Role of Glutamine as Myocardial Protector In Elective On-Pump Coronary Artery Bypass Graft Surgery With Low Ejection Fraction

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STUDY SUMMARY

Title	Myocardial Protecting Role of Glutamine in Patients with Low Ejection Fraction Undergoing Elective On-Pump Coronary Artery Bypass Graft Surgery
Methodology	Randomized, double blinded, controlled study
Study Duration	Estimated duration for the main protocol (e.g. from start of screening to last subject processed and finishing the study) is approximately 1 year
Study Center	National Cardiovascular Center Harapan Kita, West Jakarta, Jakarta, Indonesia
Objectives	Primary Objective: To determine whether intravenous glutamine could mitigate the negative impact of on-pump CABG procedures and provide better clinical outcome in patients undergoing coronary artery bypass graft surgery under cardiopulmonary bypass. Secondary Objective: To determine whether intravenous glutamine could prevent the decline of plasma glutamine level, reduce myocardial damage, improve hemodynamic profile, and reduce morbidity low ejection fraction patients undergoing coronary artery bypass graft surgery under cardiopulmonary bypass.
Number of Subjects	60 randomized patients divided into two groups; Glutamine and Control
Diagnosis and Main Inclusion Criteria	**Inclusion Criteria** – Male and female patients, aged ≥ 18 years old with coronary heart disease indicated for elective coronary artery bypass grafting under cardiopulmonary bypass – Left ventricle ejection fraction of 31-50%, confirmed by echocardiography or radionuclide imaging – No history of heart surgery – Agree to participate in the study and signed a written informed consent

	Exclusion Criteria – Change of surgical plan from elective into emergency CABG surgery – Additional procedures other than coronary artery bypass graft procedure – Onset of myocardial infarction within the last three months – Blood creatinine level > 2 mg/dL – ALT/AST level > 1.5x of normal value – Use of preoperative intra-aortic balloon pump – History of stroke with onset of less than 3 months – Preoperative atrial fibrillation – Heart conduction problem or pacemaker use – Contraindications to pulmonary artery catheter insertion **Drop out criteria** – Stroke after surgery – Perioperative myocardial infarction based on type 5 myocardial infarct criteria – Haemorrhage complications requiring repeat surgery – Use of continuous veno-venous hemofiltration or haemodialysis after coronary artery bypass graft surgery – Delayed sternal closure – Aortic cross-clamp duration of > 120 minutes and/or cardiopulmonary bypass duration of >180 minutes
Study Product, Dose, Route, Regimen	– Glutamine Group: will receive intravenous infusion of 0.5 mg/kgbw L-alanyl-L-glutamine dipeptide (Dipeptiven, Fresenius Kabi, Bad Homburg, Germany) diluted in normal saline up to 500 mL, started after induction of anesthesia for 24 hours.

	– Control Group: will receive intravenous infusion of 500 mL normal saline, started after induction of anesthesia for 24 hours
Statistical Methodology	Primary Endpoint Plasma glutamine before induction to anesthesia and 24 hours after CPB, and plasma troponin I before induction to anesthesia, 5 minutes, 6 hours, 24 hours and 48 hours after CPB. Secondary Endpoint Alpha-Ketoglutarate, myocardial injury score, apoptosis index, anti-cardiac troponin I expression, ejection fraction, cardiac index, plasma lactate, intensive care unit ventilation time, intensive care unit length of stay and vasoactive inotropic score.

Purpose:

The primary objective is to determine whether intravenous glutamine could prevent the decline of plasma glutamine level, reduce myocardial damage, improve hemodynamic profile, and reduce morbidity low ejection fraction patients undergoing coronary artery bypass graft surgery under cardiopulmonary bypass.

Background:

Coronary artery disease has the highest mortality rate worldwide and coronary artery bypass grafting (CABG) is the most common cardiac surgery performed in patients with coronary artery disease to revascularize the heart. Despite improvement in operation techniques, cardioplegia, cardiopulmonary bypass, myocardial injury related to on-pump CABG is still prominent. In patient with low ejection fraction (EF) undergoing on-pump CABG, myocardial injury is related to worse outcome and prognosis during peri-operative and postoperative period. On-pump CABG patients with low ejection fraction has increased (up to four times higher) postoperative in hospital mortality rate compared to patient with normal ejection fraction. Administration

of intravenous glutamine had been documented in reducing myocardial damage during cardiac surgery and previous studies indicated that glutamine can protect against myocardial injury by various mechanism during ischemia and reperfusion.

