Assessment of Myocardial Ischemic-Reperfusion Injury During Off- and On- Pump CABG (ClinicalTrials.gov Identifier: NCT03050489). Corresponding author: Bunenkov Nikolay bunenkov2006@gmail.com +7-950-028-17-40
Date of the document 06 December 2016

Statistical Analysis

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2021

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CONSORT 2010 checklist of information to include when reporting a pilot or feasibility randomized trial in a journal or conference abstract

Table 1 CONSORT 2010 checklist of information to include when reporting a pilot or feasibility randomized trial in a journal or conference abstract

Item	Description	Reported on line number
Title	Assessment of Myocardial Ischemic-Reperfusion Injury During Off- and On- Pump CABG (AMIRI-CABG) ClinicalTrials.gov Identifier: NCT03050489	
Authors *	Bunenkov N. S.	
Trial design	Prospective non-randomized single center	
Methods		
Participants	Eligibility criteria: multivessel coronary artery disease with indications for elective coronary artery bypass grafting	
Interventions	Group 1: off-pump CABG Group 2: on-pump CABG Group 3: pump-assisted CABG (on-pump CABG without aortic cross-clamping)	
Objective	To compare level of MPO between three groups of intervention	
Primary objective	To compare ischemic-reperfusion injury between three groups of intervention	

Secondary objective	To assess ability of MPO to predict worse outcome (death) To assess relation between MPO and TnI	
Outcome	MPO level after CABG, death after CABG	
Randomization	Non-randomized allocation. Heart Team decision.	
Blinding (masking)	None	
Results		
Numbers randomized	Number of participants screened n=500 Allocated (non-randomized): off-pump CABG (n=181), on-pump CABG (n=128), pump-assisted CABG (n=27)	
Recruitment	Complete	
Numbers analyzed	Off-pump CABG: 181 On-pump CABG: 128 Pump-assisted CABG: 27	
Outcome	Could MPO predict death during 30 days after CABG	
Harms	Important adverse events or side effects	
Conclusions	CPB activates leucocytes that cause myocardial damage Preoperative MPO level could evaluated as a predictor of myocardial damage and worse outcome after CABG	
Trial registration	ClinicalTrials.gov Identifier: NCT03050489	
Funding	Assessment of regenerative ability after cardiac surgery	

Table 2 Statistical analysis synopsis

Assessment of Myocardial Ischemic-Reperfusion Injury During Off- and On- Pump CABG ClinicalTrials.gov Identifier: NCT03050489	
Hypothesis	Ischemic – reperfusion injury are comparable between groups
Primary objective	To compare ischemic-reperfusion injury during off-pump, on-pump and pump – assisted CABG
Secondary objective	To assess ability of myeloperoxidase to predict worse outcome after CABG

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Type of trial	Prospective non-randomised single-centre
Type of research	Explarotory
Timeline	2015-2019
Groups	Off-pump On – pump Pump-assisted (on-pump without aortic cross-clamping)
Sample size estimation	> 300 patients
Planned sample size	Averall: 300 Off-pump: 100 On-pump: 100 Pump-assissted: 100
Actual sample size	Averall: 336 Off-pump: 181 (conversion 6) On-pump: 128 Pump-assissted: 27
Baseline charachteristics comparing	Testing for type of distribution of baseline characteristics: ANOVA for normal distribution Kruskal-Wallis test with multiple groups comparison adjustment for non-normal distribution Chi-squared test or exact Fisher's test for nominal data
Statistics hypothesis testing	ANOVA/ANCOVA for MPO level, troponin I level
Missing Data Handling	Drop observations with missing data
Evaluating of reason of missingness	Hypothesis: Missing data depend on severity of complications Hypothesis testing with logistic regression model: Missingness = complications

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Abbreviations

AEs – Adverse events

CABG – coronary artery bypass grafting

CPB – cardiopulmonary bypass grafting

ECG – elecrocardiogram

IL-8 - interleukin 8

IQR – interquartile range

LCx – left circumflex artery

LDL - low-density lipoprotein

MPO – myeloperoxidase

Nmiss – number of missing values

RCA – right coronary artery

Rpm – rate per minute

SAE - Serious Adverse Event

URL – upper reference limit

Introduction

Coronary artery bypass grafting (CABG) is worldwide performed procedure. This procedure could be performed with cardiopulmonary bypass with aortic cross-clamping, without aortic cross-clamping (pump-assissted on beating heart with mechanical support of circulation) and off-pump. Some authors reported better outcomes for off-pump CABG, but others prefered on-pump CABG due to comfortable circumstances for coronary artery suture and pointed out on the risk of incomlete revascularization for off-pump CABG. Pump-assissted CABG could be favorable for myocardial tissue due to maintaining coronary flow as well as stable hemodynamics. There were a lot of clinical trials comparing short- and long-term outcomes of on-pump and off-pump CABG. But there is litle evidence about comparison of myocardial damage during on-pump CABG, off-pump CABG and pump-assissted CABG. Most common timepoints for cardiac troponin level were within 2 days postoperatively. A few clinical trials monitored cardiac troponin level after second day postoperatively and lack thereof, of precise data about cardiac troponin dynamic after different types of CABG. Another important issue is inflammation response during CABG, wich is lower in off-pump CABG. But latest trials reported that CPB-mediated inflammation response play a less important role than surgical wound-mediated inflammation response. It has been reported that myeloperoxidase(MPO) involved in ischemic-reperfusion myocardial damage [1]. Some clinical trials evaluated prognostic value of MPO for acute coronary syndrome [2 , 9]. The goal of current clinical trial is to evaluate MPO-level during off-pump, on-pump and pump-assisted CABG as well as myocardial damage and outcomes. Serum level of MPO as it has been reported raise fast during minutes after ischemia-reperfusion and could be measured during surgical procedure and served as a predictor major adverse cardiac events [1].

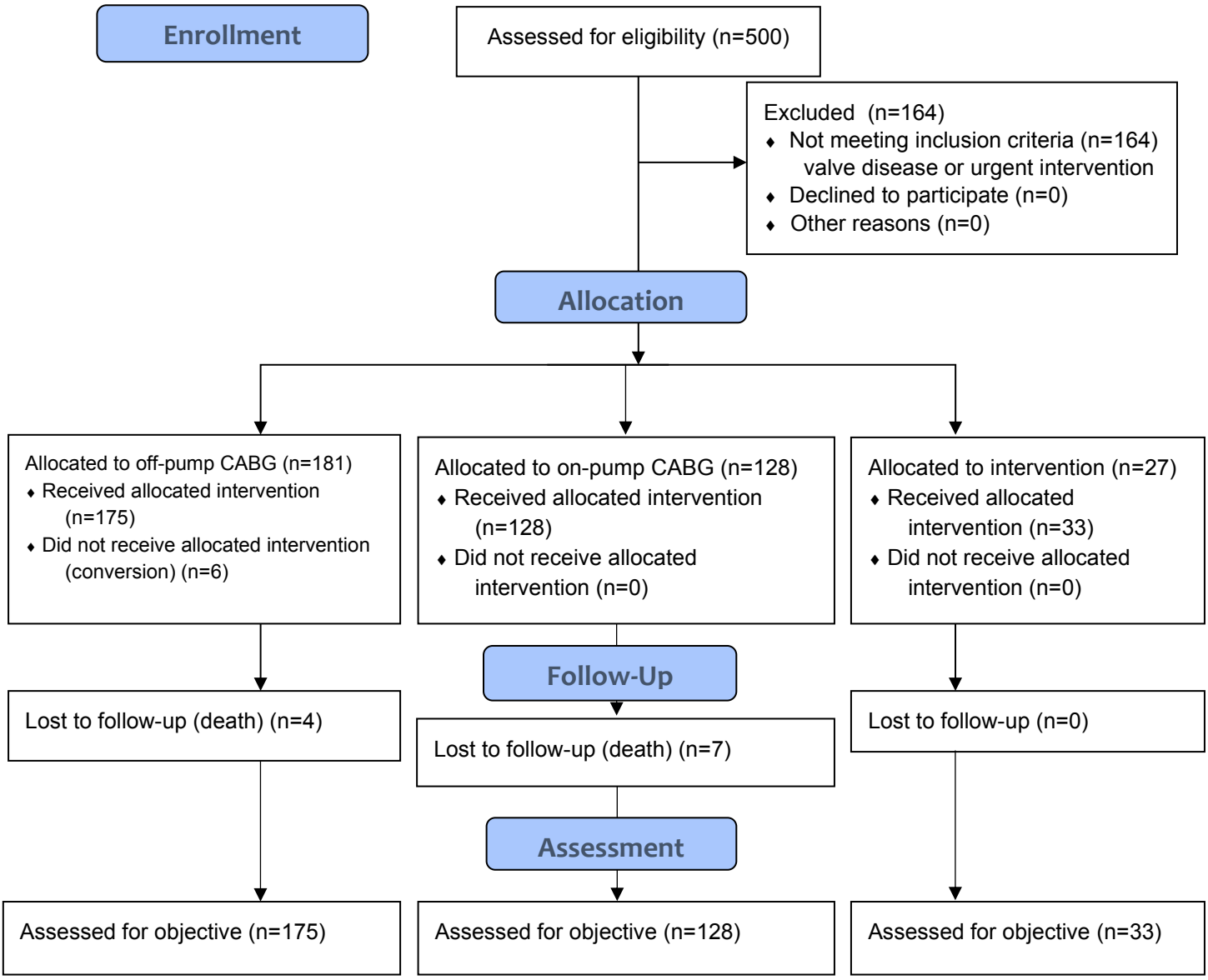
Cardiac troponin is a specific and sensitive marker of myocardial necrosis and has found wide application in clinical practice. Nevertheless, the links of the pathogenesis that precede its release into the systemic circulation have not been sufficiently studied [7]. As early and specific markers of myocardial damage, MPO activated by ischemia-reperfusion of leukocytes, which are released into circulation and participate in myocardial damage, can act [7]. By measuring the concentration of inflammatory mediator MPO that degranulate the white blood cells and which can damage cardiomyocytes, it is possible to predict the extent of myocardial damage [6].

