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# The preoperative myocardial perfusion and internal mammary artery graft blood flow relationship in patients with ischemic cardiomyopathy

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**Objective.** The purpose of this study was to determine the association between preoperative myocardial perfusion data (obtained by SPECT) with transit time blood flow characteristics in left internal mammary artery (LIMA) to left anterior descending artery (LAD) grafts in patients with ischemic cardiomyopathy.

**Methods.** The study group consisted of 57 patients with ischemic cardiomyopathy. Intraoperative transit-time flow measurement (TTFM) of LIMA-LAD grafts were performed in all patients. All patients were also examined with preoperative stress and rest myocardial perfusion SPECT with  $^{99m}\text{Tc}$ -MIBI. Anastomotic patency was considered satisfactory with a normal waveform of blood flow, diastolic-dominant blood filling, and a mean flow value greater than 11.5 ml/min.

**Results.** All 57 patients with LIMA-LAD grafts were divided into two groups; those with graft satisfactory patency ( $n = 40$ ) and those with unsatisfactory patency ( $n = 17$ ) as determined by TTFM. We found differences among these groups in values of global summed rest score ( $20.7 \pm 7.5$  vs.  $29.8 \pm 4.0$ ;  $p = 0.002$ ), global total perfusion deficit (TPD) at rest ( $32.0 \pm 11.4$  vs.  $43.0 \pm 7.2$ ;  $p = 0.01$ ), and regional TPD at rest in the LAD territory ( $20.7 \pm 7.5$  vs.  $29.8 \pm 4.0$ ;  $p = 0.002$ ). Additionally, the flow characteristics were different in patients with and without surgical left ventricle reconstruction (Q (ml/min): 17 (11.5, 40.8) vs. 47 (25, 69.5),  $p = 0.013$ ; PI: 3.9 (3.2, 7.4) vs. 2.4 (2.0, 3.6),  $p = 0.001$ ; DF (%): 63.5 (44.5, 70.8) vs. 74 (66.0, 79.7),  $p = 0.019$ ). TPD at rest was the best predictor of the LIMA-LAD graft satisfactory: area under curve = 0.771, cut-off value = 26.85 with 83.3% sensitivity and 78.1% specificity.

**Conclusions.** Preoperative myocardial perfusion characteristics are associated with blood flow in LIMA-LAD graft in patients with ischemic cardiomyopathy. TPD at rest (assessed globally and in the LAD region) as well as global SRS value are potential predictors of early graft failure.

**Keywords:** transit-time flow measurement, myocardial perfusion imaging, coronary artery bypass grafting, coronary artery disease, ischemic cardiomyopathy

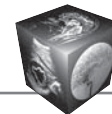
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# Взаимосвязь дооперационных показателей перфузионной сцинтиграфии миокарда и флоуметрии маммарокоронарных шунтов у больных с ишемической кардиомиопатией

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**Цель.** Целью данного исследования было определение связи между предоперационными показателями перфузии миокарда по данным ОФЭКТ (ПСМ) и характеристиками кровотока по маммарокоронарным шунтам (МКШ) по данным интраоперационной флоуметрии у пациентов с ишемической кардиомиопатией (ИКМП).

**Материал и методы.** В исследование вошли 57 больных с ИКМП. Всем пациентам была выполнена предоперационная ПСМ с  $^{99m}\text{Tc}$ -MIBI и интраоперационная флоуметрия кровотока по МКШ. Вычислялись следующие численные показатели флоуметрии: объемная скорость кровотока (Q), индекс сопротивления (PI), и диастолическое наполнение (DF). Пройодимость анастомоза считалась удовлетворительной при нормальной форме флоуметрической волны, диастолически-доминантном кровенаполнении и значении Q более 11,5 мл/мин.