Goals of the study:

To analyze the effect of intravenous glutamine in low EF patients undergoing on-pump CABG surgery in:

1. Reducing myocardial damage by a decrease of myocardial injury score, apoptotic index and increase of anti-cardiac troponin I expression through right atrial appendage tissue sample, as well as decrease of troponin I level.
2. Improving myocardial metabolism by a decrease in plasma lactate levels, increase of plasma glutamine levels and alpha ketoglutarate (α-KG) levels in the right atrial appendage tissue sample.
3. Improving hemodynamic profile through an increase in EF and cardiac index after CPB
4. Reducing postoperative morbidity by the decrease of ventilator duration, duration of intensive care, and use of postoperative vasoactive and inotropes

Duration of the Study:

The study is estimated to complete within 2 years from study initiation.

Potential Benefits and Risks:

Every effort is taken during the study period to maximize patient safety. To fulfil this goal, the study staff employs stringent procedures to reduce the risk of adverse events during the study period. The result of this study can be applied in clinical practice to ascertain the benefits of glutamine as a myocardial protector to reduce perioperative risks and treatment costs of elective on-pump CABG for patients with low EF.

Methods:

Study Design

This is a double-blind, randomized controlled trial involving sixty (60) subjects undergoing elective on-pump coronary artery bypass graft will be randomized into two groups.

Study Population and Selection Criteria

All participants will be required to sign a written informed consent, be willing and able to comply with all study requirements and should meet the following criteria:

- Male and female patients, aged ≥ 18 years old with coronary heart disease indicated for elective coronary artery bypass grafting under cardiopulmonary bypass
- Left ventricle ejection fraction of 31-50%, confirmed by echocardiography or radionuclide imaging
- No history of heart surgery
- Agree to participate in the study and signed a written informed consent

Subjects will be **excluded** from the study based on the following criteria:

- Change of surgical plan from elective into emergency CABG surgery
- Additional procedures other than coronary artery bypass graft procedure
- Onset of myocardial infarction within the last three months
- Blood creatinine level > 2 mg/dL
- ALT/AST level > 1.5x of normal value
- Use of preoperative intra-aortic balloon pump
- History of stroke with onset of less than 3 months
- Preoperative atrial fibrillation
- Heart conduction problem or pacemaker use
- Contraindications to pulmonary artery catheter insertion

Recruitment Methods

All patients aged above 18 years old with coronary artery disease indicated for elective CABG surgery at the National Cardiovascular Center Harapan Kita are offered to be

a participant in this study. The primary investigator, dr. I Made Adi Parmana Sp.An, KAKV and his partners (co-investigators) will be performing the procedures accordingly for both control and treatment groups.

Data Collection

Data on sex, age, weight, height and preoperative EF are collected through direct history-taking and preoperative medical records. Data on CPB time, aortic cross-clamping time, number of distal coronary artery grafts are collected from surgery reports. Arterial blood sampling for troponin I levels measurement are collected: (1) before induction, (2) at 5 minutes, (3) at 6 hours, (4) at 24 hours, and (5) at 48 hours after CPB. Plasma troponin I is measured using the troponin I (human) ELISA kit (Abnova, KA0233) with colorimetry method. Arterial blood samples for plasma glutamine levels measurement are collected before induction and 24 hours after the CPB. Plasma glutamine levels is measured using the Sigma–Aldrich GLN1 glutamine/glutamate determination kit (Sigma–Aldrich, GLN1-1KT) using colorimetry method. To obtain plasma samples, blood is centrifuged for 15 minutes at a speed of 3500 X G within a maximum period of 30 minutes after collection and is stored at -80^{o}C.

A 5×5 mm sample of the right atrial appendage tissue are collected at 5 minutes after CPB and are immediately transported to the laboratory at 4^{o}C within 30 minutes of collection. The tissue sample is divided for α-ketoglutarate (α-KG) measurement and paraffin block preparation for histopathological examinations. A total of 20 mg of tissue is homogenized and centrifuged to obtain the supernatant. A protease inhibitor is added to the supernatant and then stored at -80^{o}C until cellular α-KG levels are examined. The examination of α-KG is performed using α-KG assay kit (Abcam, ab83431) with colorimetry method.

