage lies in providing the surgeon and assistant with a wide field of view and the ability to adjust magnification according to the diameter of the target coronary artery. This allows for the timely identification and correction of technical imperfections during the formation of the distal anastomosis, ultimately facilitating the creation of hemodynamically optimal and durable connections.

The history of this method in cardiovascular surgery dates back to 1968, when J. Green first performed an anastomosis of the internal thoracic artery to the left anterior descending artery using an operating microscope and microsurgical instruments [1].

As highlighted in the work of Katsumoto K., the use of an operating microscope becomes particularly important when constructing an anastomosis between the internal thoracic artery and the left anterior descending artery (LAD). The internal thoracic artery typically has a smaller diameter than a saphenous vein graft, and its walls are exceptionally thin, demanding maximum precision and control from the surgeon during manipulation [2].

Data from a 20-year follow-up of post-CABG patients indicate that the use of an operating microscope is an independent factor positively influencing survival at various postoperative time points [3].

A study published by Akchurin R.S. and colleagues in 2016 demonstrated the superior efficacy of the microsurgical CABG technique over the conventional method. Analysis of 10-year survival revealed a significant advantage for the microsurgical approach: 84.3 % versus 70.2 %, respectively ($p = 0.03$). Furthermore, the microsurgery group exhibited a reduced incidence of non-fatal myocardial infarctions (9.6 % vs 21.2 %; $p = 0.03$) and repeat revascularizations (10.8 % vs 22.3 %; $p = 0.04$) [4].

In their study, which included 388 patients who underwent myocardial revascularization using microsurgical and standard techniques, Spagnolo S. and colleagues reported a graft patency rate of 83 % in the microsurgical group, compared to 52 % in the conventional group. Follow-up angiography was performed at an average of 6.7 ± 5 years postoperatively in the standard group and 5.8 ± 4 years in the microsurgical group. Regardless of the conduit type, patency was consistently higher with microsurgery. However, due to the relatively small sample size, the difference between techniques reached statistical significance only for venous grafts [5].

The importance of stenosis at the distal anastomotic site resulting from suboptimal suturing technique is often overlooked. The technical difficulty of constructing a high-quality anastomosis increases with decreasing vessel diameter, and indeed, an inverse correlation exists between recipient vessel size and graft occlusion rates. For instance, the 10-year patency of saphenous vein grafts anastomosed to the left anterior descending (LAD) artery was 90 % if the vessel caliber was ≥ 2 mm, but only 52 % if the LAD diameter was < 2 mm [6].

The challenge of myocardial revascularization is compounded in patients with diabetes mellitus, which is characterized by diffuse coronary artery disease. This pathological feature leads to reduced target artery diameter, a factor predisposing to an elevated risk of early graft occlusion (within the first month and year after surgery) and, consequently, adverse outcomes of surgical revascularization. These findings are corroborated by studies confirming the association between diabetes mellitus, small coronary artery diameter, and the risk of graft occlusion [7–10].

Analysis of data from 377,909 UK Biobank participants revealed that ischemic heart disease combined with diabetes mellitus more than doubles the risk of cardiovascular mortality [11]. Notably, up to 75 % of patients with coronary artery disease may have concomitant diabetes mellitus [12].

Given the aforementioned factors influencing graft patency, anastomotic quality is of paramount importance. The application of an operating microscope for surgical field visualization, ensuring precise and atraumatic suturing, appears critically important for optimizing myocardial revascularization outcomes, particularly in patients with diabetes mellitus and distal coronary artery disease.

Furthermore, diabetes is a condition associated with chronic inflammation and macro- and microvascular dysfunction. Some of its most serious complications, such as chronic kidney disease and myocardial infarction, manifest not immediately but after a prolonged period. Therefore, long-term follow-up and the study of postoperative outcomes in large patient cohorts warrant significant attention.

This study aimed to compare the long-term efficacy and safety of microsurgical versus conventional CABG in a cohort of patients with concomitant diabetes mellitus.

Methods

This retrospective cohort study analyzed data from 478 patients (268 men (56.1 %) and 210 women (43.9 %)) who underwent isolated coronary artery bypass grafting (CABG) at a single center (Clinic N) between January 2012 and December 2022. The study included only patients with a confirmed diagnosis of diabetes mellitus. Based on the myocardial revascularization technique, patients were divided into two groups: the OPT group (n = 186), comprising patients who underwent standard CABG using surgical binoculars with 4.5x magnification, and the MICRO group (n = 292), comprising patients who underwent microsurgical CABG using an operating microscope with 6–8x magnification. All patients underwent elective, isolated CABG via median sternotomy under cardiopulmonary bypass. In all cases, the left internal thoracic artery was used to revascularize the LAD, while autovenous conduits were used for branches of the circumflex (CX) and right coronary arteries (RCA).

Clinic N has developed its own methodology for microsurgical CABG [13; 14]. During the formation of the distal anastomosis, standard suture material is used, but the anastomosis is constructed using only one short end of the thread (approximately 5–7 cm). This ensures a consistently visible needle path for both the surgeon and the assistant. The anastomosis to the coronary artery begins with a stitch in the adventitia of the conduit (autologous artery or vein), approximately 1 mm from the "toe". Suturing continues along the far side, inserting the needle from the adventitia to the intima of the conduit and then into the coronary artery, also maintaining a 1 mm distance from the distal edge of the arteriotomy. A continuous suture is performed towards the "heel" of the conduit, after which the sutures are secured and tightened to "seat" the anastomosis. Subsequently, the near side is sutured by inserting the needle from the adventitia to the intima and into the artery, continuing the suture line to the "toe" and distal portion. Finally, the needle is cut, and knots are tied using an instrument (ligature forceps or needle holder). The application of this technique eliminates the need to procure short threads for coronary microsurgery purposes.

Inclusion and exclusion criteria

Inclusion criteria: Patients with ischemic heart disease and hemodynamically significant lesions in 2–3 coronary arteries, with indications and no contraindications for surgery; stable exertional angina pectoris of Canadian Cardiovascular Society (CCS) functional class II–IV; age > 18 years; left ventricular ejection fraction > 35 %; target vessel diameter ≤ 1.5 mm based on selective coronary angiography; and a diagnosis of diabetes mellitus.

Exclusion criteria: Need for emergency coronary artery bypass grafting (CABG); acute coronary syndrome; concomitant cardiac pathology requiring simultaneous intervention; previous cardiac surgery; off-pump CABG; and severe comorbid conditions with an expected life expectancy of less than one year.