Inflammation plays a crucial role in plaque destabilization and rupture. MPO belong to the marker of plaque instability and degranulated by leukocytes and produces active forms of halogens that is an important in antibacterial protection [12]. An important advantage of MPO in comparison with other markers is the presence of intrinsic activity, which, in the presence of fluorogenic substrates, allows to shorten the time of performance of enzyme-linked immunosorbent assays to two stages - sorption of the enzyme from the sample and detection of its activity, which is especially important for emergency diagnosis . Mediators of inflammation, secreted by the activation of leukocytes after ischemia-reperfusion, contribute to myocardial damage, accelerate the development of atherosclerosis and destabilize atherosclerotic plaques[12].

At present, a large number of works are devoted to the problem of ischemic-reperfusion injury, however, the molecular-biological aspects have not been fully elucidated. A number of clinical studies of the diagnostic value of myeloperoxidase in relation to acute coronary syndrome was conducted, and the prognostic value for cardiovascular complications in patients after PCI of was studied [3 , 5]. There are also studies evaluating the concentration of MPO in the coronary sinus after restoration of blood flow in aorto-coronary bypass surgery. Modern ideas about the mechanisms of MPO-dependent modification of low-density lipoprotein (LDL), their role in initiating inflammation and destabilization of atherosclerotic plaque are presented in the following reviews [8]. In brief, the meaning of the participation of modified LDL in atherogenesis is reduced to the following. Activation of monocytes and neutrophils leads to their degranulation and release of MPO into the extracellular space. Due to its polycationic properties (pI> 9), MPO binds to the negatively charged surface of LDL, as well as the cells of the vascular wall. As a result of activation of NADPH oxidase on the surface of leukocytes and endotheliocytes, the production of superoxide anion radical is enhanced. Spontaneous or catalyzed by the enzyme superoxide dismutase dismutation of the latter leads to the formation of hydrogen peroxide. Conditions are created for MPO-dependent synthesis of HOCl, which modifies LDL, and also causes endothelial dysfunction. Modified LDLs penetrate the damaged endothelium into the subendothelial space, where they are captured by macrophages. The accumulation of modified LDL leads to the transformation of macrophages into foam cells and the accumulation of lipids in the arterial intima. In addition, native LDL can also penetrate through the endothelium, where they undergo oxidative / halogen modifications from the active forms of halogens formed with the participation of MPO. Finally, modified LDLs activate endotheliocytes and monocytes, which results in the secretion of interleukin 8 (IL-8) and tumor necrosis factor (TNFα), respectively. In turn, IL-8 and TNFα activate monocytes and endothelial cells, closing the vicious circle of LDL modification. Also, modified LDL, interacting with the endothelium, inhibit the fibrinolysis process, contributing to the formation and subsequent destabilization of atherosclerotic plaque. Recently, we have shown that MPO are secreted by

neutrophils in response to LDL-modified oxidants . Thus, there is reason to assume the diagnostic significance of identifying active leukocyte enzymes in cardiovascular diseases [10].

Study Design



Prospective single cente non-randomized clinical trial.

Study Centers: First Saint Petersburg State Medical University.

Number of groups: 3

Intervention:

Group 1: off-pump CABG

Group 2: on-pump CABG

Group 3: pump-assisted CABG (on-pump CABG without aortic cross-clamping)

Sample size: >300.

Table 3 Number of patients

Intervention	Number of patients	
	Planned	Actual
off-pump CABG	100	181 (175)
on-pump CABG	100	128 (127)
pump-assisted CABG	100	27 (33)
Total	300	336
Conversion	N/A	6

181 patient planned for elective CABG. There were 6 conversions to pump – assisted CABG (on-pump CABG without aortic cross-clamping). 175 recived off-pump-CABG. 27 patient planned for elective pump – assisted CABG (on-pump CABG without aortic cross-clamping). 33 pump – assisted CABG were performed.

Primary Endpoint: MPO level after operation.

Secondary Endpoints: low output syndrome, length of stay in intensive care unit, length of stay in hospital, inotrope and vasopressor agents demand, duration of pulmonary ventilation, end systolic volume, end dyastolic volume, ejection fraction, reoperation, renal dysfunction, atrial fibrillation, death during 30 days after CABG, stroke during 30-days after CABG.

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Patients allocation

Patients were allocated into one of three groups of treatment by Heart Team. Patients consecutively admitted in the Department of Cardiac Surgery #1 and #2. All patients who admitted in the Department of Cardiac Surgery #1 allocated into off-pump CABG group. Patients who admitted in the Department of Cardiac Surgery #2 allocated into off-pump CABG group, on-pump CABG group (when have proximal lesions of RCA or LCx), off-pump CABG group (when have more distal lesion of coronary arteries) or pump-asssisted CABG group (when have difusse coronary artery lesions). Heart Team includes three or more cardiac surgeons who performes off-pump, on-pump or pump-assisted CABG more than 10 years, two or more interventional cardiologists, one neurologist, two ore more anesthesiologist, two ore more reanimatologist, one perfusiologist and two cardiologist. After debating patients were alocatted into one of threy groups for elective CABG.

