

# Perioperative factors of fast track extubation success following coronary artery bypass graft surgery: a literature review

Siddiq Wiratama<sup>1</sup>, Yan Efrata Sembiring<sup>1\*</sup>, Philia Setiawan<sup>2</sup>

## ABSTRACT

**Introduction:** Various studies have shown that fast-track cardiac care which its final aim is for early extubation after surgery, reduces hospital length of stays, cost, and post-operative morbidity rate. The main purpose of this study is to evaluate some perioperative factors as an independent predictor for a successful outcome for fast-track extubation (FTE) in patients undergoing coronary artery bypass graft surgery (CABG).

**Method:** This study analyzed multiple references using the keyword "Fast track Extubation", "Perioperative Factors", and "CABG". Search engines such as PubMed, Google Scholar, ProQuest, and ClinicalKey were used to search for relevant papers from the last 15 years. We obtained total of 6 articles that meet our review criteria. We excluded some articles for not meeting our review methods considerations and by the year of publication that does not meet our standard.

**Result:** A total of 6 studies were identified regarding fast tract extubation post-CABG procedure. Numerous risk factor has been identified for successful of fast tract intubation after intubation such as post-operative bleeding, aortic cross-clamp time, cardio-pulmonary bypass time, chronic obstructive pulmonary disease, atrial fibrillation, ejection fraction pre-operative, diabetes mellitus, renal function, and patient age.

**Conclusions:** This study confirms that better perioperative profile such as age, good ejection fraction >40% has better chance for FTE success in patients undergoing CABG surgery.

**Keywords:** fast-track extubation, perioperative factors, bypass graft surgery.

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<sup>1</sup>Department of Thoracic, Cardiac and Vascular Surgery, Faculty of Medicine, Universitas Airlangga - Dr. Soetomo General Hospital, Surabaya, Indonesia;

<sup>2</sup>Department of Anaesthesiology and Reanimation, Faculty of Medicine, Universitas Airlangga - Dr. Soetomo General Hospital, Surabaya, Indonesia.

\*Corresponding author:

Yan Efrata Sembiring;  
Department of Thoracic, Cardiac and Vascular Surgery, Faculty of Medicine, Universitas Airlangga - Dr. Soetomo General Hospital, Surabaya, Indonesia;  
yan-e-s@fk.unair.ac.id

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## INTRODUCTION

Fast-track cardiac surgery programs have been practiced as an established standard approach in more than three decades.<sup>1</sup> Previous study stated that the fast-track approach is associated with shorter Intensive Care Units (ICU) utility without the risk of increasing morbidity and mortality.<sup>1,2</sup> Other studies stated the safety and efficacy of the FTE in patients undergoing open cardiac surgery other than isolated CABG.<sup>3</sup> FTP being said to reduce cardiovascular mortality, increase in cardiac performance, and decrease the nosocomial infection rate, with better patient comfort.<sup>3</sup>

Although its safety and its effectiveness are proven, there is an 11-16% failure rate incidence of fast-track in cardiac surgery.<sup>2</sup> The objective of this study was to profile the perioperative factors for a successful FTE practice in CABG patients, thus giving us insight to know factors that impact for

early extubation to reduce length of stay, reduce hospital cost and to optimize ICU utility especially in developing country and Covid-19 era.<sup>4</sup>

## EVIDENCE ACQUISITION

This study was conducted by analysis and synthesis from various references. The author uses "Fast Track Extubation" AND "Perioperative Factors" AND "CABG" as keywords for exploring the literatures from search engines such as PubMed, Google Scholar, ProQuest and ClinicalKey. Inclusion criteria are the paper published in the last fifteen years and exclusion criteria are non-full paper text. The paper included in our search criteria is analyzed to answer the purpose of this study.

From total of 22 articles, we obtained 6 articles that met our criteria from search engines such as PubMed, Google Scholar, ProQuest and ClinicalKey. Many articles

are being excluded as they didn't meet our inclusion criteria or the year of publication didn't meet our review criteria.

## EVIDENCE SYNTHESIS

The information from the articles are Author's name (Study location and the year of study publication are included), design of the study, population, and journal's result and discussion are included. The findings are being presented in [Table 1](#).