**Результаты.** Пациенты были разделены на две группы: с удовлетворительной ( $n = 40$ ) и неудовлетворительной ( $n = 17$ ) проходимостью шунта по данным интраоперационной флоуметрии. По данным ПСМ различия между группами были выявлены в показателях перфузии покоя (summed rest score, SRS) –  $20,7 \pm 7,5\%$  и  $29,8 \pm 4,0\%$ ;  $p = 0,002$ , общего дефицита перфузии (total perfusion deficit, TPD) в покое –  $32,0 \pm 11,4$  и  $43,0 \pm 7,2$ ;  $p = 0,01$  и TPD в покое на территории передней нисходящей артерии –  $20,7 \pm 7,5$  и  $29,8 \pm 4,0$ ;  $p = 0,002$ . Кроме того, показатели флоуметрии различались у пациентов с хирургической реконструкцией левого желудочка и без нее (Q: 17 (11,5, 40,8) и 47 (25, 69,5) мл/мин,  $p = 0,013$ ; PI: 3,9 (3,2, 7,4) и 2,4 (2,0, 3,6),  $p = 0,001$ , DF: 63,5 (44,5, 70,8) и 74 (66,0, 79,7)%,  $p = 0,019$ ). TPD в покое, равный 26,85, был лучшим предиктором удовлетворительного состояния шунта (AUC = 0,771, чувствительность 83,3%, специфичность 78,1%).

**Выводы.** Предоперационные характеристики перфузии миокарда ассоциированы с показателями кровотока по МКШ у пациентов с ишемической кардиомиопатией. TPD в покое и SRS могут являться потенциальными предикторами ранней недостаточности шунта.

**Ключевые слова:** перфузионная сцинтиграфия миокарда, интраоперационная флоуметрия, измерение аорт-коронарное шунтирование, ишемическая болезнь сердца, ишемическая кардиомиопатия

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### List of abbreviations

CABG	– coronary artery bypass grafting
DF	– diastolic filling
DS	– regional difference score
ICM	– ischemic cardiomyopathy
LAD	– left anterior descending artery
LIMA	– left internal mammary artery
MPI	– myocardial perfusion imaging
PI	– pulsatility index
Q	– mean graft flow
RS	– regional rest score
SDS	– summed difference score
SPECT	– single photon emission computed tomography
SRS	– summed rest score
SS	– regional stress score
SSS	– summed stress score
SVR	– surgical ventricular reconstruction
TPD	– total perfusion deficit
TTFM	– transit-time flow measurement

### Introduction

Coronary artery bypass grafting (CABG) is a widely used method applied in presence of severe coronary artery disease, and it is mandatory for patients with ischemic cardiomyopathy (ICM) [1]. While most chronic atherosclerotic narrowing of coronary arteries can be successfully bypassed, revascularization failures do happen [1–3]. Thus, the literature suggests that roughly 10% of all by-pass grafts occluded in the short-term and some of the authors call graft patency the “Achilles heel” of CABG [4, 5].

Graft patency is influenced by many factors including intramyocardial tension, graft conduits and design (Y and T configuration), graft destination artery, and pacing modality and atrioventricular delay value [6].

Thus, internal mammary artery is frequently used for CABG as the most reliable conduit. It is of great importance to select coronary artery for internal mammary artery grafts carefully. In some cases the blood flow of the internal graft may be low due to severe vasoconstriction or the morphological condition of the myocardial territory, referred to the target artery, which may ultimately lead to graft failure [7–9].

Until recently, there was not an “on-table” complete and user-friendly technique for graft patency assessment, which would not drastically increase operation time. Transit-time flow measurement (TTFM) became such a method [10]. In 2010 it was included in the ESC (European Society of Cardiology) and EACTS (European Association for Cardio-Thoracic Surgery) Guidelines on myocardial revascularization [4, 11–16]. Nevertheless, the data about relevant cut-off

point for different types of conduits are still controversial [17].

The preoperative assessment of myocardial perfusion by means of single photon emission computed tomography (SPECT-MPI) was considered to be a useful tool for predicting regional functional recovery in akinetic areas after CABG [18]. Alas, only 29% of patients underwent preoperative SPECT-MPI in that study [2]. Moreover, preoperative myocardial perfusion imaging can provide clinicians with vital information about coronary vessel perfusion area, including extent of scar and ischemia [19]. This study aimed to assess the association between preoperative myocardial perfusion data with transit time blood flow characteristics in left internal mammary artery to left anterior descending artery grafts in patients with ischemic cardiomyopathy.

### Materials and methods

#### Study population

The study group comprised 57 consecutive patients (mean age  $61.1 \pm 5.1$  years, 95.7% male) with ICM, who underwent CABG with LIMA-LAD graft and left ventricle (LV) reconstruction according to standard indications [20].