Study objectives

- To compare ischemic-reperfusion injury after off-pump, on-pump and pump-assisted - CABG

Primary objective

- To compare MPO level before and just after performing coronary anastomosis during off-pump CABG, on-pump CABG and pump-assisted CABG (with cardiopulmonary bypass without aortic cross-clamping)
- To compare TnI level between groups

Secondary objectives

- To compare incidence of low output syndrome after off-pump CABG, on-pump CABG and pump-assisted CABG (with cardiopulmonary bypass without aortic cross-clamping)
- To compare length of stay in intensive care unit after off-pump CABG, on-pump CABG and pump-assisted CABG (with cardiopulmonary bypass without aortic cross-clamping)
- To compare length of stay in hospital care unit after off-pump CABG, on-pump CABG and pump-assisted CABG (with cardiopulmonary bypass without aortic cross-clamping)

- To compare inotrope and vasopressor agents demand after off-pump CABG, on-pump CABG and pump-assisted CABG (with cardiopulmonary bypass without aortic cross-clamping)
- To compare duration of pulmonary ventilation after off-pump CABG, on-pump CABG and pump-assisted CABG (with cardiopulmonary bypass without aortic cross-clamping)
- To compare end systolic volume, end dyastolic volume, ejection fraction after off-pump CABG, on-pump CABG and pump-assisted CABG (with cardiopulmonary bypass without aortic cross-clamping)
- To investigate whether MPO level could predict outcomes after CABG
- To compare incidence of reoperation after off-pump CABG, on-pump CABG and pump-assisted CABG (with cardiopulmonary bypass without aortic cross-clamping)
- To compare incidence of renal dysfunction after off-pump CABG, on-pump CABG and pump-assisted CABG (with cardiopulmonary bypass without aortic cross-clamping)
- To compare incidence of atrial fibrillation after off-pump CABG, on-pump CABG and pump-assisted CABG (with cardiopulmonary bypass without aortic cross-clamping)
- To compare incidence of death during 30 days after off-pump CABG, on-pump CABG and pump-assisted CABG (with cardiopulmonary bypass without aortic cross-clamping)
- To compare incidence of stroke during 30-days after off-pump CABG, on-pump CABG and pump-assisted CABG (with cardiopulmonary bypass without aortic cross-clamping)

Study population

- Patients with mutivessel coronary artery lesions with indications for elective CABG

Inclusion criteria

- Multivessel coronary artery disease with indications for CABG
- Single CABG procedure

Exclusion criteria

- Valve disease
- Acute coronary syndrome or urgent CABG

Study timepoints

- During 30 days after CABG

Myeloperoxidase Test

Biomaterial production protocol:

1st test before surgery. Blood is obtained from a central venous catheter in a volume of 4 ml into a violet tube. Within 7 minutes, centrifugation at 3000 rpm at 4 ° C is carried out. The plasma is then collected into an eppendorf-type tube of 1 ml and frozen at -40 or below.

The 2nd test immediately after performing coronary artery suture. Blood is obtained from a central venous catheter in a volume of 4 ml into a violet tube. Within 7 minutes, centrifugation at 3000 rpm at 4 ° C is carried out. The plasma is then collected into an eppendorf-type tube of 1 ml and frozen at -40 or below. Samples, they are delivered to the laboratory of biochemical genetics of the Institute of Experimental Medicine, where molecular and biological studies are performed. The receipt of the material was approved by the ethical committee of the First State Medical University after I.P.Pavlov, protocol 03 / 17-11.

Earlier we worked out methods for isolating homogeneous preparations of myeloperoxidase (MPO) [11]. The preparations of MPO (M ~ 145 kDa, RZ ~ 0.85) obtained with the help of original approaches do not contain impurities of leukocyte proteinases and differ in the specific activity that exceeds commercially available analogs. For the quantitative determination of MPO, previously used solid-phase enzyme-linked immunosorbent assays will be used, which are characterized by high sensitivity and specificity due to the independent production of monovalent antibodies against the proteins.

The activity of MPO in the samples is estimated from the fluorescence of resorufin, which is formed by oxidation of 10-acetyl-3,7-dihydroxyphenoxazine with brominating MPO, which binds when the samples are incubated in plates with adsorbed on the surface of the wells with affinity antibodies against MPO obtained from rats [4]. Antibodies (5 µg / ml) dissolved in 40 mM Na2CO3, 80 mM NaHCO3, pH 9.4, are adsorbed in 96-well polystyrene plates overnight at 4 ° C. After 3 washes of PBS containing 0.05% Tween 20, the purified MPO was placed in the wells at 0 concentrations; 0.625; 1.25; 2.5; 5; 10; 20; 40 ng / ml and samples diluted 10 to 80 times with PBS containing 0.05% Tween 20. After 60 min incubation in a thermoshaker at 37 ° C and 270 rpm, the wells of the plate are washed 3 times with PBS containing 0.05% Tween 20. A solution containing 1 µM 10-acetyl-3,7-dihydroxyphenoxazine, 10 µM H2O2, 20 mM NaBr, 200 mM (NH4) 2SO4, 24 mM sodium citrate buffer, pH 6.0 is placed in the wells. After 30 minutes of incubation in a thermoshaker at 37 ° C and 270 rpm, the fluorescence of the resorufin at 580-620 nm (535-555 nm excitation) was measured using a flatbed monochromator fluorimeter-luminometer

spectrophotometer ("CLARIOstar", BMG LABTECH, Germany). The calibration plot of the fluorescence intensity I from [MPO] is processed in the MS Excel 2002 program as the binomial function I = a [MPO] 2 + b [MPO] + c (the coefficient of determinism R2 normalized from 0 to 1). The activity of MPO in the samples was calculated taking into account the dilution of the sample and expressed as ng / ml of purified MPO.

In order to optimize the methods for determining the activity of these enzyme, the conditions of sorption from plasma of blood on solid-phase immobilized antibodies, dissociation conditions of inhibitors will be studied when their activity is detected. The results obtained will be compared with the results of the determination using traditional methods of enzyme immunoassay. As a result, optimal protocols will be obtained for rapid tests to detect the activity of myeloperoxidase in blood plasma after immunosorption.

Safety Analysis

Adverse events (AEs)/serious AEs.

Study Duration

The date of the first subject inclusion – 15 September 2015.

Estimated date of the last subject inclusion – May 2019 .

Expected date of database closing – October 2019.

Study report ready –2020

Definitions

Ischemic-Reperfusion Injury

Myocardial ischemic – reperfusion injury defined as troponin I elevation after CABG hihgher than upper reference limit (URL) in patients who does not met current criteria for myocardial infarction 5 type diagnosis.

Myocardial Infarction 5 Type

Myocardial Infarction 5 type defined as a troponin I elevation heigher than 10 time 99th percentile URL with new Q-vawe onset (ECG) or new regional wall motion abnormality (echocardiography) or graft/new coronary artery occlusion (angioangiography).

Adverse Events

An Adverse Event (AE) is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in a clinical investigation of procedure and not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (such as an abnormal laboratory finding), symptom, or disease temporally associated with the use of investigational procedure, whether or not considered related to the investigational procedure.

The causal relationship to study drug is determined by a physician and should be used to assess all adverse events (AE). The casual relationship can be one of the following:

Related: There is a reasonable causal relationship between study procedure and the AE.

Not related: There is not a reasonable causal relationship between study procedure and the AE.

The term "reasonable causal relationship" means there is evidence to suggest a causal relationship.

Adverse events can be spontaneously reported or elicited during open-ended questioning, examination, or evaluation of a subject. (In order to prevent reporting bias, subjects should not be questioned regarding the specific occurrence of one or more AEs.)

Serious Adverse Events

A Serious Adverse Event (SAE):

results in death is life-threatening (defined as an event in which the subject was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe) requires inpatient hospitalization or causes prolongation of existing hospitalization (see NOTE below) results in persistent or significant disability/incapacity is a congenital anomaly/birth defect is an important medical event (defined as a medical event(s) that may not be immediately life-threatening or result in death or hospitalization but, based upon appropriate medical and scientific judgment, may jeopardize the subject or may require intervention [eg, medical, surgical] to prevent one of the other serious outcomes listed in the definition above.) Examples of such events include, but are not limited to, intensive treatment in an emergency room or at home for allergic bronchospasm; blood dyscrasias or convulsions that do not result in hospitalization.)

Nonserious Adverse Events

A nonserious adverse event is an AE not classified as serious.

Laboratory Test Abnormalities

All laboratory test results captured as part of the study should be recorded following institutional procedures. Test results that constitute SAEs should be documented and reported as such.

Collection and reporting

Nonserious Adverse Event Collection and Reporting

The collection of nonserious AE information will begin at initiation of study.

All nonserious adverse events (not only those deemed to be treatment-related) should be collected during the treatment period for a minimum of 365 days following the procedure.

Serious Adverse Event Collection and Reporting

Following the subject's written consent to participate in the study, all SAEs, whether related or not related to study drug, must be collected. All SAEs must be collected that occur within 365 days after procedure.

SAEs, whether related or not related to study procedure, and pregnancies must be reported. SAEs must be recorded an approved form; SAE report should be sent within 24 hours.

Pregnancy

There will be no pregnancy cases.