Endpoints

The **primary endpoint** for long-term outcome assessment was major adverse cardiac and cerebrovascular event (MACCE)-free survival, defined as a composite of cardiac death, myocardial infarction, stroke, and repeat revascularization.

Secondary endpoints included overall survival and the individual components of MACCE (cardiac death, myocardial infarction, and repeat revascularization).

Patient follow-up and statistical analysis

The study initially included 478 patients. There were 7 in-hospital mortalities (OPT, $n = 3$; MICRO, $n = 4$). Follow-up information was obtained via telephone contact with the patients or their next of kin. Successful contact was established for 319 patients (67.73 % of the total cohort), while contact could not be established with 152 patients (32.27 %). For patients lost to follow-up, the last available medical documentation recording the patient's status was used. To control for potential selection bias and balance baseline characteristics, propensity score matching (PSM) was performed on the initial cohort of 478 patients (excluding 2 patients due to missing data for matching variables). Following 1:1 nearest-neighbor matching without replacement, 167 matched pairs were generated ($n = 167$ per group). The overall median follow-up time was 35.7 months (range: 0.2–132.8 months). The median follow-up was 31.3 months (range: 0.5–132.8 months) in the MICRO group and 40.6 months (range: 0.2–131.8 months) in the OPT group.

Ethical considerations

All patients provided written informed consent, and the study was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical analysis

For the comparative assessment of long-term outcomes between the OPT and MICRO groups, propensity score matching (PSM) was performed in a 1:1 ratio. Nearest neighbor matching without replacement was employed, with a caliper width set to 0.1 of the propensity score standard deviation for the probability of assignment to the MICRO group. The propensity score was estimated using logistic regression incorporating the following covariates: sex, age, height, weight, body mass index (BMI), body surface area (BSA), smoking, chronic obstructive pulmonary disease (COPD), arterial hypertension, prior percutaneous coronary intervention (PCI), multifocal atherosclerosis, history of stroke, chronic kidney disease (CKD)/chronic renal failure (CRF), angina functional class, prior myocardial infarction (MI), number of grafts (as a categorical variable), left ventricular ejection fraction (LVEF), end-diastolic volume (EDV), and end-systolic volume (ESV).

To evaluate the balance between the groups after matching, absolute standardized differences (ASD) were calculated. For continuous variables, ASD was computed as the absolute standardized difference of means, and for binary variables, as the absolute difference in proportions. Additionally, variance ratios were calculated for continuous variables. A variable was considered balanced between groups if the ASD was < 0.1 and, for continuous variables, the variance ratio was between 0.5 and 2. Continuous variables are presented as medians with interquartile ranges. Categorical variables are presented as absolute counts and percentages.

Long-term outcomes for the matched data were compared using univariate Cox proportional hazards regression. Kaplan – Meier curves were used for graphical representation, with hazard ratios (HR) presented alongside their 95 % confidence intervals (CI) and corresponding p-values. Furthermore, multivariate Cox regression analysis was performed on the matched data to identify independent risk factors. The multivariate model included the following explanatory variables: microsurgical technique, sex, age, body mass index, body surface area, smoking, COPD, CKD/CRF, stroke, multifocal atherosclerosis, prior MI, angina functional class, LVEF, LVEDV, LVESV, cardiopulmonary bypass (CPB) time, aortic cross-clamp (ACC) time, duration of mechanical ventilation and inotropic support. A p-value of < 0.05 was considered statistically significant. All statistical analyses were conducted using R software, version 4.3.3 (R Foundation for Statistical Computing, Vienna, Austria; https://www.R-project.org/).

Results

An acceptable balance across all variables was achieved following propensity score matching. The results are presented in Table 1.

Analysis of MACCE

Analysis of MACCE-free survival demonstrated a statistically significant advantage for the microsurgical revascularization technique (Fig. 1). The ten-year MACCE-free survival rate was 59.4 % in the MICRO group, compared to 44.3 % in the standard OPT group ($p = 0.012$; HR = 0.49; 95 % CI [0.28; 0.86]).

Predictors of MACCE were identified within the study. Univariate regression analysis revealed the following statistically significant predictors: microsurgical revascularization technique ($p = 0.012$; HR = 0.49; 95 % CI [0.28; 0.86]), CPB time ($p = 0.041$; HR = 1.13; 95 % CI [1.01; 1.26]), and aortic cross-clamp (ACC) time ($p = 0.043$; HR = 1.18; 95 % CI [1.01; 1.38]). Multivariate regression analysis identified duration of inotropic support, female sex, number of grafts, LVEDV as independent predictors of MACCE (Table 2).

Survival and Its Predictors

Assessment of overall survival revealed no statistically significant difference between the OPT and MICRO groups ($p = 0.060$; HR = 0.54; 95 % CI [0.28; 1.03]) (Fig. 2). The ten-year survival rates for the MICRO and OPT groups were 82.0 % and 65.8 %, respectively (Table 3).

CPB time and ACC time showed a negative association with survival in the univariate analysis; however, their significance was attenuated upon adjustment for other factors in the multivariate model. Similarly, LVEF was a significant predictor of survival only in the univariate analysis, losing its independent prognostic value in the multivariate model.

Multivariate regression analysis identified female sex and the number of grafts as independent predictors influencing survival (Table 4).

Table 1. Comparative patient characteristics and procedural data (number of grafts) before and after propensity score matching

