Intensive Care Unit Length of Stay and Mortality Comparison between On-pump and Off-pump Coronary Artery Bypass Graft

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Research Article

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Abstract

Background

Coronary artery bypass graft (CABG) techniques, both on-pump (ONCABG) and off-pump (OPCABG), were compared recently in order to seek the most effective technique to reduce the cost of prolonged intensive care unit length of stay (ICU LOS) and mortality. This study aim to compare ICU LOS and mortality in ONCABG and OPCABG

Methods

Secondary data was used in this study. Statistical analyses were performed in SAS 9.4 (SAS Institute Inc, Cary, NC). The analyses included descriptive statistics for all variables, generalized linear models for ICU LOS, and logistic regression for mortality. All models were fitted in bivariate and multivariate forms to consider multiple factors (i.e., age, sex, race, EF, comorbidities such as hypertension, diabetes, and obesity). Statistical significance was determined at the level of alpha = 0.05.

Results

Demographic data of 1569 patients shows variance of characteristics. The analysis shows significant and longer ICU LOS in OPCABG (Mean = 0.558; SE = 0.026 vs Mean = 0.408; SE = 0.633; $p < 0.001$). Similar results were demonstrated after adjustment of covariates effects (OPCABG Mean = 0.816; SE = 0.073 vs ONCABG Mean = 0.661; SE = 0.091). Logistic regression shows that there was no significant difference of mortality in OPCABG and ONCABG, both in the unadjusted (OR = 1.165, 95%, CI = 0.485-2.8) and the adjusted model (OR = 1.165, 95% CI = 0.482–2.817).

Conclusion

ICU LOS was significantly longer in OPCABG patients than in ONCABG patients. There was no significant difference in mortality between the two groups.

Background

Cardiovascular disease (CVD) frequency increases as the number of the old age population rise year by year. [1] The global burden of CVD was estimated to be 29.6% of all death worldwide in 2010. [2] It becomes the leading cause of death in developing and developed regions, more than all communicable diseases, maternal, neonatal, and nutritional disorders combined, and twice the number of deaths caused by cancers. [2] The most common CVD developing in the population is Coronary Artery Disease (CAD), followed by acute myocardial infarct (AMI), heart failure, and cardiac arrhythmias. [3] Most CVD variants can be managed with medical therapy, except for CAD, which depends on medical and surgical approaches like percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG).

Coronary artery bypass graft surgery became the most popular surgical technique to manage CAD. It was first introduced in the early 20th century when a scientist named Alexis Carrel applied this technique to an animal model. [4] This method emerged as a new technique to prolong survival and improve the quality of life for those suffering from CAD. Despite the success of the animal model, CABG needs to apply to the human subject. In the early 60s, a cardiothoracic surgeon named Konstantinov had successfully brought this method into a human trial. Since then, CABG has become the most popular method used by cardiothoracic surgeons to manage CAD surgically. [4] In the late 60s, a more extensive scientific trial was carried out by Favaloro on approximately 15 human subjects. [4] Those researches marked the start of CABG as a new therapeutic modality for CAD today. CABG has appeared to be a better method to manage advanced CAD surgically, especially in high-risk patients. Compared to medication approaches like the administration of beta-blockers and nitrates, CABG appears to provide a better survival rate in high-risk patients. [4] It also gives a lower mortality percentage, up to 10.2%, compared to 15.8% ($p < 0.001$) in medical therapy after five years of treatment. [4] These facts support CABG as the first surgical method used in advanced CAD management.

Treatment options for CAD have progressed rapidly due to market demands. Many techniques from medical and also surgical approaches have been developed to fulfil the needs. From an economic point of view, The Health Care Financing Administration reported almost $11 billion in expenses for Medical care expenditure in 2000 for CAD. [5] This promotes health care providers and insurers to look for the most cost-effective way of managing this problem. Therefore, many new treatment options have been compared over the past decades to seek the most effective treatment to reduce cost and hospital length of stay for patients. [5]

CABG techniques applications available today, namely on-pump and off-pump CABG, are still controversial despite the advantages and disadvantages of these two techniques. Both treatment options have been compared over the past decades to seek the most effective treatment to reduce cost from the possibility of prolonged intensive care unit stay and decrease perioperative mortality.