Other Safety Considerations

Any significant worsening noted during interim or final physical examinations, electrocardiograms, x-rays, and any other potential safety assessments, whether or not these procedures are required by the protocol, should also be recorded as a nonserious or serious AE, as appropriate, and reported accordingly.

ETHICAL CONSIDERATIONS. INFORMED CONSENT

This study will be conducted in accordance with International Society for Pharmacoepidemiology (ISPE) Guidelines for Good Pharmacoepidemiology Practices (GPP), in accordance with Good Clinical Practice (GCP), as defined by the International Conference on Harmonisation (ICH) and in accordance with the ethical principles the Declaration of Helsinki of 2000, Russian version – September 20, 2002.

The study will also be carried out in keeping with federal, state, and local laws, rules and regulations.

The study will be conducted in compliance with the protocol. The protocol, any amendments, and the subject informed consent will receive Institutional Review Board/Independent Ethics Committee (IRB/IEC) approval/favorable opinion before initiation of the study.

Investigators must ensure that subjects are clearly and fully informed about the purpose of the study in which they participate. Freely given written informed consent must be obtained from every subject before participation in the study and the Informed Consent Form (APPENDIX 1) should be signed. Two copies of the Informed Consent Form will be signed by the patient. One copy of the Informed Consent Form will be taken by the patient; another remains with the investigator and is placed in the records. The rights, safety, and well-being of the study subjects are the most important considerations and should prevail over interests of science and society.

All subject names will be kept confidential. Subjects will be identified throughout documentation and evaluation by the Individual Identification code allotted to them during the study. The subjects will be told that all study findings will be handled in strictest confidence.

DATA ANALYSIS

Sample Size Justification

Since it is exploratory study and no statistical hypotheses will be tested, sample size calculation was not conducted for this study. Thus, about 300 patients is planned to be included in the analysis.

Baseline Characteristics

Hypothesis: baseline characteristics are comparable between groups.

Hypothesis testing:

- Normality test (Kolmogorov-Smirnov test, Shapiro-Wilk test)

Group comparing:

Continuous variables

- Non-normal distribution: Kruskal-Wallis test with adjustment for multiple comparisons
- Normal distribution: t-test with multiple comparison adjustment

Nominal variables

- Chi-squared test/ Fisher's exact test

Baseline characteristics:

Table 4 Baseline characteristics specification

Characteristic	Variable name in database	Test
Age	Age	t-test
Gender	Sex	Chi-squared test/ exact Fisher's test
Syntax Score I	SS1	Kruskal-Wallis test
Syntax Score II	SS2	Kruskal-Wallis test
Euroscore II	EII	Kruskal-Wallis test
Charlson/ Deyo Index	ICD	Kruskal-Wallis test
Ejection Fraction	EFPreOp	Kruskal-Wallis test
End diastolic volume	EDVPreOp	Kruskal-Wallis test
End systolic volume	ESVPreOp	Kruskal-Wallis test

Table 5 Baseline characteristics

Variables	off-pump CABG (N=181)	on-pump CABG (N=128)	pump-assisted CABG (N=27)	P Value
Age in years				0.7836*
Mean±SD	63.5±7.3	63.6±7.1	64.3±8.9	
Min–Max	43.0–79.0	33.0–80.0	46.0–80.0	
Median (IQR)	63.0 (59.0–68.0)	64.0 (59.0–68.0)	66.0 (58.0–69.0)	
Syntax Score I				0.3667**
Nmiss (%)	1 (0.6)	2 (1.6)	1 (3.7)	

Variables	off-pump CABG (N=181)	on-pump CABG (N=128)	pump-assisted CABG (N=27)	P Value
Mean±SD	26.2±9.4	27.4±7.7	27.8±6.7	
Min–Max	2.0–61.0	10.0–52.5	14.0–43.5	
Median (IQR)	24.4 (22.0–31.8)	25.8 (22.0–31.5)	27.0 (22.0–33.0)	
Syntax Score II				0.6002
Nmiss (%)	1 (0.6)	2 (1.6)	1 (3.7)	
Mean±SD	41.7±11.6	40.9±12.5	43.5±11.6	
Min–Max	8.1–68.0	3.7–68.3	24.6–67.6	
Median (IQR)	41.4 (32.7–50.8)	42.3 (31.1–49.9)	43.5 (34.5–53.6)	
EuroScore I				0.3137
Mean±SD	1.4±1.3	1.3±1.0	1.4±1.4	
Min–Max	0.5–10.8	0.5–5.5	0.5–6.7	
Median (IQR)	1.0 (0.7–1.5)	1.0 (0.6–1.5)	0.8 (0.6–1.4)	
Index Charlson/Deyo				0.1141
Nmiss (%)	1 (0.6)			
Mean±SD	5.4±2.0	5.0±1.8	4.9±2.0	
Min–Max	1.0–11.0	0.0–10.0	2.0–10.0	
Median (IQR)	5.0 (4.0–7.0)	5.0 (4.0–6.0)	5.0 (4.0–6.0)	
Ejection Fraction before operation				0.9090
Nmiss (%)	1 (0.6)	2 (1.6)		
Mean±SD	60.2±10.4	60.9±8.5	58.4±11.7	
Min–Max	30.0–85.0	28.0–85.0	30.0–72.0	
Median (IQR)	62.0 (55.0–67.0)	62.0 (59.0–66.0)	63.0 (55.0–65.0)	
End diastolic volume				0.2187
Nmiss (%)	5 (2.8)	5 (3.9)		
Mean±SD	115.7±41.5	115.7±34.8	131.1±53.6	
Min–Max	11.0–270.0	44.0–224.0	81.0–367.0	
Median (IQR)	109.0 (91.0–131.5)	114.0 (90.0–139.0)	121.0 (101.0–141.0)	
End Systolic Volume				0.4178
Nmiss (%)	5 (2.8)	5 (3.9)		
Mean±SD	48.0±28.0	46.8±23.0	50.5±20.7	
Min–Max	11.0–178.0	12.0–138.0	23.0–107.0	

Variables	off-pump CABG (N=181)	on-pump CABG (N=128)	pump-assisted CABG (N=27)	P Value
Median (IQR)	40.5 (31.0–55.0)	43.0 (32.0–54.0)	44.0 (38.0–55.0)	
Gender				0.6268***
Male	142 (78.5)	95 (74.2)	20 (74.1)	
Female	39 (21.5)	33 (25.8)	7 (25.9)	

* ANOVA, ** Kruskal-Wallis test, Nmiss – number of missing values, SD – standard deviation, IQR – interquartile range, *** - Chi-squared test, CABG – coronary artery bypass grafting

Primary endpoint analysis

Hypothesis: MPO levels after procedure are different between groups.

Hypothesis testing:

- Normality test (Kolmogorov-Smirnov test, Shapiro-Wilk test)

Group comparing:

Continuous variables

- Non-normal distribution: Kruskal-Wallis test with adjustment for multiple comparisons

Table 6 Myeloperoxidase variables specifications

Characteristic	Variable name in database	Test
MPO level before procedure	MPOPreOp	Kruskal-Wallis test
MPO level after procedure	MPOPostOp	Kruskal-Wallis test

Table 7 Myeloperoxidase before and during coronary artery bypass grafting (CABG)

Variables	off-pump CABG (N=181)	on-pump CABG (N=128)	pump-assisted CABG (N=27)	P Value*
MPO before CABG				0.2904
Nmiss (%)	34 (18.8)	21 (16.4)	9 (33.3)	
Mean±SD	35.8±32.1	39.9±30.6	29.2±14.8	
Min–Max	2.8–237.8	4.0–168.9	5.6–65.4	
Median (IQR)	27.7 (17.0–41.0)	31.0 (19.0–48.7)	29.0 (18.7–34.0)	
MPO after CABG				<.0001
Nmiss (%)	28 (15.5)	26 (20.3)	13 (48.1)	

Variables	off-pump CABG (N=181)	on-pump CABG (N=128)	pump-assisted CABG (N=27)	P Value*
Mean±SD	96.2±75.3	210.9±138.7	175.0±102.6	
Min–Max	9.1–410.3	16.7–824.6	63.4–374.5	
Median (IQR)	66.5 (41.3–135.8)	184.3 (135.0–250.0)	144.7 (95.0–284.9)	