Characteristics	Unmatched			Matched		
	OPT	MICRO	ASD	OPT	MICRO	ASD
Number of patients, *n* (%)	186 (100)	292 (100)		167 (100)	167 (100)	
Female Sex, *n* (%)	65 (34.9)	145 (49.7)	0.147	64 (38.3)	73 (43.7)	0.054
Age, years	63 (59–68)	65 (60–69)	0.121	63 (59–68)	64 (59.5–69)	0.07
Height, cm	168 (160–173)	164 (158–171)	0.21	167 (160–172.5)	166 (159–172)	0.053
Weight, kg	85 (78–96)	84 (76–95)	0.133	84 (78–96)	84 (76–95)	0.069
Body Mass Index, kg/m^2	30.4 (28.1–35)	31.1 (28.3–34.5)	0.018	30.4 (28–35)	30.6 (28–34)	0.047
Body Surface Area, m^2	2 (1.9–2.1)	2 (1.8–2.1)	0.157	2 (1.9–2.1)	2 (1.9–2.1)	0.081
Smoking, *n* (%)	47 (25.3)	44 (15.1)	0.102	35 (21)	29 (17.4)	0.036
COPD, *n* (%)	9 (4.8 %)	5 (1.7)	0.031	5 (3)	2 (1.2)	0.018
Arterial Hypertension, *n* (%)	184 (98.9)	290 (99.3)	0.004	165 (98.8)	165 (98.8)	0
Prior PCI, *n* (%)	0 (0)	2 (0.7)	0.007	0 (0)	0 (0)	0
Multifocal Atherosclerosis, *n* (%)	61 (32.8)	107 (36.6)	0.038	52 (31.1)	60 (35.9)	0.048
History of Stroke, *n* (%)	12 (6.5)	25 (8.6)	0.021	11 (6.6)	13 (7.8)	0.012
CKD/CRF, *n* (%)	40 (21.5)	65 (22.3)	0.008	37 (22.2)	44 (26.3)	0.042
Angina Functional Class, *n* (%)						
Class 0, *n* (%)	0 (0)	5 (1.7)	0.017	0 (0)	0 (0)	0
Class I, *n* (%)	2 (1.1)	6 (2.1)	0.01	2 (1.2)	2 (1.2)	0
Class II, *n* (%)	52 (28)	47 (16.1)	0.119	40 (24)	32 (19.2)	0.048
Class III, *n* (%)	117 (62.9)	209 (71.6)	0.087	112 (67.1)	116 (69.5)	0.024
Class IV, *n* (%)	15 (8.1)	25 (8.6)	0.005	13 (7.8)	17 (10.2)	0.024
Prior Myocardial Infarction, *n* (%)	114 (61.3)	192 (65.8)	0.045	105 (62.9)	114 (68.3)	0.054
3 Grafts, *n* (%)	84 (45.2)	163 (55.8)	0.106	83 (49.7)	83 (49.7)	0
LV Ejection Fraction, %	60 (53–65)	60 (54–65)	0.017	60 (52.5–65)	60 (54–65)	0.006
LVEDV, ml	95 (81.2–122)	94 (78–118.2)	0.104	93 (80.5–120)	94 (79–121)	0
LVESV, ml	38 (28–51.5)	37 (28.8–51.2)	0.082	36 (28–50)	38 (28.5–53)	0.016

Note. CCS FC – Canadian Cardiovascular Society functional class; CKD/CRF – Chronic kidney disease / Chronic renal failure; COPD – Chronic obstructive pulmonary disease; LVEF – Left ventricular ejection fraction; LVEDV – Left ventricular end-diastolic volume; LVESV – Left ventricular end-systolic volume; PCI – Percutaneous coronary intervention.

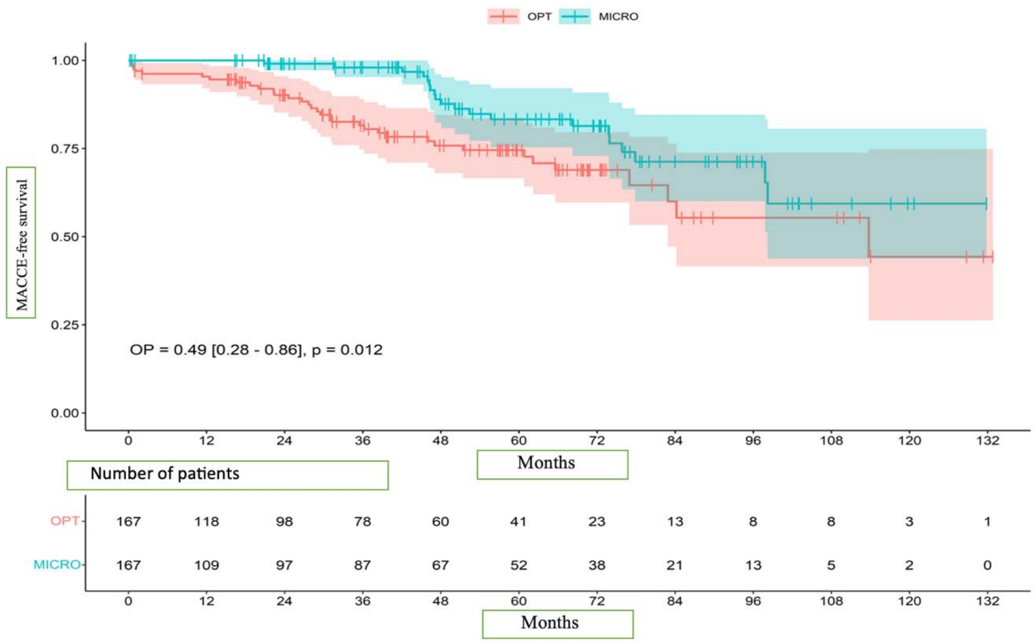

Fig. 1. Major adverse cardiac and cerebrovascular event (MACCE)-free survival.

Note. MACCE – major adverse cardiac and cerebrovascular events; MICRO – microsurgical intervention group; OPT – standard technique group.

Table 2. Predictors of major adverse cardiac and cerebrovascular events (MACCE)