Methods

This is a descriptive study. Secondary data were collected from medical records of post-CABG patients in National Cardiovascular Center Harapan Kita from June 2010 until January 2014. Statistical analyses were performed in SAS 9.4 (SAS Institute Inc, Cary, NC). Descriptive statistics were reported for all variables of interest. Mean and standard deviation were reported for continuous outcomes, and frequency and percentages were reported for categorical outcomes. Logistic regression models were used to model the probability of death (from patient status) to assess the difference in mortality between ONCABG and OPCABG patients. The odds ratios were computed using the ONCABG group as the reference. Generalized linear models were fitted assuming gamma-distributed errors and a natural log link function to compare intensive care unit length of stay (ICU LOS) between the two groups. The distribution was chosen due to the skewness of the data. All models were fitted in bivariate and multivariate forms to account for the multiple factors that might affect the dependent variables. The factors considered in the adjusted models were age, sex, race, ejection fraction status, and comorbidities such as high blood pressure, diabetes, and obesity. Statistical significance was determined at the level of alpha = 0.05.

Results

Sample demographic data

The total study sample was 1569. It showed a range from 27 to 89 years old with a mean age of 58 ± 8.302 years old. The bodyweight profile ranged from 30 kg to 130 kg, with a mean bodyweight of 67.41 ± 11.252 kg. The body height profile ranged from 136 cm to 188 cm, with a mean body height of 163.41 ± 6.681 cm. Body mass index (BMI) profile ranged from 13.36 kg/m^2 to 42.94 kg/m^2, with BMI mean of 25.19 ± 3.629 kg/m^2. Length of stay profile ranged from 1 day to 27 days, with a mean length of stay of 2 ± 2.184 days.

The majority of samples were males with 1361 (87.13%), and the rest were females with 201 (12.87%). Sample age was then classified into early adult (20-39 years old), middle adult (40-59 years old), late adult (60-65 years old), and old age (>65 years old). The majority of the sample classified as middle adults was 871 (55.98%), followed by late adults by 355 (22.81%), old age 313, and the last early adult by only 17 (1.09%). Total ONCABG procedures were 1232 (83.41%), and OPCABG was 245 (16.59%). Hypertensive patients were 567 (36.75%), and obesity among the study sample was 152 (10.04%). Approximately 150 patients (13.66%) had diabetes. Intensive care unit length of stay (ICU LOS) was classified into short (≤ 2 days) and prolonged (> 2 days). Short ICU LOS was observed in 775 cases (87.07%), and only 115 cases (12.93%) had prolonged ICU LOS. Mortality among CABG patients was 44 (2.8%) from the 1569 data collected. These results are included in Table 1.

Analysis of CABG technique, ICU Length of Stay, and Mortality

The analysis of CABG technique and ICU LOS shows a significant longer ICU LOS in OPCABG patients (Mean = 0.558, SE = 0.026) compared to ONCABG patients (Mean = 0.408, SE = 0.633) with a *p*-value < 0.001. Similar results were found when the models were adjusted for the effects of covariates, with an adjusted mean of ICU LOS of 0.816 (SE = 0.073) for OPCABG patients and 0.661 (SE = 0.091) for ONCABG patients. The information is included in Table 2. The analysis of the CABG technique and mortality by using logistic regression models shows that there was no significant difference in mortality between OPCABG and ONCABG patients both in the unadjusted model (OR = 1.165, 95%, CI = 0.485-2.8) and the adjusted model (OR = 1.165, 95% CI = 0.482-2.817). Results of the CABG technique analysis and mortality were included in Table 3.

Discussion

Intensive care unit length of stay in OPCABG and ONCABG

Our study found that ICU LOS was significantly longer in OPCABG patients than in ONCABG patients. The result shows a gap between recent theories and practices in the authors' study centre. Some information regarding the issue was collected to explain the phenomenon. The authors found some problems arise following the CABG procedure, regardless of the technique; the problems are transient left ventricular dysfunction, capillary leak, warming from hypothermia, and emergence from anaesthesia. These problems contribute to the course of treatment in the intensive cardiac care unit. [6]