* Kruskal-Wallis test, Nmiss – number of missing values, SD – standard deviation, IQR – interquartile range, CABG – coronary artery bypass grafting

Ischemic – reperfusion injury analysis (MPO level)

Hypothesis: MPO level after suture performing depends on length of operation, length of cardiopulmonary bypass, MPO level before procedure and associated with complications

Method of hypothesis testing: ANCOVA

ANCOVA model: LGMPOPostOp = LGMPOPreOp CPBTYPE LGMPOPreOp*CPBTYPE COMPLICATION AoClamp CPBTime OpTime

Table 8 Variables description

Variable	Description	Note
LGMPOPostOp	Logarithm of MPO level during CABG (after suture performing)	Log – transformation for normal distribution
LGMPOPreOp	Logarithm of MPO level before CABG (after suture performing)	Log – transformation for normal distribution
CPBTYPE	Group of intervention	1 – off-pump CABG 2 – on – pump CABG 3 – pump-assisted CABG
COMPLICATION	Cumulative number of complications	Ordinal variable
AoClamp	Length of aortic cross-clamping, min	Continuous variable
CPBTime	Length of cardiopulmonary bypass, min	Continuous variable
OpTime	Length of procedure, min	Continuous variable
*	Interaction effect	

Table 9 Characteristics of model

Source	Sum of Squares	df	Mean Square	F	p	Eta Square
Model	51.9	9	5.77	12.13	0.0001	0.34

*Table 10 General linear model LGMPOPostOp = LGMPOPreOp CPBTYPE LGMPOPreOp*CPBTYPE COMPLICATION AoClamp CPBTime OpTime*

Source	Sum of Squares (Type III)	df	Mean Square	F	p	Partial Eta Squared
LGMPOPreOp	0.9	1	0.9	0.2	0.0001	0.009
CPBType	6.2	2	3.1	6.6	0.0001	0.06
LGMPOPreOp*CPBTYPE	3.5	2	1.7	3.6	0.0499	0.03
Complication	0.02	1	0.02	0.04	0.6	0.0002
AoClamp	0.03	1	0.03	0.05	0.3	0.0002
CPBTime	0.05	1	0.05	0.1	0.1	0.0004
OpTime	1.3	1	1.3	2.8	0.1	0.01

Ischemic – reperfusion injury analysis (TnI level 1st day after CABG)

Hypothesis: TnI level 1st after CABG depends on length of operation, length of cardiopulmonary bypass, MPO level before procedure and just after suture performing

Method of hypothesis testing: ANCOVA

ANCOVA model: LGTnI1 = LGMPOPostOp LGMPOPreOp CPBTYPE LGMPOPreOp*CPBTYPE AoClamp CPBTime AoClamp*CPBTime OpTime CPBTime* OpTime AoClamp*OpTime

Table 11 Variables descriptions

Variable	Description	Note
TnI1	Troponin I level 1st day after procedure	Continuous variable
LGMPOPostOp	Logarithm of MPO level during CABG (after suture performing)	Log – transformation for normal distribution
LGMPOPreOp	Logarithm of MPO level before CABG (after suture performing)	Log – transformation for normal distribution
CPBTYPE	Group of intervention	1 – off-pump CABG 2 – on – pump CABG 3 – pump-assisted CABG
AoClamp	Length of aortic cross-clamping, min	Continuous variable
CPBTime	Length of cardiopulmonary bypass, min	Continuous variable
OpTime	Length of procedure, min	Continuous variable
*	Interaction effect	

Table 12 Characteristics of model

Source	Sum of Squares	df	Mean Square	F	p	Eta Square

Model	249.3	14	17.8	10.4	0.0001	0.44

*Table 13 General linear model characteristics LGTnI1 = LGMPOPostOp LGMPOPreOp CPBTYPE LGMPOPreOp*CPBTYPE AoClamp CPBTime AoClamp*CPBTime OpTime CPBTime* OpTime AoClamp*OpTime*

Source	Sum of Squares (Type III)	df	Mean Square	F	p	Partial Eta Squared
LGMPOPostOp	2.0	1	2.6	1.2	0.3	0.006
LGMPOPreOp	0.8	1	0.8	0.5	0.5	0.002
AoClamp	2.3	1	2.3	1.4	0.2	0.007
CPBTime	2.2	1	2.2	1.3	0.3	0.007
OpTime	23.3	1	23.3	13.6	0.0003	0.07
CPBType	3.9	2	1.9	1.1	0.3	0.01
CPBTime*OpTime	0.7	1	0.7	0.4	0.5	0.002
AoClamp*CPBTime	0.4	1	0.4	0.22	0.6	0.001
AoClamp*OpTime	3.5	1	3.5	2.1	0.2	0.01
LGMPOPostOp*CPBTYPE	4.1	2	2.1	1.2	0.3	0.01
LGMPOPreOp*CPBTYPE	0.4	2	0.2	0.1	0.9	0.001

Summary: troponin I level 1st day postoperatively depends on length of operation

Ischemic – reperfusion injury analysis (TnI level 1st day after on – pump CABG)

Hypothesis: TnI level 1st day after on-pump CABG depends on length of operation, length of cardiopulmonary bypass, MPO level before procedure and after suture performing

Method of hypothesis testing: ANCOVA

ANCOVA model: LGTnI1 = LGMPOPostOp LGMPOPreOp CPBTYPE LGMPOPreOp*CPBTYPE AoClamp CPBTime AoClamp*CPBTime OpTime CPBTime* OpTime AoClamp*OpTime

Table 14 Variables description

Variable	Description	Note
TnI1	Troponin I level 1st day after procedure	Continuous variable
LGMPOPostOp	Logarithm of MPO level during CABG (after suture performing)	Log – transformation for normal distribution
LGMPOPreOp	Logarithm of MPO level before CABG (after suture performing)	Log – transformation for normal distribution
CPBTYPE	Group of intervention	1 – off-pump CABG 2 – on – pump CABG 3 – pump-assisted CABG
AoClamp	Length of aortic cross-clamping, min	Continuous variable
CPBTime	Length of cardiopulmonary bypass, min	Continuous variable
OpTime	Length of procedure, min	Continuous variable
*	Interaction effect	

Table 15 Characteristics of model

Source	Sum of Squares	df	Mean Square	F	p	Eta Square
Model	39.7	8	4.96	5.4	0.0001	0.4

*Table 16 Characteristics of model LGTnI1 = LGMPOPostOp LGMPOPreOp CPBTYPE LGMPOPreOp*CPBTYPE AoClamp CPBTime AoClamp*CPBTime OpTime CPBTime* OpTime AoClamp*OpTime*

Source	Sum of Squares (Type III)	df	Mean Square	F	p	Partial Eta Squared
LGMPOPostOp	1.3	1	1.3	1.4	0.2	0.02
LGMPOPreOp	3.9	1	3.9	4.2	0.04	0.06
AoClamp	0.9	1	0.9	1.0	0.3	0.02
CPBTime	7.4	1	7.4	8.1	0.006	0.1
OpTime	3.4	1	3.4	3.7	0.06	0.05
CPBTime*OpTime	0.01	1	0.1	0.1	0.8	0.0009
AoClamp*CPBTime	5.5	1	5.5	5.9	0.02	0.08
AoClamp*OpTime	1.6	1	1.6	1.7	0.2	0.026

Summary: troponin I level 1st day after on-pump CABG affected by length of cardiopulmonary bypass, preoperative MPO level and interaction of duration of aortic cross clamping and length of cardiopulmonary bypass.