Characteristics	Results of Cox Regression Models with MACCE as the Outcome (After Matching)					
	Univariate Regression Model			Multivariate Regression Model		
	HR	95 % CI	*p*-value	HR	95 % CI	*p*-value
Microsurgical Technique	0.49	[0.28; 0.86]	**0.012**	0.60	[0.26; 1.37]	0.22
Female Sex	0.67	[0.38; 1.19]	0.17	0.29	[0.11; 0.76]	**0.012**
Age, per 10-year increment	1.17	[0.79; 1.74]	0.42	0.91	[0.57; 1.47]	0.71
BMI	1.03	[0.97; 1.08]	0.36	1.07	[0.95; 1.20]	0.28
Body Surface Area, m^2	1.60	[0.44; 5.91]	0.48	0.42	[0.02; 9.77]	0.59
Smoking	0.92	[0.46; 1.82]	0.80	0,90	[0.43; 1.91]	0.79
COPD	1.78	[0.43; 7.37]	0.42	1.13	[0.23; 5.63]	0.88
CKD/CRF	1.03	[0.58; 1.85]	0.91	0.76	[0.40; 1.48]	0.42
History of Stroke	0.53	[0.13; 2.19]	0.38	0.58	[0.12; 2.75]	0.49
Multifocal Atherosclerosis	0.64	[0.35; 1.17]	0.14	0.80	[0.39; 1.66]	0.55
Prior Myocardial Infarction	1.34	[0.74; 2.43]	0.34	1.48	[0.74; 2.96]	0.26
CCS FC III vs I-II	2.20	[0.87; 5.56]	0.10	1.52	[0.58; 4.02]	0.39
CCS FC IV vs I-II	2.00	[0.48; 8.40]	0.34	0.85	[0.09; 7.60]	0.88
LVEF, %	1.00	[0.97; 1.03]	0.79	1.05	[0.99; 1.11]	0,11
LVEDV, mL	1.00	[0.99; 1.01]	0.83	0.98	[0.96; 0.99]	**0.007**
LVESV, мл	1.00	[0.99; 1.01]	0.47	1.02	[1.00; 1.05]	0.053
Number of Grafts (3 vs other)	0.67	[0.39; 1.14]	0.14	0.33	[0.16; 0.69]	**0.003**
CPB Time, per 10-min increment	1.13	[1.01; 1.26]	**0.041**	1.37	[0.90; 2.09]	0.14
ACC Time, per 10-min increment	1.18	[1.01; 1.38]	**0.043**	0.78	[0.42; 1.47]	0.45
Duration of MV	0.99	[0.96; 1.02]	0.61	0.97	[0.90; 1.04]	0.35
Duration of Inotropic Support	1.01	[1.00; 1.02]	0.14	1.03	[1.01; 1.05]	**0.006**

Note. ACC – Aortic cross-clamp; BMI – Body mass index; CCS FC – Canadian Cardiovascular Society functional class; CKD/CRF – Chronic kidney disease / chronic renal failure; COPD – Chronic obstructive pulmonary disease; CPB – Cardiopulmonary bypass; HR – Hazard ratio; LVEDV – Left ventricular end-diastolic volume; LVEF – Left ventricular ejection fraction; LVESV – Left ventricular end-systolic volume; MV – Mechanical ventilation.

Table 3. Survival Rates at Different Time Points, %

Groups	Months Post-Operation				
	12 mo.	36 mo.	60 mo.	72 mo.	120 mo.
MICRO	98.2	96.9	91.9	91.9	82.0
OPT	96.4	91.6	89.0	86.5	65.8
p-value = 0. 060					

Analysis of Cardiac Mortality and Its Predictors

Analysis of cardiac mortality-free survival demonstrated a significant advantage for the microsurgical technique, providing higher patient survival compared to the standard technique (Fig. 3).

The cardiac mortality-free survival rates at 1, 3, 6, and 10 years postoperatively were: 100 % vs 97 % (p = NS); 100 % vs 94.9 % (p = NS); 98.3 % vs 90.5 % ($p < 0.05$; HR 0.15); and 95.8 % vs 77.6 % ($p = 0.003$; HR 0.16), respectively.

Univariate regression analysis identified the following predictors of cardiac mortality: microsurgical technique ($p = 0.003$), patient age ($p = 0.039$), cardiopulmonary bypass duration ($p < 0.001$), and aortic cross-clamp time ($p < 0.001$). Multivariate regression analysis indicated female sex, patient age, and the number of grafts as significant independent predictors of cardiac mortality (Table 5).

Repeat Revascularization

Over the ten-year follow-up period, analysis of repeat revascularization-free survival revealed a trend toward a higher rate in the microsurgical technique group; however, the difference did not reach statistical significance (Fig. 4).

The repeat revascularization-free survival rate was 84.3 % in OPT group and 89.9 % in the MICRO group ($p = 0.17$; HR 0.47; 95 % CI [0.16; 1.39]) (Table 6). It is noteworthy that none of the patients available for follow-up required repeat coronary artery bypass grafting. Our analysis did not identify statistically significant predictors of repeat revascularization following coronary artery bypass grafting.

Myocardial Infarction-Free Survival

Assessment of myocardial infarction-free survival revealed statistically significant differences between the study groups, indicating an advantage for the MICRO technique ($p < 0.001$; HR = 0.09; 95 % CI [0.02; 0.37]) (Fig. 5).

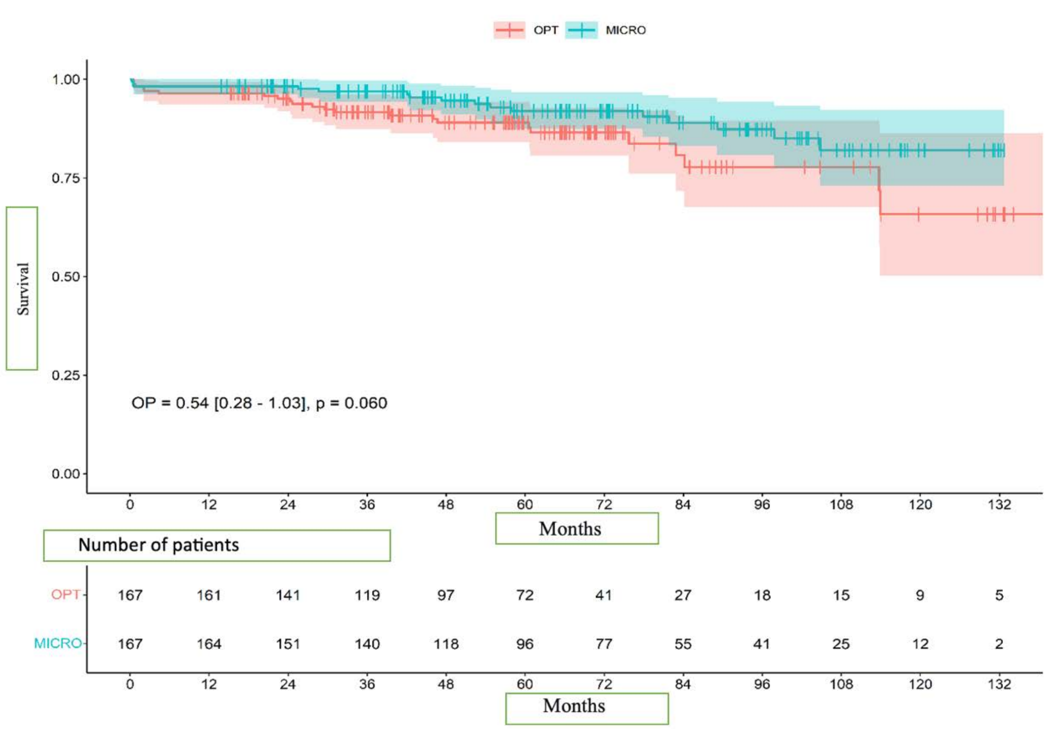

Fig. 2. Survival Curve
Note. MICRO – microsurgical intervention group; OPT – standard technique group.