Myocardial injury score is measured on preparations stained with hematoxylin and eosin (H&E) with a scoring system from 0 to 3 as follows: 0 = no change; 1 = slight changes: focal myocyte damage or small multifocal degeneration with slight degree of inflammation; 2 = moderate changes: extensive myofibrillar degeneration and/or diffuse inflammatory process; 3 = severe changes: necrosis with diffuse inflammatory process.[12] Terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate nick end-labelling (TUNEL) staining is performed using the TUNEL assay kit (Abcam, ab206386). Cell nuclei with positive TUNEL staining is colored brown. The apoptotic

index is calculated based on the average number of cells with positive TUNEL staining.[12] Expression of anti-cardiac troponin I is observed using anti-cardiac troponin I antibody (Abcam, ab47003). Measurement of anti-cardiac troponin I expression is performed on preparations stained with anti-cardiac troponin I antibody using a scoring system ranging from 0 to -3, as follows: 0 = no loss of staining; -1 = minimal decrease in staining, compared to normally stained tissue; -2 = clear decrease in staining with some positivity (brown color) remaining; -3 = no positive (brown color) staining.[13] For quantitative analysis, histopathological examinations are made on as many as six fields of view per specimen under a light microscope (Olympus BX50, Tokyo, Japan) and photographed for further analysis. The histopathological specimens are assessed separately by two blinded examiners to get an average score.

Arterial blood samples for plasma lactate levels measurement are collected: (1) before induction, (2) at 5 minutes, (3) at 6 hours, (4) at 24 hours, and (5) at 48 hours after CPB. Lactate examination is performed using the Nova Biomedical Stat Profile® pHOX Ultra analyzer (Nova Biomedical, Waltham, MA, USA) with basic enzymatic method.

Ejection fraction measurements are taken: (1) after induction and (2) at 5 minutes after CPB, through TEE examination using the modified Simpson method. Cardiac index (CI) measurements are taken: (1) after induction, (2) at 5 minutes, (3) at 2 hours, (4) at 6 hours, and (5) at 24 hours after CPB. The values are obtained from calculating cardiac output (CO) per body surface area (in m^2). Cardiac output is measured via a pulmonary artery catheter using thermodilution method. The measurements are performed three times, averaged, and considered valid if the variation between the three values is less than 10%. Body surface area is calculated using the Mosteller formula. Morbidity variables consist of ventilator time, postoperative use of vasoactive and inotropic agents, and duration of intensive care are collected from the medical record. Vasoactive and inotropic score (VIS) is calculated (VIS = dopamine dose [μg kg^{-1} min^{-1}] + dobutamine [μg kg^{-1} min^{-1}] + 100 × epinephrine dose [μg kg^{-1} min^{-1}] + 10,000 × vasopressin [units kg^{-1} min^{-1}] + 100 × norepinephrine dose [μg kg^{-1} min^{-1}]) using the maximum dosing rates of vasoactive and inotropic medications (μg kg^{-1} min^{-1} or IU kg^{-1} min^{-1}) during the first 24 hours after postoperative ICU admission.

Expected Outcomes

It is the investigator's expectation that administration of intravenous glutamine will be beneficial as a myocardial protector in low EF patients undergoing on-pump CABG surgery.

Adverse Reactions

There is no expectation of any adverse outcomes or reactions, should there be any adverse outcome or reactions, necessary management and will be taken in accordance with the standard medical protocol at the National Cardiovascular Center Harapan Kita Hospital. All participants will be given access to contact information of the primary investigator performing this study. Any adverse reactions will be reported immediately to the primary investigator or co-investigators.

Reasons for Withdrawal or Termination:

A subject may be discontinued from the study at any time if the subject or the investigator feels that it is not in the subject's best interest to continue. The following is a list of possible reasons the subjects will be **dropped out** from the study:

- Stroke after surgery
- Perioperative myocardial infarction based on type 5 myocardial infarct criteria
- Haemorrhage complications requiring repeat surgery
- Use of continuous veno-venous hemofiltration or haemodialysis after coronary artery bypass graft surgery
- Delayed sternal closure
- Aortic cross-clamp duration of > 120 minutes and/or cardiopulmonary bypass duration of >180 minutes

All subjects are free to withdraw from participation at any time, for any reason, specified or unspecified, and without prejudice. Reasonable attempts will be made by the investigator to provide a reason for subject withdrawals. The reason for the subject's withdrawal from the study will be specified in the subject's source documents and the Case Report Form (CRF). If a subject is withdrawn from treatment due to and adverse event, the subject will be followed and treated by the investigator until the adverse event has resolved or stabilized.