Ischemic – reperfusion injury analysis (TnI level 1st day after off – pump CABG)

Hypothesis: TnI level 1st day after off-pump CABG depends on length of operation, MPO level before procedure and after suture performing

Method of hypothesis testing: ANCOVA

ANCOVA model: LGTnI1= LGMPOPostOp LGMPOPreOp OpTime

Table 17 Variables description

Variable	Description	Note
TnI1	Troponin I level 1st day after procedure	Continuous variable
LGMPOPostOp	Logarithm of MPO level during CABG (after suture performing)	Log – transformation for normal distribution
LGMPOPreOp	Logarithm of MPO level before CABG (after suture performing)	Log – transformation for normal distribution
OpTime	Length of procedure, min	Continuous variable

Table 18 Characteristics of model

Source	Sum of Squares	df	Mean Square	F	p	Eta Square
Model	43.7	3	14.6	7.0	0.0002	0.15

Table 19 Characteristics of model LGTnI1= LGMPOPostOp LGMPOPreOp OpTime

Source	Sum of Squares (Type III)	df	Mean Square	F	p	Partial Eta Squared
LGMPOPostOp	0.1	1	0.1	0.06	0.8	0.0005
LGMPOPreOp	4.9	1	4.9	2.36	0.1	0.02
OpTime	38.5	1	38.5	18.58	0.0001	0.1

Summary: troponin I level 1st day after on-pump CABG affected by length of operation.

Ischemic – reperfusion injury analysis (TnI level 1st day after pump – assisted CABG)

Hypothesis: TnI level 1st day after pump – assisted CABG depends on length of operation, MPO level before procedure and after suture performing and cardiopulmonary bypass.

Method of hypothesis testing: ANCOVA

ANCOVA model: LGTnI1= LGMPOPostOp LGMPOPreOp OpTime CPBType

Table 20 Variables description

Variable	Description	Note
TnI1	Troponin I level 1st day after procedure	Continuous variable
LGMPOPostOp	Logarithm of MPO level during CABG (after suture performing)	Log – transformation for normal distribution
LGMPOPreOp	Logarithm of MPO level before CABG (after suture performing)	Log – transformation for normal distribution
OpTime	Length of procedure, min	Continuous variable
CPBType	Group of intervention	1 – off-pump CABG 2 – on – pump CABG 3 – pump-assisted CABG

Table 21 Characteristics of model

Source	Sum of Squares	df	Mean Square	F	p	Eta Square
Model	3.7	4	0.9	0.8	0.6	0.45

Summary: TnI level 1st day after pump – assisted CABG does not depend on MPO level and length of cardiopulmonary bypass grafting.

Hypothesis: Myeloperoxidase can predict death after CABG.

Missing data handling: exclude from logistic regression model.

Hypothesis testing: logistic regression model **death=MPO**

Table 22 Logistic regression variables specification

Characteristic	Variable name in database	Description	Type of variable
Death after CABG	Death30	Response	Binary
MPO level after CABG	MPOPostOp	Predictor	Continuous

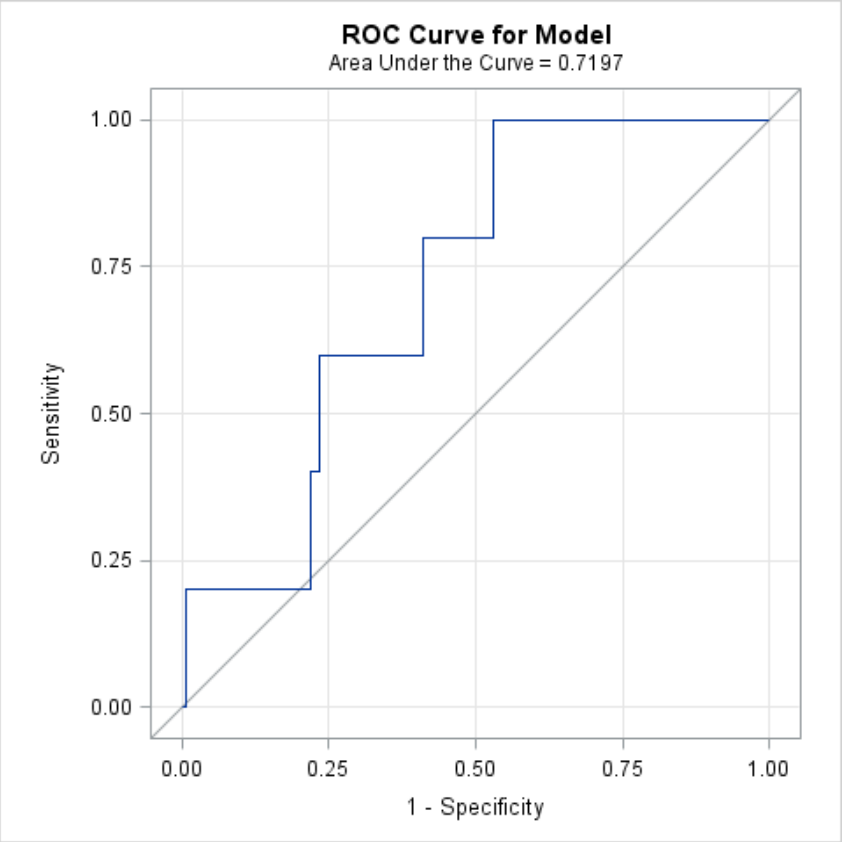
Table 23 Logistic regression model Death = MPO after CABG

Predictor	β	SE β	Wald's χ^2	*df*	*p*	e^{β} (odds ratio)
Constant	0.0047	0.0022	4.4592	1	0.0001	0.0078
MPOPostOp	-4.8498	0.7172	45.7300	1	0.00347	1.0047

Test	χ^2	*df*	*p*
Overall model evaluation			
Likelihood ratio test	3.33	1	0.0679
Score test	5.3072	1	0.0347
Wald test	4.4592	1	0.0347
Goodness-of-fit test			
Hosmer & Lemeshow	9.14	8	0.3305

Cox and Shnell R^2 = 0.052, Nagelkerke R^2 (Max rescaled R^2) = 0.0726. Kendall's Tau-a = 0.011. Goodman – Kruskal Gamma = 0.276. Sommer's D_{xy}=0.27. c-statistics = 63.6%. All statistics reported herein use 4 decimal places in oder to maintain statistical precision.

Table 24 ROC-curve for model death=MPO



Missing data analysis

Table 25 Missing data analysis

MPOPostOp	off-pump CABG (N=181)	on-pump CABG (N=128)	pump-assisted CABG (N=27)
Present	153 (84.5)	102 (79.7)	14 (51.9)
Missing	28 (15.5)	26 (20.3)	13 (48.1)

CABG – coronary artery bypass grafting.

Reason of missingness: laboratory test shows exceeding upper scale limit. Results could be biased.

Hypothesis: postoperative MPO level too high to determine with current assay.

Hypothesis testing: new clinical trial with larger number of patients could this hypothesis tested.

Mechanism of missingness detecting

Hypothesis: missingness due to severity of postoperative status.

Hypothesis testing: logistic regression model missing data (MPOPostOp)= (complications + group)

Table 26 Variables specification for missing data analysis

Characteristic	Variable name in database/ SAS-code	Description	Type of variable
Complications	Complication	Summarize all complications	Ordinal
Group	CPBType	Grouping variable	Ordinal
Missing data (MPO level after CABG)	MISSING	MISSING=1 when data omitted	Binary

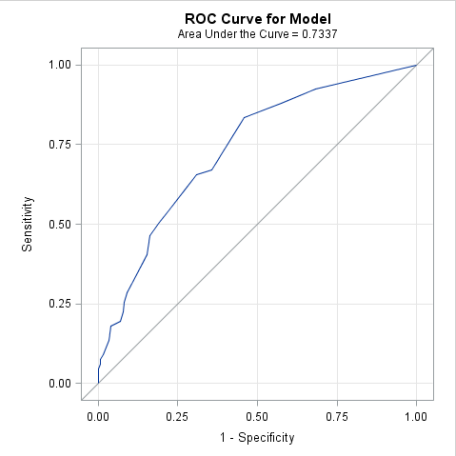
MPO – myeloperoxidase, CABG – coronary artery bypass grafting.

Table 27 Logistic regression model Missing data = complications

Predictor	β	SE β	Wald's χ^2	*df*	*p*	e^{β} (odds ratio)
Constant	-3.6145	0.5957	36.8138	1	0.0001	0.02693
Complication	0.8242	0.2453	11.2900	1	0.0008	2.2801
CPBType	0.8871	0.3168	7.8406	1	0.0051	2.4282
CPBType*Complication	-0.2294	0.1238	3.4338		0.0639	0.7950
Test			χ^2	*df*	*p*	
Overall model evaluation						
Likelihood ratio test			39.0463	3	0.0001	
Score test			39.5144	3	0.0001	
Wald test			32.6207	3	0.0001	
Goodness-of-fit test						
Hosmer & Lemeshow			6.7779	6	0.3419	

Cox and Shnell R^2 = 0.1097, Nagelkerke R^2 (Max rescaled R^2) = 0.1736. Kendall's Tau-a = 0.15. Goodman – Kruskal Gamma = 0.505. Sommer's D_{xy}=0.467 c-statistics = 0.734. All statistics reported herein use 4 decimal places in order to maintain statistical precision.