Inclusion criteria were:  $\geq 75\%$  stenosis of left main or proximal LAD or  $\geq 75\%$  stenosis of two or more major epicardial vessels; left ventricular ejection fraction (EF)  $\leq 40\%$ ; left ventricular end-systolic index  $\geq 60$  ml/m<sup>2</sup> (by transthoracic echocardiography) [20].

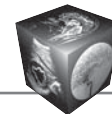
Exclusion criteria were:  $< 3$  months after acute myocardial infarction; rheumatic or inflammatory heart disorders; acute coronary syndrome; recent ( $< 6$  months) cerebral ischemic attack; acute or chronic right ventricle failure (by transthoracic echocardiography); severe pulmonary hypertension; contraindications for cardiopulmonary bypass; contraindication to adenosine administration.

The study was approved by the Local Ethical Committee and conformed to the Declaration of Helsinki on Human Research. Written informed consent was obtained from each patient after explanation of the protocol, its aims, and potential risks.

After surgery patients were divided into two groups according to the TTFM results (cut-off value for  $Q = 11.5$  ml/min) [2].

#### Surgical technique

All surgical operations were performed under conditions of norm-thermal cardiopulmonary bypass standard procedure. A great saphenous vein and a LIMA were harvested according to the routine procedure [21]. In all cases, the LIMA was grafted to the left anterior descending artery. No sequential anasto-



moses were included in this series. The LV reconstruction was performed in the case of an LV aneurysm (based on preoperative examination and intraoperative evaluation [22, 23]) using one of the following methods: D. Cooley or V. Dor method with L. Menicanti modification.

### **Coronary angiography**

Quantitative coronary angiography was performed after catheterization of the femoral artery by the Seldinger's technique on the Axiom Artis coronary angiography system (Siemens; Erlangen, Germany) in a single scheme: a multi-projection right then left coronary angiography according to the method of M. Judkins [24]. All coronary angiographies were performed during the preoperative period.

### **TTFM and evaluation criteria for anastomosis satisfactory**

Transit-time flow measurement was performed with VeriQ System (Medi-StimAS, Oslo, Norway) after finishing all internal surgical manipulations (anastomoses sewing, ventricle and valves reconstructions), off-pump, after reaching a stable hemodynamic parameters (mean arterial pressure fixed of 75–85 mmHg) [4, 25]. Flow parameters recorded in this study included mean graft flow (Q, ml/min), pulsatility index (PI), and diastolic filling (DF, %).

A Q-value greater than 11.5 ml/min, a normal waveform of blood flow, and diastolic-dominant blood filling was considered as a surrogate marker for satisfactory anastomotic patency [2].

### **Myocardial perfusion imaging**

Patients were instructed to refrain from caffeine, substances containing methylxanthine, and to avoid nitrates, calcium channel blockers, and beta-blockers for at least 24 h before the scan. All scans were performed after overnight fasting.

All patients underwent a 2-day stress/rest protocol within 1 week before surgery. A pharmacological stress test (adenosine, 140 mg/kg/min for 6 minutes) combined with low-level exercise was performed in all patients [26]. The heart rate, systemic blood pressure, and 12-lead electrocardiogram were monitored before, during, and after the stress test. A dose of 370 MBq of  $^{99m}\text{Tc}$ -sestamibi was injected after 3 minutes of stress testing and the same dose on the next day for rest study like described in ASNC guidelines for SPECT nuclear cardiology procedures [26]. Pharmacologic stress testing did not lead to atrioventricle (AV) conduction delay and/or to ST-segment depression in any patient. The total effective radiation dose was 5.8–7.0 mSv.

The SPECT-MPI data were acquired one hour after injection for both the rest and the stress studies with a solid-state detector CZT cardiac SPECT/CT system (GE Discovery NM/CT 570c). The acquisition time was 7 minutes. Scans were acquired using low energy multi-pinhole collimator and 19 stationary detectors which simultaneously imaged 19 different views without detector rotation. The acquisition matrix was  $32 \times 32$  pixels (pixels sizes  $4 \times 4 \times 4$  mm). Each detector contains  $32 \times 32$  pixelated ( $2.46 \times 2.46$  mm) CZT elements. A 20% energy window at 140 keV was used. Patients were imaged in the supine position with arms placed over their heads.