Although improvements in surgical procedures, cardioplegia delivery, and other myocardial protective characteristics over the last decade, the observed prevalence of transient left ventricular systolic failure (90%) did not vary between the late 1970s and the early 1990s. Transient myocardial depression has been linked by some authors to a lack of myocardial protection or the effects of cold cardioplegia. However, the majority of data points to cardiopulmonary bypass's (CPB) inflammatory condition as the primary causal component. OPCABG is expected to prevent myocardial harm by lowering the inflammatory response, whether the lowered ventricular function is caused by oxygen free radicals or myocardial ischemia associated with cardioplegia. OPCABG significantly reduces the inflammatory response. However, it is essential to note that OPCABG does not entirely reduce the inflammatory response, as other factors such as surgical trauma and anaesthetic drugs have a role. [6]While systemic vascular resistance does not arise immediately after surgery, it does rise as ventricular function deteriorates. This increase in systemic vascular resistance is most likely a result of decreased ventricular function and the need to maintain systemic blood pressure rather than being a primary cause of decreased cardiac contractility. It is essential to notice the confusing effect of vasopressor medicines to raise systemic blood pressure. [6]Endothelial cells are also damaged by the inflammation-induced generation of oxygen free radicals and the release of proteolytic enzymes by neutrophils. [6] The endothelium's "gatekeeper" function is disrupted, and capillary permeability rises, resulting in oedema. Depending on the degree of CPB duration, the capillary leak syndrome might continue anywhere from a few hours to 1 to 2 days. Intravascular volume overload is a risk when the capillary leak stops and the interstitial oedema fluid is mobilized. [6]. Hypothermia raises systemic vascular resistance, causes shaking (which increases O consumption and CO generation), and affects coagulation. [6] Severe postoperative bleeding (more than 10 U of blood transfused) is common after heart surgery, with an incidence of 3-5%. [6]

Advantages of OPCABG over ONCABG demonstrate that transient left ventricular dysfunction and capillary leak are minimal since the inflammatory effect of CPB usage is avoided; moreover, warming from hypothermia seems not to be a significant problem. We believe that issues with the anaesthetic strategy may cause the longer intensive care treatment course in OPCABG patients based on that description. [6] The provision of safe induction and maintenance of anaesthesia using a technique that offers maximum cardiac protection, maintenance of hemodynamic stability throughout surgery with the help of adequate monitoring and pharmacological support, and early emergence and ambulation in conjunction with excellent postoperative analgesia are among the anaesthetic goals of management of

OPCABG surgery. [7] Hemmerling et al. [8] discuss the anaesthetic technique utilized for OPCABG to fulfil the goals. Hemmerling et al. state that the heart rate should be kept between 70 and 80 beats per minute, MAP > 70 mmHg, and SvO2 > 70%, and that clinicians should ensure adequate preload and apply for Trendelenburg position, repositioning the heart in the holding device, and vasopressors and/or inotropes (phenylephrine, dopamine, or norepinephrine) administration to treat hypotension. Fast extubation is a difficult decision for OPCABG patients due to hemodynamic instability caused by ischemia prevention and heart position throughout the operation. Anesthesiologists will utilize a lot of intravenous fluid and vasoconstrictor agents if there is hypotension during the surgery. This might result in volume overload and later interstitial oedema, which must be addressed during postoperative care, extending the treatment course by inadvertently delaying extubation. [9]However, our data never mention any information about hypotension, vasoconstrictor agent use, volume overload, or duration of intubation in OPCABG patients.

In many studies, there has been mentioned that OPCABG shortens hospital of ICU LOS. Studies that support the statement are those conducted by Islam *et al.* [4] and Brewer *et al*. [10].Both studies mention that the off-pump technique shortens the course of treatment in hospitals and ICUs. Nonetheless, the study never discusses why off-pump can shorten the length of stay. In contrast, our study found that the length of stay in OPCABG patients was longer than in ONCABG patients. Unfortunately, information regarding the possibility of prolonged hospital and ICU length of stay in OPCABG was never demonstrated in other articles. The authors reflect on the results and found that the application of OPCABG still relies on clinicians' preparation, operators, and other supporting clinicians like anesthesiologists and cardiologists in dealing with the technique to get the desired outcome, especially to shorten the length of stay. The above explanation about post-CABG problems that usually arise and anaesthetic consideration for extubation in OPCABG might explain prolonged ICU LOS in OPCABG patients; despite many results in other centres, OPCABG can shorten the length of stay. However, the data from the authors' centre to support the explanation was still unclear.

Mortality in OPCABG and ONCABG

The degree to which a patient tolerates the CABG treatment, the natural course of the disease, the procedural complexity, and the postoperative recovery are all factors that influence mortality. [11] In this scenario, post-CABG mortality is linked to complications following the surgery, and ONCABG is the most common cause of these issues. It explains why ONCABG was found to have a lower death rate than OPCABG. [12]However, there was no significant difference in mortality between the two groups in this study.