Table 28 ROC - curve for model Missing data = complications



Summary: Missing data can be classified as 'missing not at random (MNAR)'.

Bias estimation: underestimating predictive value of MPO.

Missing data handling: exclude from logistic regression model. Missing data imputation is not applicable due to MNAR.

Secondary Endpoint Analysis

Hypothesis testing:

- Normality test (Kolmogorov-Smirnov test, Shapiro-Wilk test)

Group comparing:

Continuous variables

- Non-normal distribution: Kruskal-Wallis test with adjustment for multiple comparisons

Table 29 Postoperative characteristics

Variables	off-pump CABG (N=181)	on-pump CABG (N=128)	pump-assisted CABG (N=27)	P Value
ICU days				<.0001*
Mean±SD	2.5±2.2	3.1±3.1	3.3±1.9	
Min–Max	1.0–20.0	1.0–26.0	2.0–7.0	
Median (IQR)	2.0 (1.0–2.0)	2.0 (2.0–3.0)	2.0 (2.0–5.0)	
Days in hospital after CABG				0.0066*
Mean±SD	12.6±6.1	13.6±5.5	12.9±4.1	
Min–Max	0.0–50.0	0.0–33.0	3.0–25.0	
Median (IQR)	12.0 (10.0–13.0)	13.0 (11.0–15.0)	13.0 (10.0–15.0)	
Vasopressor and inotrope demand				0.0204*
Mean±SD	0.1±0.5	0.2±0.9	0.2±0.5	
Min–Max	0.0–4.2	0.0–8.4	0.0–2.1	
Median (IQR)	0.0 (0.0–0.1)	0.0 (0.0–0.1)	0.0 (0.0–0.1)	
Levosimendan demand				0.0220*
Mean±SD	0.0±0.1	0.2±1.8	0.7±3.8	
Min–Max	0.0–0.8	0.0–20.0	0.0–20.0	

Variables	off-pump CABG (N=181)	on-pump CABG (N=128)	pump-assisted CABG (N=27)	P Value
Median (IQR)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	
Lenght of pulmonary ventilation				0.0181*
Mean±SD	1.2±1.2	1.5±1.6	1.4±0.7	
Min–Max	0.0–14.0	0.0–13.0	1.0–3.0	
Median (IQR)	1.0 (1.0–1.0)	1.0 (1.0–1.0)	1.0 (1.0–2.0)	
ESV after CABG				0.1283*
Nmiss (%)	22 (12.2)	22 (17.2)	3 (11.1)	
Mean±SD	42.7±23.5	45.2±21.0	50.9±32.2	
Min–Max	10.0–149.0	19.0–155.0	19.0–170.0	
Median (IQR)	37.0 (27.0–50.0)	40.5 (31.0–52.0)	40.5 (34.0–52.5)	
EDV after CABG				0.0508*
Nmiss (%)	22 (12.2)	22 (17.2)	3 (11.1)	
Mean±SD	103.7±37.7	107.2±32.6	122.3±40.4	
Min–Max	41.0–243.0	44.0–212.0	73.0–222.0	
Median (IQR)	97.0 (79.0–122.0)	106.0 (81.0–131.0)	109.5 (96.0–136.5)	
EF after CABG				0.9820*
Nmiss (%)	22 (12.2)	21 (16.4)	4 (14.8)	
Mean±SD	59.6±10.3	59.8±7.7	60.5±12.3	
Min–Max	29.0–86.0	28.0–73.0	23.0–88.0	
Median (IQR)	61.0 (54.0–66.0)	61.0 (58.0–65.0)	60.0 (55.0–67.0)	
End Systolic Volume				0.4178*
Nmiss (%)	5 (2.8)	5 (3.9)		
Mean±SD	48.0±28.0	46.8±23.0	50.5±20.7	
Min–Max	11.0–178.0	12.0–138.0	23.0–107.0	

Variables	off-pump CABG (N=181)	on-pump CABG (N=128)	pump-assisted CABG (N=27)	P Value
Median (IQR)	40.5 (31.0–55.0)	43.0 (32.0–54.0)	44.0 (38.0–55.0)	
Low Cardiac Output Syndrome				0.3945*
No	166 (91.7)	113 (88.3)	26 (96.3)	
Yes	15 (8.3)	15 (11.7)	1 (3.7)	
Reoperation Cardio				0.8361**
No	176 (97.2)	126 (98.4)	27 (100)	
Yes	5 (2.8)	2 (1.6)		
Reoperation non cardio				0.0740**
No	177 (97.8)	119 (93.0)	27 (100)	
Yes	4 (2.2)	9 (7.0)		
Kidney Damage				<.0001**
Cr< URL	130 (71.8)	52 (40.6)	17 (63.0)	
Cr> 25% URL	49 (27.1)	70 (54.7)	7 (25.9)	
Hemodialisys	2 (1.1)	6 (4.7)	3 (11.1)	
Atrial fibrillation				0.0784**
No	155 (85.6)	101 (78.9)	19 (70.4)	
Yes	26 (14.4)	27 (21.1)	8 (29.6)	
Multiorgan dysfunction after CABG				0.0017**
No	179 (98.9)	116 (90.6)	25 (92.6)	
Yes	2 (1.1)	12 (9.4)	2 (7.4)	
Infection or leukocytosis or febril >7 days				0.8634**
No	166 (91.7)	117 (91.4)	26 (96.3)	
Yes	15 (8.3)	11 (8.6)	1 (3.7)	
Bleeding after CABG				0.0014**
No	178 (98.3)	114 (89.1)	26 (96.3)	
Yes	3 (1.7)	14 (10.9)	1 (3.7)	
Graft thrombosis within 30d after CABG				0.8295**
No	175 (96.7)	122 (95.3)	26 (96.3)	

Variables	off-pump CABG (N=181)	on-pump CABG (N=128)	pump-assisted CABG (N=27)	P Value
Yes	6 (3.3)	6 (4.7)	1 (3.7)	
Pulmonary dysfunction after CABG				0.0492**
No	171 (94.5)	117 (91.4)	21 (80.8)	
Yes	10 (5.5)	11 (8.6)	5 (19.2)	
Neurological complications within 30d after CABG				0.0322**
No	175 (96.7)	124 (96.9)	23 (85.2)	
Yes	6 (3.3)	3 (2.3)	3 (11.1)	
Death within 30d after CABG				0.2545**
No	177 (97.8)	121 (94.5)	27 (100)	
Yes	4 (2.2)	7 (5.5)		
Intestinal complications within 30d after CABG				0.2773**
No	180 (99.4)	127 (99.2)	26 (96.3)	
Yes	1 (0.6)	1 (0.8)	1 (3.7)	

* Kruskal-Wallis test, ** exact Fisher's test. Nmiss – number of missing values, SD – standard deviation, IQR – interquartile range, CABG – coronary artery bypass grafting

Table 30 Troponin I level after CABG

Variables	off-pump CABG (N=181)	on-pump CABG (N=128)	pump-assisted CABG (N=27)	P Value
TnI before CABG				0.0938
Nmiss (%)	145 (80.1)	99 (77.3)	19 (70.4)	
Mean±SD	0.0±0.1	0.0±0.1	0.0±0.0	
Min–Max	0.0–0.5	0.0–0.2	0.0–0.1	
Median (IQR)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.1)	
TnI 1st day				<.0001
Nmiss (%)	17 (9.4)	10 (7.8)	1 (3.7)	
Mean±SD	2.5±8.9	6.0±10.3	4.7±7.3	
Min–Max	0.0–98.0	0.0–93.0	0.3–31.1	
Median (IQR)	0.4 (0.2–1.0)	3.1 (1.8–6.3)	1.4 (0.7–6.8)	
TnI 2st day				<.0001
Nmiss (%)	104 (57.5)	39 (30.5)	9 (33.3)	
Mean±SD	3.5±8.2	3.9±7.9	4.5±5.9	