Images post processing was performed on the dedicated workstation (Xeleris 4.0; GE Healthcare, Haifa, Israel) using maximum-penalized-likelihood iterative reconstruction (60 iterations; Green OSL Alpha 0.7; Green OSL Beta 0.3) to acquire perfusion images in standard cardiac axes (short axis, vertical long axis, and horizontal long axis). The software Myovation for Alcyone (GE Healthcare, Haifa, Israel) was used for image reconstruction, and Butterworth post-processing filter (frequency 0.37; order 7) was applied to the reconstructed slices. The reconstruction was performed in a  $70 \times 70$  pixels matrix with 50 slices.

### **MPI interpretation**

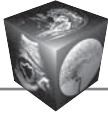
Raw data at stress and rest were visually assessed for motion and attenuation artifacts. Stress/rest images were analyzed with a commercially available software package Cedars QGS/QPS (Cedars-Sinai Medical Center, Los Angeles, CA, USA).

Left ventricle myocardium was presented in a 17-segment polar map format and was computed separately for each vascular territory by the guidelines [26]. Each of the 17 segments was scored using a semi-quantitative 5-point scoring system: 0 – normal uptake; 1 – mild uptake reduction; 2 – moderate uptake reduction; 3 – severe uptake reduction; and 4 – an absence of radiotracer.

Myocardial perfusion was assessed globally and for LAD region by following parameters: summed stress score (SSS), summed rest scores (SRS), summed difference score (SDS, difference between SSS and SRS), total perfusion defect (TPD) at stress and at rest [19, 26–29].

### **Statistical analysis**

The distribution of continuous variables was assessed with Shapiro–Wilk's *W*-test. Normally distributed continuous variables were presented as the mean  $\pm$  standard deviation and not normally distributed parameters were shown as the median and interquartile



range (Q25, Q75). Categorical variables were presented as numbers and percentages. Group comparisons were analyzed with Student t-test or the Mann-Whitney U-test for continuous variables, and the  $\chi^2$  or Fisher's exact test for categorical variables. The Spearman test was used to estimate the correlation coefficient between quantitative variables. The receiver-operating-characteristic (ROC) curve analysis was performed to evaluate the sensitivity and specificity, as well as optimal cut-off value of a modality in terms of predicting of graft satisfactory. Areas under the ROC curves were compared using the DeLong method. A value of  $p < 0.05$  was considered statistically significant. All analyses were performed

using SPSS statistical software 19.0 (SPSS Inc., Chicago, IL, USA) and MedCalc version 17.4 (MedCalc Software, Mariakerke, Belgium).

## Results

### Clinical Outcomes

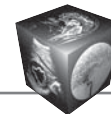
The characteristics of the study groups are presented in Table 1. In 12 cases intra-aortic balloon counterpulsation was used intraoperatively or in the early postoperative period for circulatory assistance. The early mortality rate (within 30 days after surgery) was 10% (6/57). The causes of early death were associated with acute heart failure in four cases and gastrointestinal bleeding in one case.

**Table 1.** The clinical characteristics of study groups

	Q > 11,5 ml/min, n = 40	Q ≤ 11,5 ml/min, n = 17	p-value
Age, years	61.4 ± 4.9	59.9 ± 5.2	0.5
Diabetes Mellitus (2nd type)	8 (20%)	1 (6%)	0.06
NYHA class, n (%)			
I	1 (3%)	1 (6%)	0.09
II	22 (55%)	2 (12%)	
III	14 (35%)	4 (24%)	
IV	3 (7%)	0 (%)	
CCS angina class, n (%)			
I	1 (3%)	1 (6%)	0.6
II	11 (27%)	4 (24%)	
III	27 (67%)	2 (12%)	
IV	1 (3%)	0 (%)	
The operation type, n (%)			
CABG	25 (63%)	2 (12%)	0.72
CABG+SVR (D. Cooley)	7 (17%)	1 (6%)	
CABG+SVR (L. Menicanti)	8 (20%)	4 (24%)	
Ultrasound data			
LV ESV	136 (120, 184)	169 (150, 185)	0.79
LV EDV	201 (189, 251)	237 (223, 272)	0.08
LV EF (%)	31.1 ± 6.1	30.1 ± 5.1	0.7
Others			
Body-mass index (kg/m <sup>2</sup> )	27.4 (25.3, 30.9)	27.5 (25.7, 31.5)	0.8
EuroSCORE 2	4.5 ± 2.1	4.0 ± 2.2	0.32

Q – mean graft flow; NYHA – functional class of heart failure according to the New York Heart Association; CCS CABG – Coronary artery bypass grafting; SVR – surgical ventricular reconstruction; LV – left ventricle; ESV – end-systolic volume; EDV – end diastolic volume; EF – ejection fraction; EuroSCORE – European System for Cardiac Operative Risk Evaluation.