The use of a CPB machine in ONCABG, as well as the manipulation of the ascending aorta, has been linked to several perioperative complications, including myonecrosis during aortic occlusion, cerebrovascular accidents, generalized neurological deficits (e.g., stroke, coma, postoperative neurocognitive dysfunction), renal dysfunction (increased incidence of postoperative renal failure requiring dialysis), and the Systemic Inflammatory Response (SIRS). [12]

Many studies have attempted to propose strategies for dealing with such issues. Some researchers have utilized S100 beta serum concentrations to measure brain injury, and increased serum levels have been linked to the number of microemboli exiting the CPB circuit during CABG. On the other hand, others have observed a higher incidence of microemboli with on-pump CABG (as compared to off-pump CABG) but have not observed a comparable impairment in neurocognitive function one week to six months after surgery. Lipid material and particle matter have been highlighted as possible causes of postoperative neurocognitive dysfunction in blood collected from the operating field after on-pump CABG. [12]

After significant morbid events such as trauma, infection, or major surgery, SIRS manifests as a broad systemic inflammation. [12] Surgical trauma, contact of blood with nonphysiological surfaces (e.g., pump tubing, oxygenator surfaces), myocardial ischemia and reperfusion, and hypothermia all combine to cause a dramatic release of cytokines (e.g., interleukin (IL-6 and IL-8) and other inflammatory mediators after on-pump cardiac surgery. SIRS has been observed in patients undergoing CPB, prompting the development of measures to avoid or reduce its recurrence. [16] Increased serum concentrations of cytokines (e.g., IL-2R, IL-6, IL-8, tumour necrosis factor-alpha) and other inflammatory modulators (e.g., P-selectin, sE-selectin, soluble intercellular adhesion molecule-1, plasma endothelial cell adhesion molecule-1, and plasma malondialdehyde) that reflect leukocyte and platelet activation have been linked [12] A study found that patients who had a 50% increase in serum creatinine concentration after CPB had more elevation of neutrophil CD11b expression (a sign of leukocyte activation), indicating activated neutrophils in the pathogenesis of SIRS and the incidence of post-CPB renal impairment. The effects of modifying neutrophil activation to lessen the development of SIRS have been studied; however, the results have been mixed. [12] These cytokines had lower serum concentrations after CPB after preoperative intravenous methylprednisolone (10 mg/kg). This reduction, however, was not linked to improved hemodynamic indicators, reduced blood loss, less use of inotropic drugs, shorter ventilation times, or shorter ICU stays. [12] Similarly, intravenous immunoglobulin G has not been linked to lower rates of short-term morbidity or 28-day mortality in patients with post-CPB SIRS. Other strategies for preventing SIRS after CPB have been investigated, such as using CPB circuits (including oxygenators) coated with materials known to reduce complement and leukocyte activation, CPB tubing covalently bonded to heparin, and CPB tubing coated with polyethylene oxide polymer or Polyethylene oxide polymer (2-methoxyethyl acrylate). [12] After CPB, plasma concentrations of P-selectin, intercellular adhesion molecule-1, IL-8, plasma endothelial cell adhesion molecule-1, and plasma malondialdehyde were lower after leukocyte depletion via customized filters in the CPB circuits. Finally, closed CPB microcircuits have been designed to reduce blood–air interface and blood interaction with nonbiological surfaces, stimulating cytokine generation. However, whether these manoeuvres and procedures have a discernable impact on CABG outcomes is unknown. [12]

OPCABG, unlike ONCABG, is done on a beating heart utilizing stabilizing devices (which minimize cardiac motion). It also includes strategies to reduce myocardial ischemia and systemic hemodynamic instability. As a result, CPB is no longer required. This approach does not eliminate the requirement to manage the ascending aorta during the proximal anastomosis creation. [12] According to Head et al. [11], 25% of CABG procedures were conducted off-pump in 2001. The current rate of OPCABG procedures in the

Western world is 20%, but in Asia, most treatments are performed off-pump. By avoiding cardiopulmonary bypass, which is linked with microemboli formation, increased blood-brain barrier permeability, and aortic manipulation during cross-clamping and cannulation, OPCABG could theoretically reduce morbidity, notably stroke and mortality. In that study, the off-pump method was superior to ONCABG in terms of mortality (OR = 0.69, 95 per cent CI 0.60-0.75, p = 0.0001). [11]