Handling of Participant Withdrawals or Termination:

Although subjects may withdraw from the study at any time and for any reason, (or may be withdrawn at the investigator's discretion), subject withdrawal should be avoided as much as reasonably possible. In any case, appropriate follow-up for withdrawals or termination. Subjects who are discontinued are not to be replaced. For subjects considered discontinued, the CRF must be completed up to the last visit performed.

Methods of Intervention:

Subjects eligible for the study will review and undergo informed consent. Once consented, subjects will be randomly assigned to undergo:

- Glutamine Group, blind: will receive intravenous infusion of 0.5 mg/kgbw L-alanyl-L-glutamine dipeptide (Dipeptiven, Fresenius Kabi, Bad Homburg, Germany) diluted in normal saline up to 500 mL, started after induction of anesthesia for 24 hours
- Control Group, blind: will receive intravenous infusion of 500 mL normal saline, started after induction of anesthesia for 24 hours

STATISTICAL ANALYSIS PLAN

RANDOMIZATION

Subjects who meet all inclusion and exclusion criteria will be randomized into two groups, glutamine and control group. Subject allocation will be carried out through block randomization and known only by the pharmacist, and the confidentiality are maintained so that subjects, doctors/nurses, researchers, and data analysers does not know the allocation of each subject.

SAMPLE SIZE JUSTIFICATION

Sample size calculations

The sample size of this study is obtained from the two-way hypothesis testing formula for the two mean values in two independent groups with a confidence index (α) of 95% and power of 80%. Results are considered statistically significant if p < 0.05. The details of the estimated size of the research subject are as follows:

$$\mathrm{n1} = \mathrm{n2} = 2\left[\frac{(Z_\alpha + Z_\beta)s}{(X_1 - X_2)}\right]^2 = 2\left[\frac{(1{,}96 + 0{,}84)\ 0{,}04}{(0{,}032)}\right]^2$$

n1 = n2 = **24,5 subjects → 25 subjects per group**

Legend:

n1 : Number of subjects in the intervention group (glutamine group)

n2 : Number of subjects in the control group

s : Standard deviation = 0.0415

Z_α : Z value in 95% confidence index = 1.96

Z_β : Z value of test power = 0.84

$X_1 - X_2$: Difference in mean value = 0.032

Assuming a 20% drop out event, the final sample size are:

n = 50 + (50 * 20%)

n = 50 + 10

n = **60 subjects**

For a fixed sample size design, the sample size required to achieve a power of 1-β=0.84 for a two sided t-test at level α=0.05 under these assumptions amounts to a total of 60 patients, or 30 patients in each treatment group.

Primary Endpoint

Plasma glutamine before induction to anesthesia and 24 hours after CPB, and plasma troponin I before induction to anesthesia, 5 minutes, 6 hours, 24 hours and 48 hours after CPB.

Secondary Endpoint

Alpha-Ketoglutarate, myocardial injury score, apoptosis index, anti-cardiac troponin I expression, ejection fraction, cardiac index, plasma lactate, intensive care unit ventilation time, intensive care unit length of stay and vasoactive inotropic score.

ASSESSMENT OF SAFETY

Adverse events will be monitored and collected by the study team from the point of signed consent until the adverse event(s) are resolved and subjects are stabilized. For each adverse event, a detailed explanation will be obtained from the subject and subject's medical record. All adverse events will be recorded on the CRFs.

DATA MONITORING

The principal investigator will be responsible to ensure the study is conducted in accordance with the protocol, Declaration of Helsinki, and that the data recorded is valid. To achieve this objective the study will be continuously monitored and reviewed by the study team.

Clinical site monitoring is conducted to ensure that the rights and well-being of human subjects are protected, that the reported trial data are accurate, complete, and verifiable, and that the conduct of the trial is in compliance with the currently approved protocol/amendment(s) with the Good Clinical Practice (GCP).