**Table 2.** Results of intraoperative transit-time flow measurements in left internal mammary artery to left anterior descending artery grafts

Transit-time flow measurements	Q > 11,5 ml/min, n = 40	Q ≤ 11,5 ml/min, n = 17	p-value
Q (ml/min)	43 (23, 61.8)	8 (5.9, 10)	0.003
PI	3.0 (2.4, 3.7)	7.6 (4.3, 10.8)	0.002
DF (%)	69.5 (58.5, 74.5)	59 (37.5, 64)	0.12

Q – mean graft flow; PI – pulsatility index; DF – diastolic filling.

**Table 3.** The impact of CTO and SVR on results of intraoperative transit-time flow measurements in LIMA-LAD grafts

Transit-time flow measurements	With LAD CTO	Without LAD CTO	p-value
Q (ml/min)	36.5 (13.5, 53.5)	31 (16, 58)	0.73
PI	3.6 (2.8, 5.3)	2.9 (2.1, 4.1)	0.44
DF (%)	67.5 (56.8, 73.3)	68.5 (60.3, 76)	0.7
Transit-time flow measurements with SVR		without SVR	p-value
Q (ml/min)*	17 (11.5, 40.8)	47 (25, 69.5)	0.013
PI*	3.9 (3.2, 7.4)	2.4 (2.0, 3.6)	0.001
DF (%)*	63.5 (44.5, 70.8)	74 (66.0, 79.7)	0.019

\* – a statistically significant difference,  $p < 0.05$ ; CTO – chronically totally occlusion; SVR – surgical ventricular reconstruction; LIMA – left internal mammary artery; LAD – to left anterior descending; Q – mean graft flow; PI – pulsatility index; DF – diastolic filling.

### Coronary angiography results

The stenosis of the main left coronary artery (ranged from 40 to 75%) was found in 9 cases. There were chronically totally occluded left descending artery in 20 cases (35%), more than 75% stenosis in 25 cases (44%), and less than 70% in 10 cases (17%). There were the following numbers of cases with stenosis in range 30 to 100 percentage: median artery in 5 cases, a diagonal branch of LAD in 19 cases, left circumflex artery in 13 cases, left marginal artery in 33 cases, a right coronary artery in 36 cases, a posterior descending artery in 11 cases.

### The results of CABG

Of the 57 patients with LIMA-LAD grafts, there were 40 patients (70%) with graft satisfactory patency ( $Q > 11.5$  ml/min) and 17 (30%) poor graft patency ( $Q \leq 11.5$  ml/min).

In two cases, LIMA-LAD was the only graft. In 17 cases, there were two grafts and in 28 cases – three grafts, while in the 10 cases more than three grafts were applied.

### Transit-time flow measurement

The blood flow characteristics in the grafts are presented in Table 2. Patient groups had a statistically

significant difference in the PI. The Q-values correlated with PI ( $r = -0.611$ ,  $p < 0.001$ ) and diastolic flow ( $r = 0.418$ ,  $p = 0.003$ ) values.

Despite the presence of LAD chronic total occlusion in 20 cases, there were no statistically significant difference in flow measurements between patients with and without LAD chronic total occlusion. However, such differences were found between groups with and without surgical left ventricle reconstruction (Table 3).

### SPECT myocardial perfusion imaging

All patients had at least 3 segments with abnormal myocardial perfusion. We found differences for both global and LAD territory myocardial perfusion characteristics only on rest MPI but not on stress (Table 4). The representative examples of myocardial SPECT with satisfactory and not-satisfactory TTFM are presented in Fig. 1.

According to the ROC analysis, TPD at rest was the best predictor of the LIMA-LAD graft satisfactory: area under curve = 0.771, cut-off value = 26.85 with 83.3% sensitivity and 78.1% specificity.