A study conducted by Brewer *et al.* [10] supports our findings. The study demonstrates no difference in operative mortality for OPCAB patients compared within ONCAB patients (ONCABG, 1.8%; OPCABG, 2.3%; p = 0.259). However, another study conducted by Islam *et al*. [4] mentions the risk of mortality increases with the ONCABG technique as it increases SIR's incidence, which can cause mortality from septic shock. Hillis *et al*. [12] mention in the ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery that around the year 2005, an AHA scientific statement comparing the two techniques concluded that regardless of some studies about the comparison of both procedures, both generally result in excellent outcomes and that neither technique should be considered superior to the other. Because CPB maintains systemic circulation, surgeons often favour ONCABG in patients with hemodynamic impairment. OPCABG, on the other hand, is favoured by some surgeons who have substantial experience with it and are therefore familiar with its technical aspects. According to the explanations, ONCABG was better for mortality than OPCABG because of the impacts of the CPB machine, SIRS, and cerebrovascular accidents. However, our study suggests that there is no significant difference in mortality in both techniques in the authors' centre.

Conclusion

The study conducted by the authors found that ICU LOS was significantly longer in OPCABG patients compared to in ONCABG patients, and there was no significant difference in mortality in the two groups. The results suggest that clinicians have to pay more attention to some suspected problems as the reasons behind OPCABG's prolonged ICU so that the goal of OPCABG application can be achieved. In addition, some improvements still need to significantly decrease mortality in applying the OPCABG procedure in the authors' centre.

Abbreviations

AMI	Acute myocardial infarction
BMI	Body mass index
CABG	Coronary artery bypass graft
CAD	Coronary artery disease
CVD	Cardiovascular disease
CPB	Cardiopulmonary bypass

ICU LOS	Intensive care unit length of stay
ONCABG	On-pump coronary artery bypass graft
OPCABG	Off-pump coronary artery bypass graft surgery
PCI	Percutaneous coronary intervention
SIRS	Systemic inflammatory response

Declarations

The authors declare that they have no conflict of interest.

Ethics approval and consent to participate

Ethics approval and waiver of consent were granted by the Ethical Committee Board of National Cardiovascular Center Harapan Kita Hospital and has therefore been performed following the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Consent was waivered because this study only involves the use of secondary data, which involves no risk to the subject.

Consent for publication

Not applicable.

Availability of data and materials

Data is not available for third-party use as the Ethics approval does not cover this for this project.

Competing interests

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial or non-financial interest in this manuscript's subject matter or materials.

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Authors' contributions

RZI contributed substantially in the conception and design of the study, acquisition of data, interpretation of data, and finalization of the article. EOJ contributed substantially in data analysis, interpretation of data, and drafting the article. All authors read and approved the final manuscript.

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Tables

Table 1. Study sample characteristics

n=1569	Minimum	Maximum	Mean	Std. Deviation
Age	27	89	58.21	8.302
Body Weight	30	130	67.415	11.2519
Body Height	136	188	163.41	6.681
BMI	13.36	42.94	25.1963	3.62896
ICU LOS	1	27	1.68	2.184
	Frequency		Percentage	
Sex				
Male	1361		87.13	
Female	201		12.87	
Age				
Early Adult, 20-39	17		1.09	
Middle Adult, 40-59	871		55.98	
Late Adult, 60-65	355		22.81	
Old Age, > 65	313		20.12	
Ejection Fraction				
Normal, > 50 %	865		57.1	
Mild, 40-50 %	279		18.42	
Moderate, 30-39 %	217		14.32	
Severe, < 30 %	154		10.17	
CABG Technique				
On pump	1232		83.41	
Off pump	245		16.59	
Blood Pressure				
Normotensive	976		63.25	
Hypertensive	567		36.75	
Obesity				
Non-obese	1362		89.96	
Obese	152		10.04	

Diabetes Mellitus		
Non-diabetic	948	86.34
Diabetic	150	13.66
Length of Stay		
≤ 2 Days	775	87.07
> 2 Days	115	12.93
Mortality		
Survived	1525	97.2
Died	44	2.8

Table 2. Univariate and multivariate analyses of CABG technique and ICU LOS

CABG technique	Intensive Care Unit Length of Stay					
	Univariate			Multivariate		
	Mean	Standard Error	*p*-Value	Mean	Standard Error	*p*-Value
OPCABG	0.558	0.026	0.0285	0.816	0.073	0.0224
ONCABG	0.408	0.633		0.661	0.661	

Table 3. Univariate and multivariate analyses of CABG technique and mortality based on the logistic regression model

	Mortality					
	Univariate			Multivariate		
	OR	95% Confidence Interval	*p* Value	OR	95% Confidence Interval	*p* Value
OPCABG vs ONCABG	1.165	0.485-2.800	0.733	1.165	0.482-2.817	0.735