Table 4. Predictors affecting survival

Characteristics	**Results of Cox Regression Models with** Survival **as the Outcome (After Matching)**					
	Univariate Regression Model			**Multivariate Regression Model**		
	HR	**95 % CI**	***p*-value**	**HR**	**95 % CI**	***p*-value**
Microsurgical Technique	0.54	[0.28; 1.03]	0.06	0.78	[0.27; 2.22]	0.64
Female Sex	0.40	[0.18; 0.86]	**0.02**	0.26	[0.07; 0.92]	**0.037**
Age, per 10-year increment	1.49	[0.95; 2.31]	0.079	1.67	[0.95; 2.95]	0.075
BMI	1.00	[0.93; 1.07]	0.93	0.97	[0.84; 1.13]	0.71
Body Surface Area, m^2	2.23	[0.49; 10.2]	0.30	2.07	[0.05; 88.6]	0.70
Smoking	1.28	[0.61; 2.71]	0.51	1.39	[0.58; 3.32]	0.46
COPD	1.03	[0.14; 7.52]	0.98	0.94	[0.11; 8.30]	0.96
CKD/CRF	1.01	[0.49; 2.08]	0.97	0.72	[0.31; 1.69]	0.46
Stroke	1.23	[0.43; 3.47]	0.70	1.27	[0.37; 4.35]	0.70
Multifocal Atherosclerosis	1.22	[0.64; 2.33]	0.54	1.38	[0.63; 3.00]	0.42
Prior Myocardial Infarction	0.96	[0.49; 1.87]	0.91	1.47	[0.64; 3.37]	0.36
CCS FC III vs I-II	1.56	[0.60; 4.04]	0.36	1.64	[0.58; 4.59]	0.35
CCS FC IV vs I-II	2.53	[0.77; 8.34]	0.13	1.28	[0.26; 6.44]	0.76
LVEF, %	0.96	[0.93; 1.00]	**0.03**	0.97	[0.89; 1.05]	0.41
LVEDV, mL	1.01	[1.00; 1.01]	0.17	1.02	[0.99; 1.05]	0.29
LVESV, мл	1.01	[1.00; 1.02]	0.092	0.96	[0.91; 1.02]	0.19
Number of Grafts (3 vs other)	0.80	[0.42; 1.51]	0.49	0.38	[0.17; 0.86]	**0.021**
CPB Time, per 10-min increment	1.24	[1.09; 1.40]	**<0.001**	1.19	[0.74; 1.91]	0.48
ACC Time, per 10-min increment	1.34	[1.13; 1.60]	**<0.001**	1.09	[0.52; 2.29]	0.81
Duration of MV	0.99	[0.95; 1.04]	0.75	0.99	[0.92; 1.07]	0.83
Duration of Inotropic Support	1.00	[0.98; 1.02]	0.95	1.00	[0.96; 1.04]	0.95

Note. ACC – Aortic cross-clamp; BMI – Body mass index; CCS FC – Canadian Cardiovascular Society functional class; CKD/CRF – Chronic kidney disease / chronic renal failure; COPD – Chronic obstructive pulmonary disease; CPB – Cardiopulmonary bypass; HR – Hazard ratio; LVEDV – Left ventricular end-diastolic volume; LVEF – Left ventricular ejection fraction; LVESV – Left ventricular end-systolic volume; MV – Mechanical ventilation.

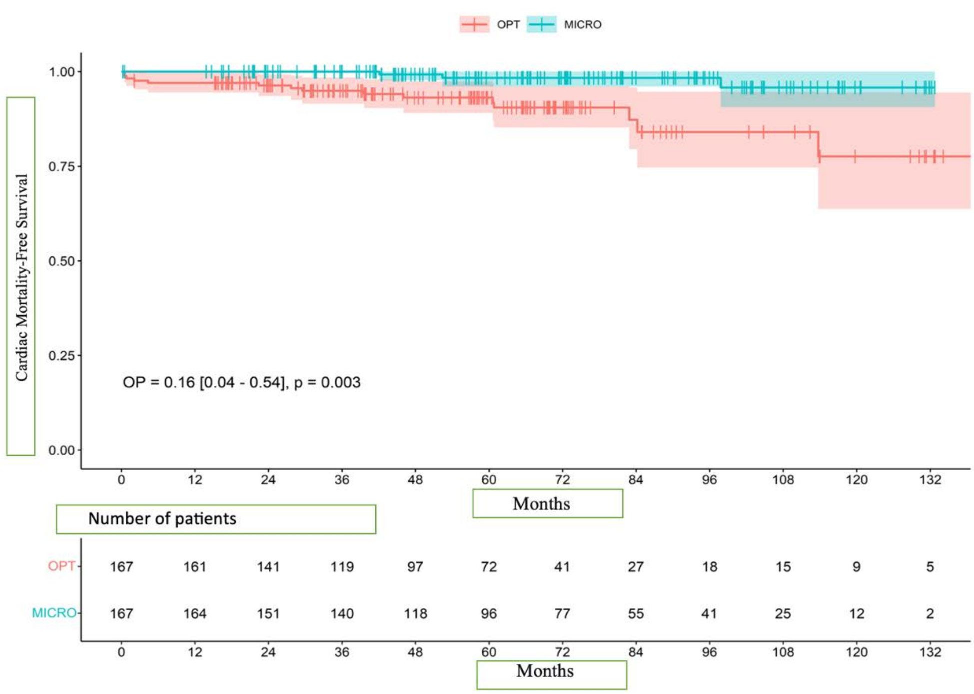

Fig. 3. Cardiac Mortality-Free Survival Curve

Note. MICRO – microsurgical intervention group; OPT – standard technique group.

The rates of myocardial infarction-free survival at various time intervals are presented in Table 7.

Predictors of Myocardial Infarction

Results of the univariate regression analysis identified the following potential predictors of myocardial infarction: microsurgical technique ($p < 0.001$), CPB duration ($p = 0.037$), ACC time ($p = 0.04$), and duration of inotropic support ($p = 0.008$).