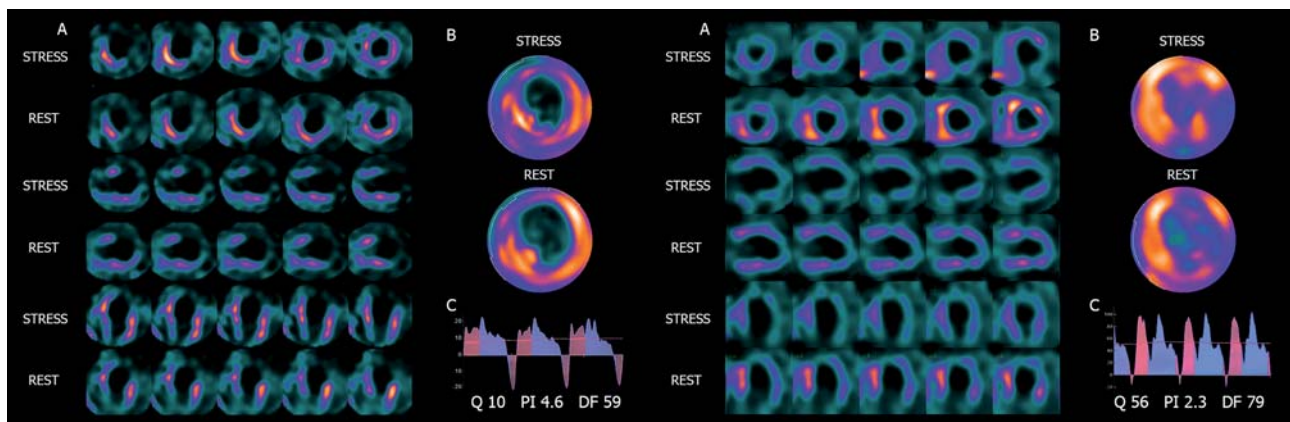
The data about association between TTFM and SPECT-MPI parameters are presented in Fig. 2.



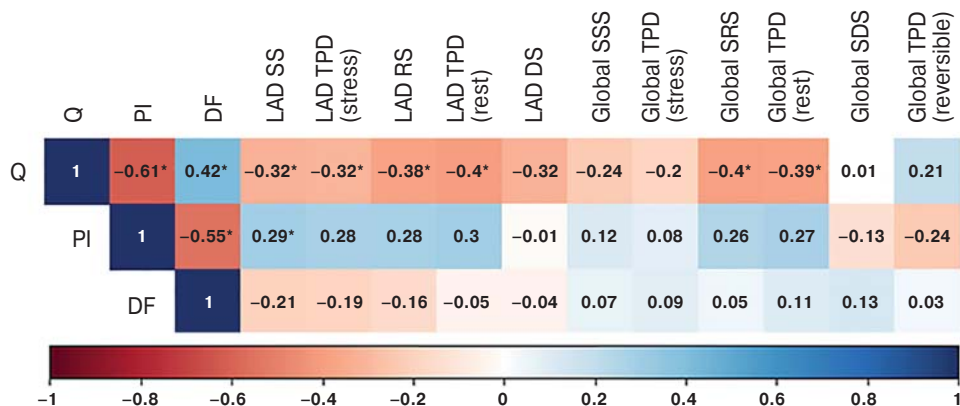
**Table 4.** Results of SPECT MPI

	Q > 11,5 ml/min, n = 40	Q ≤ 11,5 ml/min, n = 17	p-value
Global SPECT parameters			
SSS	27.3 ± 8.3	31.2 ± 5.1	0.051
TPD (stress)	38.7 ± 10.4	44.1 ± 7.3	0.088
SRS*	20.7 ± 7.5	29.8 ± 4.0	0.002
TPD (rest)*	32.0 ± 11.4	43.0 ± 7.2	0.01
SDS	4 (2, 7)	3 (2, 5)	0.9
LAD SPECT parameters			
SS	12.7 ± 6.0	15.0 ± 5.2	0.51
TPD (stress)	21.4 ± 8.9	24.1 ± 12.1	0.56
RS	10.8 ± 5.4	15.1 ± 4.7	0.06
TPD (rest)*	19.7 ± 9.6	25.1 ± 6.1	0.03
DS	0 (0, 2)	1 (0.3, 1.6)	0.53

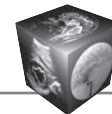
SPECT MPI – Single-photon emission computed tomography myocardial perfusion imaging; SSS – summed stress score; TPD – total perfusion deficit; SRS – summed rest score; SDS – summed difference score; LAD – left anterior descending artery; SS – stress score; RS – rest score; DS – difference score.