DATA HANDLING AND RECORD KEEPING

The collection of personal patient information will be limited to the amount necessary to achieve the aims of the research, so that no unneeded sensitive information is being collected. Only study personnel will collect data. Collected data will be de-identified and to be used for statistical analysis.

INSTITUTIONAL REVIEW BOARD

The protocol, informed consent form(s), and all participant materials will be submitted to the Ethics Committee for review and approval. Approval of both the protocol and consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval before the changes are implemented to the study.

CONSENT PROCESS

Subjects will be approached when they come through the hospital for treatment and considered for elective CABG surgery. Each potential subject must provide written informed consent with full knowledge of the procedures involved. The informed consent must be fully explained by the investigator or member of the study staff including the study aims, methods, benefits and risks, and signed by the subject before enrollment into the study. Potential subjects will be informed that study participation is voluntary and that they may withdraw at any time. The subjects will be told that choosing against participation will not affect the care received for treatment. The subjects will be informed that they will be authorizing access of investigational staff to confidential medical records. The subjects will be given sufficient time to read the consent and ask any questions. Once the informed consent is signed, the subject will be given a copy of the document.

STUDY PERSONNEL AND ROLES

I Made Adi Parmana, MD	Primary investigator	Responsible for all study related issues

CONFLICT OF INTEREST

No conflicts of interest have been reported

APPENDIX I: INFORMED CONSENT FORM

Myocardial Protecting Role of Glutamine in Patients with Low Ejection Fraction Undergoing Elective On-Pump Coronary Artery Bypass Graft Surgery Research Explanation

I, the research team led by dr. I Made Adi Parmana from Cardiovascular Anesthesia Department of National Cardiovascular Center Harapan Kita will conduct a study to examine the role of glutamine as a myocardial protector in low ejection patients undergoing elective on-pump coronary artery bypass graft surgery. The coronary artery bypass graft surgery is one of the most common procedures performed at the National Cardiovascular Center Harapan Kita for cardiac revascularization and is often performed with a cardiopulmonary bypass machine to take over the functions of the heart and lungs during surgery. Coronary artery bypass graft surgery done with the cardiopulmonary bypass machine requires cardiac protection to reduce the negative impact of the procedure. Cardiac protection serves a major role in patients with low cardiac function (low cardiac ejection fraction).

This research aims to assess the role of glutamine in myocardial protection during coronary artery bypass graft surgery with a cardiopulmonary bypass machine in patients with low ejection fraction. Myocardial protection arising from glutamine administration is expected to improve cardiac function after surgery thereby reducing the burden for patients after surgery. A total of 60 patients with low ejection fraction indicated for coronary artery bypass graft surgery using a cardiopulmonary bypass machine will participate in this research with a participation period during the patients' stay in the National Cardiovascular Center Harapan Kita.

You are one of the patients fitting these indications so we are inviting you to be a participant in this research. You are free to participate in this research without coercion after getting a full explanation of this research. Should you be willing to participate, you are also entitled to resign at any time without any consequences or any decrease in quality of service from the doctors. If you refuse to participate in the research, you will still receive services from doctors of the highest quality and standard in National Cardiovascular Center Harapan Kita Hospital.

If you choose to agree to participate in this research, you will be asked to **sign this informed consent form in duplicate, one for your keeping and one for the research team.** The next procedures are:

- You will be interviewed by the doctor to ask about your: name, age, medical history, history of drug use, history of allergies, smoking habits, alcohol consumption habits.
- Undergo a physical examination by the doctor to check your health status.
- Undergo pre-operative procedures and preparation according to National Cardiovascular Center Harapan Kita Hospital protocol until the D-day of surgery.
- Glutamine administration in liquid given via venous access route that will be done before surgery. Because there will be a group that will not be given medication or treatment in this research, it is possible that the liquid given to you will not contain glutamine.
- Undergo coronary artery bypass graft surgery with a cardiopulmonary bypass machine in accordance with the standards and protocol of the National Cardiovascular Center Harapan Kita Hospital.
- Blood sampling will be carried out five times during the research period by way of a vascular access routinely used in standard cardiac surgery services at National Cardiovascular Center Harapan Kita Hospital. First blood sampling will be taken shortly before surgery of approximately two tablespoons. Subsequent blood sampling of approximately two tablespoons each time will be taken at: 5 minutes after cardiopulmonary bypass, 6 hours after cardiopulmonary bypass, 24 hours after cardiopulmonary bypass and 48 hours after cardiopulmonary bypass. Blood collection will be carried out by experienced doctors/nurses who are accustomed to taking blood.
- Heart function measurement during the research will be carried out in accordance with standard cardiac surgery services at the National Cardiovascular Center Harapan Kita Hospital. Cardiac ejection fraction will be assessed twice using standard equipment at the National Cardiovascular Center Harapan Kita Hospital: shortly before surgery and 5 minutes after cardiopulmonary bypass. Heart pump function will be measured five times during the research: shortly before surgery, 5 minutes after cardiopulmonary bypass, 2 hours after cardiopulmonary bypass, 6 hours after cardiopulmonary bypass and 24 hours after cardiopulmonary bypass.