Multivariate regression analysis identified the following independent factors associated with the risk of myocardial infarction: MICRO technique ($p < 0.001$), female sex ($p = 0.011$), CPB duration ($p = 0.043$), ACC time ($p = 0.046$), number of grafts ($p = 0.028$), and duration of inotropic support ($p < 0.001$) (Table 8). The use of the microsurgical technique was associated with a reduced risk of myocardial infarction.

Discussion

In the Russian Federation in 2021, the mortality rate from myocardial infarction was 38.27 cases per 100,000 population [15].

The study by Parmida Sadat Pezeshki et al. included 23,873 patients. A total of 38.7 % of patients had

Table 5. Predictors of Cardiac Mortality

Characteristics	**Results of Cox Regression Models with** Cardiac Mortality **as the Outcome (After Matching)**					
	Univariate Regression Model			**Multivariate Regression Model**		
	HR	**95 % CI**	***p*-value**	**HR**	**95 % CI**	***p*-value**
Microsurgical Technique	0.16	[0.04; 0.54]	**0.003**	0.20	[0.04; 1.17]	0.074
Female Sex	0.44	[0.14; 1.34]	0.15	0.13	[0.02; 0.78]	**0.025**
Age, per 10-year increment	2.04	[1.04; 4.02]	**0.039**	3.45	[1.10; 10.8]	**0.034**
BMI	0.99	[0.89; 1.09]	0.77	1.09	[0.88; 1.34]	0.45
Body Surface Area, m^2	0.82	[0.09; 7.59]	0.86	0.02	[0.00; 2.82]	0.12
Smoking	1.24	[0.41; 3.76]	0.71	1.63	[0.35; 7.56]	0.53
COPD	2.36	[0.31; 17.9]	0.41	2.66	[0.21; 32.9]	0.45
CKD/CRF	1.90	[0.73; 4.90]	0.19	1.41	[0.42; 4.70]	0.58
Stroke	1.34	[0.31; 5.90]	0.70	1.90	[0.29; 12.5]	0.51
Multifocal Atherosclerosis	0.98	[0.37; 2.62]	0.97	1.08	[0.28; 4.17]	0.91
Prior Myocardial Infarction	1.69	[0.56; 5.13]	0.36	3.16	[0.74; 13.5]	0.12
CCS FC III vs I-II	1.95	[0.44; 8.60]	0.38	1.60	[0.27; 9.54]	0.60
CCS FC IV vs I-II	2.08	[0.29; 14.9]	0.46	1.08	[0.07; 18.1]	0.96
LVEF, %	0.96	[0.91; 1.01]	0.08	1.03	[0.91; 1.17]	0.63
LVEDV, mL	1.01	[0.99; 1.02]	0.29	1.00	[0.95; 1.05]	0.91
LVESV, мл	1.01	[1.00; 1.03]	0.14	1.01	[0.91; 1.11]	0.89
Number of Grafts (3 vs other)	0.76	[0.30; 1.94]	0.57	0.23	[0.06; 0.83]	**0.026**
CPB Time, per 10-min increment	1.45	[1.24; 1.69]	**<0.001**	1.82	[0.99; 3.35]	0.054
ACC Time, per 10-min increment	1.59	[1.27; 2.00]	**<0.001**	0,66	[0.24; 1.81]	0.42
Duration of MV	1.00	[0.98; 1.02]	0.89	1.00	[0.97; 1.03]	0.82
Duration of Inotropic Support	1.00	[0.98; 1.03]	0.74	0.99	[0.94; 1.04]	0.62

Note. ACC – Aortic cross-clamp; BMI – Body mass index; CCS FC – Canadian Cardiovascular Society functional class; CKD/CRF – Chronic kidney disease / chronic renal failure; COPD – Chronic obstructive pulmonary disease; CPB – Cardiopulmonary bypass; HR – Hazard ratio; LVEDV – Left ventricular end-diastolic volume; LVEF – Left ventricular ejection fraction; LVESV – Left ventricular end-systolic volume; MV – Mechanical ventilation.

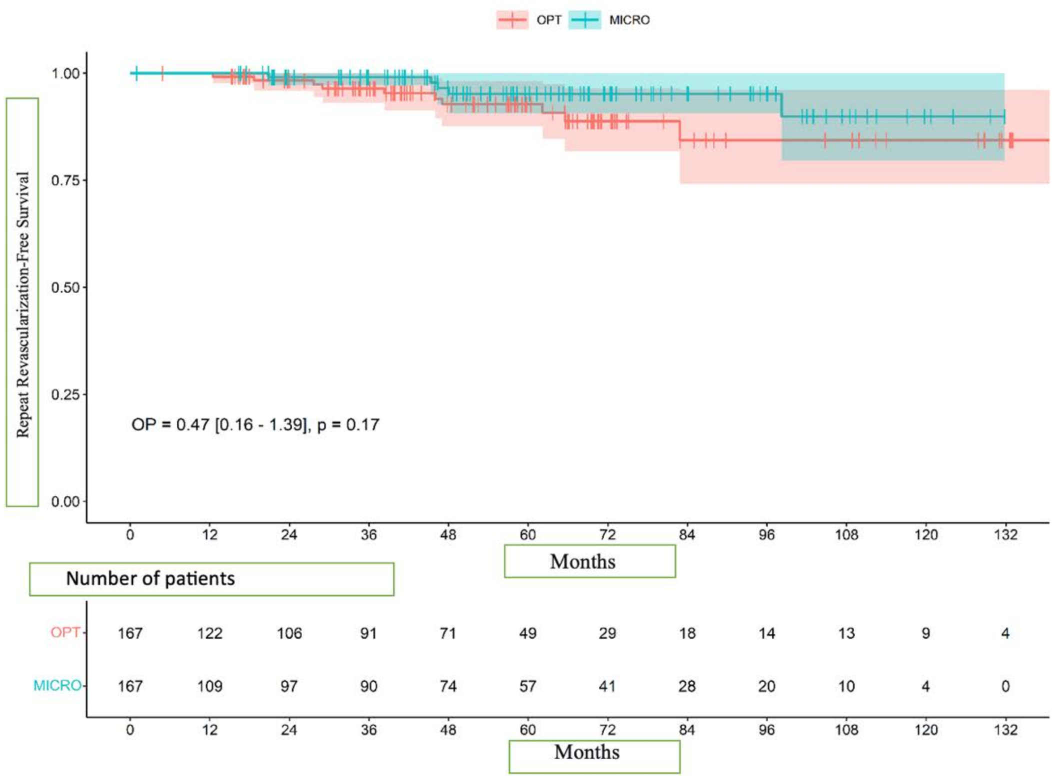

Fig. 4. Repeat Revascularization-Free Survival

Note. MICRO – microsurgical intervention group; OPT – standard technique group.