**Fig. 1.** The myocardial perfusion stress-rest SPECT (A, B) in ischemic cardiomyopathy patients with non-satisfactory (Q < 11.5, left) and satisfactory (Q > 11.5, right) flow in left internal mammary artery grafts during coronary artery bypass grafting (C).



**Fig. 2.** Correlations between TTFM and MPI estimators. Q – mean graft flow; PI – pulsatility index; DF – diastolic filling; LAD – left anterior descending artery; SS – regional stress score; SSS – summed stress score; TPD – total perfusion deficit; SRS – summed rest score; SDS – summed difference score; \* – statistically significant correlation, p < 0.05.



## Discussion

The main findings of this study are: 1) the preoperative rest myocardial perfusion indices in LAD bed are associated with TTFM parameters of LIMA-LAD grafts in ICM patients; 2) Rest TPD is a best predictor of the LIMA-LAD graft satisfactory among other perfusion parameters.

TTFM is influenced by many factors, including vasoconstriction, graft diameter, perfusion area, morphological myocardial state, myocardial viability, myocardial oxygen consumption, blood pressure, and coronary vascular resistance [5]. Some of them appear during or after surgery, but other exist before it. The assessment of myocardial perfusion by SPECT before operation allows surgeon to assess a micro-circulatory condition of myocardium and thus take into account another potential risk factor for graft failure.

### TTFM and graft patency

The low TTFM characteristics are correlated with the risk of LIMA graft failure at the one-year angiographic follow-up [14]. Even in the earliest studies, the pulsatory index was shown as a promising parameter, further it has been shown that a significant difference was shown in Q-value between patent and non-patent grafts, but not in pulsatory index or diastolic flow [30, 31].

According to the literature, the Q for non-satisfactory arterial grafts is less than 10 to 20 ml/min [6, 32]. Lehnert et al defined the Q threshold of internal mammary artery as 20 ml/min and Honda et al and G. Di Giammarco et al pointed out that reduced  $Q < 15$  ml/min was found in non-satisfactory internal mammary artery grafts [12, 13, 33]. We considered a graft satisfactory with a normal waveform of blood flow, diastolic-dominant blood filling, and a mean flow value greater than 11.5 ml/min.

A PI-value may be elevated in very long arterial conduits (a resistance to blood flow is determined by, among other factors, vessel length and increase PI associated with worse outcome) [17, 34]. However, some authors supposed that PI is clinically irrelevant [17, 25]. In our data, PI value was irritated in patients with not-satisfactory patency of LIMA-LAD grafts.

### The TTFM measurements basis

According to literature, TTFM is a quick and reproducible intraoperative method with the prognostic ability of graft potency in 5 years of the postoperative period. However, few researchers have written about causes of low Q- or high PI-values and the ability to predict them [6, 15, 33]. It is known that the technical errors in grafts installation can lead to changes in TTFM. Thus, this technic can be used for the detection

of such errors. But technical errors are not the only source of bias in TTFM values [35].

### Blood vessels

It is obvious that the blood vessels condition, including graft state, has an impact on the graft flow. The measure in proximal graft end can be viewed as a sum of the graft capacitive flow and flow that passes through the distal anastomosis. The last one depends on many factors, such as graft destination, coronary artery stenosis, collateral and competitive flows, as well as graft type [25]. The TTFM measurements do not depend on graft diameter [36].

There are no direct studies on the impact of the graft target artery on TTFM, probably because it is not possible to isolate this factor from others. However, Y. Tokuda et al. declare different cut-off value of mean graft flow for different coronary arteries (15 mL/min for LCA and 20 mL/min for RCA) that could be an indicator of such influence [37].

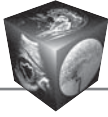
K. Honda et al showed that graft flow increases and pulsatory index decreases with progressing of coronary stenosis [33]. Niclauss L. in his review mentioned a correlation between blood flow and the severity of artery stenosis [17]. However, our data suggest that the chronically total occlusion of the destination artery does not have an impact on TTFM in grafts, as well as the low mean bypass graft flow and high pulsatory index by means of TTFM are not specific for anastomotic stenosis. These blood flow characteristics might be explained with the competitive flow and poor coronary run-off [24].