- Heart tissue sampling will be taken during surgery, using right atrial tissue and will be done by experienced cardiac surgeons who are accustomed with the procedure.

As a research sample, you are obliged to follow the procedures and pre-surgical preparations according to the National Cardiovascular Center Harapan Kita Hospital protocol. Glutamine administration so far has been widely used and does not provide significant side effects, but in some cases drug allergies could occur. Administration of glutamine at the dose used in this research never caused significant side effects in previous studies. Blood collection from blood vessel is not dangerous and is a routine procedure. Circulatory function monitoring device setup are generally harmless and beneficial as an effort to monitor patients with decreased cardiac function. Heart tissue sampling is not dangerous and so far has not caused any side effects or decreased cardiac function after surgery. During the research, the research will also prepare the necessary protection and guidance in case something untoward happens, in accordance with the medical protocol at the National Cardiovascular Center Harapan Kita Hospital.

All research information/data will be kept confidential (known only to researchers and research staff). The information will be treated with care in order to maintain the confidentiality of your identity so that people outside the research will not know the data of your identity. The research outcome will be deidentified and published. Participation in this research will be free of charge and independently funded by the research team.

You are given the opportunity to ask everything you want to know and you feel are not clear regarding this research. If at any given time side effects are to occur or if you need further explanation, feel free to contact dr. I Made Adi Parmana Sp.An, KAKV at the Cardiovascular Anesthesia Department of National Cardiovascular Center Harapan Kita Hospital, or via phone at 08124601212.

You can also inquire about our research to the National Cardiovascular Center Harapan Kita Hospital Ethics Committee, via tel. 568111 ext. 2837/2831 or via email: irb.kometik_rsjpdhk@gmail.com.

INFORMED CONSENT

Participant number : _____ _____ _____(to be filled by researcher)

I hereby signed below:

Name ……
Place/Date of Birth : ……
Address : ……
……
……
……
Relation to participant : ……
(leave empty if respondent is participant)

Claim that:

1. I have received an explanation regarding every aspect of the research: "**Myocardial Protecting Role of Glutamine in Patients with Low Ejection Fraction Undergoing Elective On-Pump Coronary Artery Bypass Graft Surgery**". If during the research period adverse events are to occur, follow-up will be carried out in accordance with the standing medical protocol at National Cardiovascular Center Harapan Kita.
2. After understanding the research, I voluntarily agree without coercion to participate in the research with:
    a. All data obtained during research to be kept confidential and used only for scientific purposes.
    b. No fees charged for examinations and management in this study
3. I allow myself or my family member to be a participant of the research until the end of time limit set by the researcher.

Jakarta, ……

Witness | Respondent

(……) (……)

APPENDIX II: CASE REPORT FORM (CRF)

CASE REPORT FORM (CRF)
MYOCARDIAL PROTECTING ROLE OF GLUTAMINE IN PATIENTS WITH LOW EJECTION FRACTION UNDERGOING ELECTIVE ON-PUMP CORONARY ARTERY BYPASS GRAFT SURGERY

Respondent code : …… …… ……
Name : .....
Medical record no.: .....
Attending doctor : .....
Date of birth / age : ……/……/…… …… years old
Sex : Male/ female (cross as not applicable)
Weight : … … … kg
Height : … … … cm
Address : .....
.....

Telephone number : ....
Alternative number : ....
Diagnosis : .....
.....