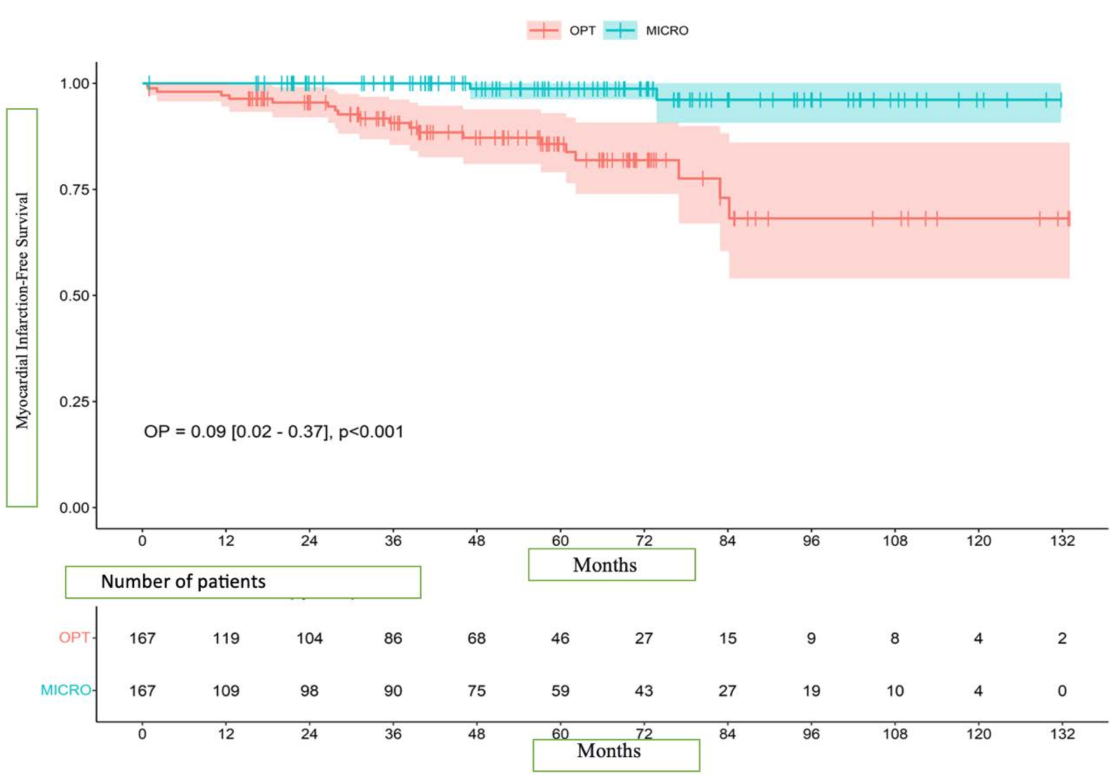

Fig. 5. Myocardial Infarction-Free Survival

Note. MICRO – microsurgical intervention group; OPT – standard technique group.

Table 6. Repeat Revascularization-Free Survival Rates at Different Time Points, %

Groups	Months Post-Operation			
	12 mo.	36 mo.	60 mo.	72 mo.
MICRO	100	99.0	95.2	89.9
OPT	100	96.4	88.8	84.3
p-value = 0.17				

Table 7. Myocardial Infarction-Free Survival Rates at Different Time Points, %

Groups	Months Post-Operation			
	12 mo.	36 mo.	72 mo.	120 mo.
MICRO	100	100	98.7	96.1
OPT	97.2	90.6	81.9	68.1
p-value < 0.001				

a history of diabetes mellitus at the time of surgery. After adjusting for potential confounding factors, patients with diabetes exhibited a 31 % increase in the rate of MACCE seven years postoperatively compared to patients without diabetes (HR = 1.31; 95 % CI [1.25; 1.38]; $p < 0.001$). The 7-year cumulative all-cause mortality rate was 19.46 % (1,796 patients) and 14.12 % (2,065 patients) in patients with and without diabetes, respectively (HR 1.59; 95 % CI [1.50; 1.68]; $p < 0.001$). After adjusting for confounders, the HR for mortality associated with diabetes remained significant. Diabetes contributed to a 52 % increased risk of post-CABG mortality (HR 1.52; 95 % CI [1.42; 1.61]; $p < 0.001$). Univariate analysis identified the following

Table 8. Predictors of Myocardial Infarction

Characteristics	Results of Cox Regression Models with Myocardial Infarction as the Outcome (After Matching)					
	Univariate Regression Model			Multivariate Regression Model		
	HR	95 % CI	*p*-value	HR	95 % CI	*p*-value
Microsurgical Technique	0.09	[0.02; 0.37]	**<0.001**	0.02	[0.00; 0.21]	**<0.001**
Female Sex	0.56	[0.22; 1.42]	0.22	0.13	[0.03; 0.62]	**0.011**
Age, per 10-year increment	1.08	[0.59; 1.97]	0.80	0.69	[0.34; 1.41]	0.31
BMI	1.02	[0.94; 1.11]	0.62	1.14	[0.96; 1.36]	0.15
Body Surface Area, m^2	1.11	[0.15; 8.42]	0.92	0.12	[0.00; 15.5]	0.40
Smoking	0.64	[0.19; 2.17]	0.48	0.58	[0.15; 2.26]	0.43
COPD	1.62	[0.22; 12.2]	0.64	0.60	[0.06; 6.10]	0.67
CKD/CRF	0.96	[0.38; 2.46]	0.93	0.51	[0.16; 1.59]	0.24
Multifocal Atherosclerosis	0.70	[0.27; 1.78]	0.45	1.59	[0.49; 5.21]	0.44
Prior Myocardial Infarction	1.39	[0.54; 3.55]	0.49	1.81	[0.62; 5.27]	0.28
LVEF, %	1.01	[0.97; 1.07]	0.56	1.06	[0.95; 1.18]	0.30
LVEDV, mL	1.00	[0.99; 1.01]	0.88	0.99	[0.95; 1.02]	0.53
LVESV, мл	1.00	[0.98; 1.02]	0.77	1.00	[0.94; 1.07]	0.96
Number of Grafts (3 vs other)	0.67	[0.29; 1.59]	0.37	0.25	[0.07; 0.86]	**0.028**
CPB Time, per 10-min increment	1.20	[1.01; 1.42]	**0.037**	2.12	[1.02; 4.40]	**0.043**
ACC Time, per 10-min increment	1.28	[1.01; 1.62]	**0.04**	0.34	[0.12; 0.98]	**0.046**
Duration of MV	1.00	[0.98; 1.01]	0.82	0.96	[0.91; 1.00]	0.052
Duration of Inotropic Support	1.02	[1.00; 1.03]	**0.008**	1.07	[1.04; 1.10]	**<0.001**