Other vessel conditions are poorly studied: Verhoye et al. [38] showed the evidence and type of relationship of collateral blood flow between left coronary artery bypass grafts and chronically occluded right coronary artery in patients with triple vessel disease. However, the influence of collateral circulation on graft patency is still not well known [2]. There is some evidence that competitive blood flow has a strong impact on graft's satisfactory [39]. The competitive blood flows can occur in the case of arterial "Y" grafting directed to different coronary beds with unbalanced stenosis [11]. These data was a reason for excluding any sequential grafts from the analysis in present study.

### Ischemia

Current scientific knowledge lacks information on the effect of transient ischemia on any TTFM measurements after CABG [1, 2]. H. Oshima et al. [2] wrote that they assessed patients using preoperative SPECT but did not describe their results in the context of TTFM prediction. In other sources, SPECT MPI was used to assess the condition of coronary artery bypass graft after CABG, but no associative analysis has been done





[40–45]. According to our data, ischemia by means of the preoperative SPECT MPI, did not affected Q, PI, or DF in the graft coronary artery bed.

### **Myocardial scar and ventricular reconstruction**

There are some studies aimed to establish the value of SPECT MPI in prediction of regional functional recovery after CABG [1, 18, 46]. Murashita T. et al. [46] demonstrated that perfusion uptake of more than 50% is a sign of such recovery after revascularization. In our study the cut-off point for LAD territory RS was 15.5/28 (55.4%) and it is very close to the T. Murashita data.

Moreover, the perfusion uptake less than 50% in a recognized criteria for scar, which often presents in ICM patients with LV aneurysm [1]. These patients usually underwent ventricular reconstruction. There was reduction of Q-values along with increase of PI-values in patients with SVR. The reasons for this could be a reduction of collateral circulation or worse morphological condition of myocardium before operation in presence of an apex/anterior LV aneurysm.

According to our study, TPD has been most associated with TTFM values in LIMA-LAD grafts in ICM patients. TPD over 14% is considered abnormal [47, 48]. Our data suggest that TPD in the LAD territory >26.85 is a predictor of early LIMA graft failure in patients with ICM.

### **Study limitations**

The present study has a few limitations: there was a relatively small number of involved patients; the wall motion in the LAD territory was not assessed and we used cut-off value for mean conduit flow revealed by H. Oshima et al (2016) [2], despite an ongoing dispute about the cut-point values in modern literature. The influence of graft number and type has not been assessed.

### **Conclusion**

We must agree with T. Kieser et al, who determined that the use of TTFM is only half of the picture [5]. TTFM is a reliable tool for preventing technical mistakes during CABG, however, its use is limited by variability in presurgical myocardial condition. Myocardial perfusion parameters, assessed by means of SPECT before surgery (more specifically, indicators such as rest TPD and SRS) are potential predictors of LIMA-LAD early graft failure in patients with ICM.

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All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Sergey S. Gutor, Sergey L. Andreev, Vladimir V. Shipulin, Andrey V. Mochula, Vasily V. Zatolokin, Andrey S. Pryahin, Vladimir M. Shipulin, Boris N. Kozlov, and Konstantin V. Zavadovsky. All authors read and approved the final manuscript.

The study was approved by the Local Ethical Committee (Committee on Biomedical Ethics, Cardiology Research Institute; Approval Number: 178) and conformed to the Declaration of Helsinki on Human Research. Written informed consent was obtained from each patient after explanation of the protocol, its aims, and potential risks.

### **Authors' participation**

Shipulin V.V. – writing text, text preparation and editing, responsibility for the integrity of all parts of the article, analysis and interpretation of the obtained data, approval of the final version of the article.

Gutor S.S. – concept and design of the study, conducting research, collection and analysis of data, statistical analysis, analysis and interpretation of the obtained data, writing text, review of publications, preparation and creation of the published work.

Andreev S.L. – concept and design of the study, conducting research, collection and analysis of data, analysis and interpretation of the obtained data.

Mochula A.V. – collection and analysis of data, participation in scientific design, preparation and creation of the published work.

Zatolokin V.V. – concept and design of the study, conducting research, collection and analysis of data, analysis and interpretation of the obtained data.

Shipulin V.M. – participation in scientific design, approval of the final version of the article.

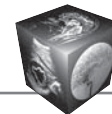
Kozlov B.N. – concept and design of the study, approval of the final version of the article.

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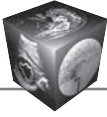
Zavadovsky K.V. – concept and design of the study, approval of the final version of the article.

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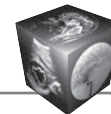
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