Note:

Pre-Operative Laboratory Parameters

Parameters	Value
Hb	
Hct	
Leukocyte	
Trombocyte	
SGOT	
SGPT	
Ur	
Cr	
Albumin	
pH	
pCO2	
pO2	
FiO2	
Na+	
K+	
HCO3-	
SatO2	
Lactate	
CRP	
HIV	
Hepatitis B	
Hepatitis C	

ECG:
CXR:

Surgical Procedure, Aortic Cross-Clamp and CPB

Parameters	Date	Time
No. of distal coronary artery graft	……..	
Induction start	……/……/…….	…. : ….
Intervention administration Bottle no. : _____	……/……/…….	…. : ….
Incision	……/……/…….	…. : ….
Start of CPB	……/……/…….	…. : ….
Aortic cross-clamp start	……/……/…….	…. : ….
Aortic cross-clamp end	……/……/…….	…. : ….
End of CPB	……/……/…….	…. : ….
Skin closure suture	……/……/…….	…. : ….
Operating room departure	……/……/…….	…. : ….
ICU admission	……/……/…….	…. : ….
Extubation	……/……/…….	…. : ….
ICU discharge	……/……/…….	…. : ….

Cardiac Index and Ejection Fraction Measurement

Parameters	**Pre-operation**	Time after CPB				
		5 minutes	**30 minutes**	**2 hours**	**6 hours**	**24 hours**
Cardiac Index	1: 2: 3:	1: 2: 3:	1: 2: 3:	1: 2: 3:	1: 2: 3:	1: 2: 3:
Ejection Fraction (EF)						
Echocardiography Operator	EF 1: dr._____ _ EF 2: dr._____ _					

Right Atrial Appendage Tissue Examination

Parameters	**Results**
α-KG level	1: 2:
Myocardial injury score	1: 2:
Apoptotic index	1: 2:
Anti-cardiac troponin I expression	1: 2:

Post-Operative Vasoactive and Inotropes

Parameters	1	4	6	8	12	18	24	36	48
Dobutamine (mcg/kg/minute)									
Epinephrine (mcg/kg/minute)									
Milrinon (mcg/kg/minute)									
Vasopressin (unit/kg/minute)									
Norepinephrine (mcg/kg/minute)									
VIS*									

*VIS = dopamine dose (in mcg/kg/minute) + dobutamine dose (in mcg/kg/minute) + 100 x epinephrine dose (in mcg/kg/minute) + 10 x milrinone doses (in mcg/kg/minute) + 10.000 x vasopressin dose (in unit/kg/minute) + 100 x norepinephrine dose (in mcg/kg/minute)

Surgery Duration, Aortic Cross-Clamp Duration, ICU Care Duration and Ventilator Usage Duration

Parameters	Results
Surgery duration (Incision – skin closure suture)	…… minutes
Aortic cross-clamp duration (Aortic cross clamp start – Aortic cross clamp end)	…… minutes
CPB duration (Start of CPB – End of CPB)	…… minutes
ICU care duration (ICU admission – ICU discharge)	…… hours
Ventilator usage duration (ICU admission – Extubation)	…… minutes

Research Sample Outcomes

Criteria	Yes	No
Post CABG surgery stroke		
Perioperative MI (based on type 5 MI criteria)		
Hemorrhage complication requiring repeat surgery		
Require CVVH / HD after surgery		
Delayed sternal closure		
AoX >120 minutes / CPB time >180 minutes		
Mortality • Time: _____ • Cause: _____		
Sepsis		
Post-operative arrhythmia		
• Onset • Arrhythmia type • Duration		
Acute renal failure		
Intubation		
• Onset • Duration • Reason		
Post-operative IABP usage		
• Onset • Duration		

Note:

Research CRF Checklist

Sample characteristics	
Preoperative laboratory parameters	
Surgical procedure, aortic cross-clamp and CPB	
Intervention liquid bottle number: _____	
Right atrial appendage tissue biopsy	
• a-KG level	
• Myocardial injury score	
• Apoptotic index	
• Anti-cardiac troponin I expression	
Plasma glutamine levels	
Troponin I levels	
Lactate levels	
Ejection Fraction	
Cardiac Index	
Post-operative vasoactive and inotropes	
Surgery duration, aortic cross-clamp duration, ICU care duration and ventilator usage duration	
Research sample outcomes	

Researcher: _____ Date: _____ Signature: _____