Variables	off-pump CABG (N=181)	on-pump CABG (N=128)	pump-assisted CABG (N=27)	P Value
Min–Max	0.0–50.0	0.0–50.0	0.2–18.8	
Median (IQR)	0.4 (0.2–2.1)	1.5 (0.7–3.4)	0.9 (0.4–6.1)	
TnI 3st day				0.1936
Nmiss (%)	149 (82.3)	90 (70.3)	21 (77.8)	
Mean±SD	3.4±7.4	2.5±2.8	4.8±4.5	
Min–Max	0.1–40.7	0.1–14.6	0.5–10.9	
Median (IQR)	1.1 (0.2–3.5)	1.4 (0.6–3.5)	2.6 (1.9–10.0)	
TnI 4st day				0.3843
Nmiss (%)	168 (92.8)	108 (84.4)	22 (81.5)	
Mean±SD	5.4±7.5	2.3±3.0	2.7±3.2	
Min–Max	0.0–27.9	0.1–10.7	0.2–8.3	
Median (IQR)	3.2 (1.3–7.5)	0.9 (0.4–2.6)	1.5 (1.4–2.0)	
TnI 5st day				0.2222
Nmiss (%)	158 (87.3)	106 (82.8)	23 (85.2)	
Mean±SD	1.5±2.1	0.9±1.4	2.4±1.9	
Min–Max	0.0–6.6	0.0–5.9	0.5–4.9	
Median (IQR)	0.3 (0.0–2.5)	0.4 (0.1–0.8)	2.2 (1.2–3.7)	

Table 30 Troponin I level after CABG in patients without low cardiac output syndrome after CABG

Variables	off-pump CABG (N=166)	on-pump CABG (N=113)	pump-assisted CABG (N=26)	P Value
MPO before operation				0.3871
Nmiss (%)	27 (16.3)	18 (15.9)	9 (34.6)	
Mean±SD	36.0±32.6	38.8±29.5	29.0±15.3	
Min–Max	2.8–237.8	4.1–168.9	5.6–65.4	
Median (IQR)	28.1 (16.4–40.6)	30.8 (19.3–47.7)	28.7 (18.7–34.0)	
MPO after operation				0.3871
Nmiss (%)	27 (16.3)	18 (15.9)	9 (34.6)	
Mean±SD	36.0±32.6	38.8±29.5	29.0±15.3	
Min–Max	2.8–237.8	4.1–168.9	5.6–65.4	
Median (IQR)	28.1 (16.4–40.6)	30.8 (19.3–47.7)	28.7 (18.7–34.0)	
TnI before CABG				0.0403

Variables	off-pump CABG (N=181)	on-pump CABG (N=128)	pump-assisted CABG (N=27)	P Value
Nmiss (%)	134 (80.7)	89 (78.8)	18 (69.2)	
Mean±SD	0.0±0.1	0.0±0.1	0.0±0.0	
Min–Max	0.0–0.5	0.0–0.2	0.0–0.1	
Median (IQR)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.1)	
TnI 1st day				<.0001
Nmiss (%)	14 (8.4)	8 (7.1)	1 (3.8)	
Mean±SD	1.1±2.6	4.1±4.0	4.1±7.0	
Min–Max	0.0–18.5	0.0–18.7	0.3–31.1	
Median (IQR)	0.4 (0.2–0.7)	2.5 (1.7–5.0)	1.4 (0.7–2.7)	
TnI 2st day				<.0001
Nmiss (%)	100 (60.2)	37 (32.7)	9 (34.6)	
Mean±SD	1.9±4.7	2.3±3.0	3.9±5.5	
Min–Max	0.0–29.8	0.0–15.0	0.2–18.8	
Median (IQR)	0.3 (0.1–1.0)	1.2 (0.6–2.5)	0.9 (0.4–5.9)	
TnI 3st day				0.0828
Nmiss (%)	140 (84.3)	84 (74.3)	21 (80.8)	
Mean±SD	1.4±2.0	1.8±1.8	3.5±3.7	
Min–Max	0.1–9.2	0.1–6.5	0.5–10.0	
Median (IQR)	0.6 (0.2–2.1)	1.1 (0.5–2.9)	2.3 (1.9–3.0)	
TnI 4st day				0.6389
Nmiss (%)	158 (95.2)	99 (87.6)	21 (80.8)	
Mean±SD	2.6±3.1	2.0±2.7	2.7±3.2	
Min–Max	0.0–9.1	0.1–8.3	0.2–8.3	
Median (IQR)	1.6 (0.3–4.1)	0.8 (0.4–2.6)	1.5 (1.4–2.0)	
TnI 5st day				0.0541
Nmiss (%)	149 (89.8)	96 (85.0)	22 (84.6)	
Mean±SD	0.8±1.6	0.7±1.0	2.4±1.9	
Min–Max	0.0–5.8	0.0–3.8	0.5–4.9	
Median (IQR)	0.1 (0.0–0.9)	0.3 (0.1–0.8)	2.2 (1.2–3.7)	

Table 31: Troponin I level in patients with low cardiac output syndrome after CABG

Variables	off-pump CABG (N=15)	on-pump CABG (N=15)	pump-assisted CABG (N=1)	P Value
MPO before operation				0.7362
Nmiss (%)	7 (46.7)	3 (20.0)		
Mean±SD	32.8±22.1	48.8±38.3	32.7±	
Min–Max	8.2–76.7	4.0–115.2	32.7–32.7	
Median (IQR)	25.8 (17.5–45.3)	37.4 (16.3–76.8)	32.7 (32.7–32.7)	
MPO after operation				0.7362
Nmiss (%)	7 (46.7)	3 (20.0)		
Mean±SD	32.8±22.1	48.8±38.3	32.7±	
Min–Max	8.2–76.7	4.0–115.2	32.7–32.7	
Median (IQR)	25.8 (17.5–45.3)	37.4 (16.3–76.8)	32.7 (32.7–32.7)	
TnI before CABG				0.8065
Nmiss (%)	11 (73.3)	10 (66.7)	1 (100)	
Mean±SD	0.0±0.0	0.0±0.0	±	
Min–Max	0.0–0.1	0.0–0.0	–	
Median (IQR)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	(–)	
TnI 1st day				0.8742
Nmiss (%)	3 (20.0)	2 (13.3)		
Mean±SD	20.0±27.0	21.0±24.8	17.6±	
Min–Max	0.2–98.0	2.6–93.0	17.6–17.6	
Median (IQR)	13.0 (4.8–20.6)	13.8 (9.7–18.0)	17.6 (17.6–17.6)	
TnI 2st day				0.6954
Nmiss (%)	4 (26.7)	2 (13.3)		
Mean±SD	13.1±15.9	13.4±16.9	14.7±	
Min–Max	0.0–50.0	1.2–50.0	14.7–14.7	
Median (IQR)	8.0 (2.6–15.2)	5.1 (4.0–14.1)	14.7 (14.7–14.7)	
TnI 3st day				0.2275
Nmiss (%)	9 (60.0)	6 (40.0)		
Mean±SD	11.7±14.6	4.7±4.2	10.9±	
Min–Max	2.1–40.7	0.6–14.6	10.9–10.9	
Median (IQR)	5.4 (4.0–12.3)	3.8 (2.0–5.1)	10.9 (10.9–10.9)	
TnI 4st day				0.1441

Nmiss (%)	10 (66.7)	9 (60.0)	1 (100)	
Mean±SD	9.9±10.5	3.2±3.8	±	
Min–Max	1.3–27.9	0.4–10.7	–	
Median (IQR)	7.5 (4.3–8.4)	2.4 (0.7–2.6)	(–)	
TnI 5st day				0.0679
Nmiss (%)	9 (60.0)	10 (66.7)	1 (100)	
Mean±SD	3.5±2.3	1.7±2.4	±	
Min–Max	0.8–6.6	0.0–5.9	–	
Median (IQR)	2.9 (2.0–6.2)	0.6 (0.4–1.7)	(–)	

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