Note. ACC – Aortic cross-clamp time; BMI – Body mass index; CKD/CRF – Chronic kidney disease / chronic renal failure; COPD – Chronic obstructive pulmonary disease; CPB – Cardiopulmonary bypass; HR – Hazard ratio; LVEDV – Left ventricular end-diastolic volume; LVEF – Left ventricular ejection fraction; LVESV – Left ventricular end-systolic volume; MV – Mechanical ventilation. The variables CCS functional class and history of stroke were excluded from the multivariate analysis due to an insufficient number of events in individual categories.

predictors that increased the risk of all-cause mortality: age, patient sex, arterial hypertension, BMI, dyslipidemia, number of grafts, duration of CPB, and time spent in the intensive care unit [16].

Finally, another Canadian study demonstrated that 10-year survival ($p = 0.006$) and major adverse cardiac event-free survival ($p = 0.02$) were reduced in the group with diabetes mellitus [17].

A similarly significant difference in survival was demonstrated in the study by Akchurin R.S. et al. [4].

In our study, univariate regression analysis of the matched cohort identified the following factors associated with patient survival: female sex, preoperative left ventricular ejection fraction, cardiopulmonary bypass time, and aortic cross-clamp time. However, we did not observe a statistically significant difference in overall survival between the study groups. This is most likely attributable to the limited sample size and the inherent homogeneity of the groups with respect to the presence of diabetes mellitus.

Analysis of MACCE-free survival revealed an advantage for the microsurgical technique over the standard approach. At 1 year of follow-up, MACCE-free survival was 100.0 % in the MICRO group versus 95.4 % in the OPT group. This advantage persisted at 3 years (36 months): 98.0 % versus 81.6 %, respectively. By 6 years (72 months), the rates were 81.4 % in the MICRO group and 68.9 % in the OPT group. According to available data, at 10 years (120 months) these rates were 59.4 % in the MICRO group and 44.3 % in the OPT group, corresponding to a hazard ratio of 0.49. It should be noted that by the end of the 10-year follow-up period, only 5 patients remained under observation in the comparative groups.

Another study conducted by Axelsson T. et al., which examined diabetic and non-diabetic patients undergoing isolated CABG with a median follow-up of 8.5 years, also demonstrated analogous findings. Patients with diabetes had an increased risk of postoperative mortality [odds ratio 2.52; 95 % CI [1.27; 4.80]), with a 5-year overall survival of 85 % compared to 91 % in favor of non-diabetic patients ($p < 0.001$) [18].

The results of our study regarding five-year survival (91.9 % in the MICRO and 89.0 % in the OPT group) demonstrate trends comparable to the data presented in the study by Axelsson T.

In a pivotal U.S. study involving 2,278 patients with diabetes and 9,920 without, diabetic patients demonstrated significantly lower 5-year (78 %) and 10-year (50 %) survival rates. This study did not report on a composite endpoint such as MACCE. However, the authors reported that the long-term incidence of myocardial infarction and repeat CABG did not differ significantly between the two groups, whereas diabetic patients had a higher risk of post-CABG percutaneous coronary intervention over a 10-year period. Furthermore, their findings indicated that insulin-dependent diabetic patients had significantly lower survival compared to those managed with diet or oral hypoglycemic agents [19].

Study limitations

Our study did not include an analysis of the impact of different diabetes mellitus management strategies on revascularization outcomes. In light of the foregoing, several limitations of our investigation must be acknowledged. The retrospective design implies reliance on existing data and the potential for loss to follow-up. We did not analyze outcomes stratified by diabetes therapy (insulin versus oral agents), which constitutes a limitation given the established influence of insulin therapy on prognosis. While we employed propensity score matching to address the initial disparities in group sizes and other characteristics, this method cannot fully eliminate all potential biases inherent to observational studies.

It is important to emphasize that this study focuses on evaluating CABG outcomes in diabetic patients stratified by surgical technique (microscope versus loupes). Given the propensity for diabetic patients to have smaller-caliber distal coronary arteries, the enhanced visualization and magnification afforded by microsurgical technique may play a particularly critical role in achieving high-quality anastomoses. However, the primary objective was to evaluate the impact of the microsurgical technique itself on anastomotic quality and long-term CABG outcomes, which prioritized the assessment of technical aspects over the influence of diabetes management.

Despite these limitations, our study provides valuable insights into the outcomes of microsurgical CABG in diabetic patients – an important consideration given that the majority of prior research has compared diabetic to non-diabetic cohorts. Our findings suggest that microsurgical technique may be associated with improved long-term outcomes, although further prospective, randomized studies are warranted to confirm these results.

Conclusion

The results of this study, which evaluated microsurgical CABG in patients with diabetes mellitus, demonstrate a significant improvement in MACCE-free survival (59.4 % in the MICRO group vs 44.3 % in the OPT group at 10 years, $p = 0.012$ over the entire follow-up period). This indicates a substantial reduction in the long-term risk of combined adverse cardiac and cerebrovascular events with the microsurgical approach. Furthermore, the use of microsurgical technique was associated with a significant reduction in the incidence of myocardial infarction ($p < 0.001$) and cardiac mortality ($p = 0.003$). Although no statistically significant difference in overall survival was observed ($p = 0.060$), which may be attributed to the limited sample size, the findings underscore the potential benefit of microsurgical technique for improving long-term outcomes in diabetic patients undergoing CABG. Further prospective studies are warranted to confirm these findings and to define the optimal revascularization strategy for this patient population.

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