## DISCUSSION

Fast-track cardiac care is now the global standard of care. New protocols are replacing conventional protocols of extubation, this fast-track cardiac care consists of some intervention involving several components of care during cardiac anesthesia and in the post-operative period. The main purpose of this fast-track cardiac care is for Fast Track Extubation,

**Table 1. Included study characteristics**

Article	Design	Objective	Population	Results	Limitation
Akhtar, et al.	Cross-sectional study	Determining FTE success or failure profile in adult open-heart surgery	290 patients at Cardiac operating room and Cardiac Intensive Care Unit (CICU) in Aga Khan University Hospital for nine months since October 2014 to June 2015. All patient age 35 to 80 years undergoing on-pump elective cardiac surgery patients (CABG, isolated valve replacement or combined valve replacements and CABG, or Aortic replacement surgery) are included in this study.	The average age is 56.3 ±10.5 years. The overall success rate was 51.9% and failure rate was 48.1%. In the success group, perioperative profiles such as renal insufficiency, cross-clamp time, and CICU length of stays are significantly lower. Reintubation rate was 0.74%. the major reason for failure in FTE were hemodynamic instability (high inotropic support) (36.9%), drowsiness (39.2%) and bleeding (21.5%).	Observational study without control group. Limited CICU stay means there is no evaluation for 30 days post-operative morbidity and mortality.
Wong, et al.	Randomized control trial	Determining the safety and effectiveness of fast-track cardiac care compared with conventional care in adult patients undergoing cardiac surgery.	28 trials (4438 participants) are included from all randomized control trials between 1994-2015 of adult cardiac surgery patients (CABG, aortic valve replacement, mitral valve replacement) that compared fast-track and conventional care groups.	No difference in risk of death, complication or reintubation in the first year after surgery.	Evidence quality are low because of study limitations and unexplained variation in study findings. There's only a number of large trials which consist of post-operative complications.
Toraman, et al.	Cross-sectional study	To investigate the applicability of FTE in open heart surgery other than isolated CABG procedure.	299 patients between March 1999 and 2003 in Siyami Ersek Cardiovascular Surgery Centre in Turkey who underwent cardiac surgery other than CABG to evaluate the safety and efficacy of fast-track care	This study uses risk stratification to reveal variables that affected the duration and ICU's length of stays, delayed extubation as a parameter for safety and efficacy of FTE. The post-operative and preoperative variables predictors for delayed intubation are perioperative congestive heart failure, peripheral vascular disease, diabetes, emergent operation, red blood cell transfusion, chest tube drainage >1000ml, EuroSCORE>5, and COPD.	There are no isolated CABG procedure data. But combined open heart surgery are included in this study.
Ott, et al.	Cross-sectional study	To determine gender-associated factors that may impact outcome and recovery in fast-track CABG grafting	517 patients underwent isolation CABG in Yale Haven hospitals in Connecticut. 315 men were compared to 160 women. A rapid recovery protocol focused on reduced cardiopulmonary bypass (CPB) time, IABP use, early extubation, perioperative administration of corticosteroids and thyroid hormone, diuresis and atrial fibrillation prevention was applied to all patients	In this study, women have longer recovery compared to men, this might be caused by preoperative risk profile. When being treated with rapid recovery protocols, even though there's no mortality rates or postoperative complications different in women and men their profile is older, higher incidence of AMI, diabetes, and symptomatic vascular disease, had shorter CPB time, and longer lengths of stays.	This study could be affected by response bias when data for patients' preoperative health status are collected retrospectively by interview. There is referral bias, the women In this study had less extensive coronary disease than men group.

Article	Design	Objective	Population	Results	Limitation
Lima, et al.	Retrospective cohort	Comparing the impact of two fast-track strategies regarding the extubation time after cardiac surgery on clinical and hospital outcomes	All patients undergoing cardiac surgery extubated in the operating room or patient remained under invasive mechanical ventilation up to 18 hours after admission to ICU, aged between 20-80 years from March 2013 to June 2013 admitted to Real Hospital Portugues de Beneficencia in Pernambuco.	Fast-track extubation group of patients with extubation within 6 hours had shorter stay in ICU without increasing post operative complication or death.	Retrospective data obtained from medical records result in no control regarding sample selection or randomization in the stratification of the groups. The baseline characteristics of the patients could have influenced the result.
Gu, et al.	Meta-analysis	To assess the efficacy of intravenous magnesium on the prevention of postoperative atrial fibrillation (POAF)	7 double blinds, placebo-controlled Randomized Control Trials and 1.028 participants are being reviewed.	The study result showed that intravenous magnesium reduced the incidence of POAF by 36%.	Some of the clinical study has small sample size, bias in effect caused by few study sizes, no standardized follow-up up and magnesium dosage among studies

defined as early removal of the tube that provides mechanical breathing support to enable cardiac surgery within six hours or earlier.<sup>2,6</sup> This paradigm shifts toward newer cardiac care aiming to lower the burden of hospitalization and lowering the length of stay such that the patient turnover in ICU could be faster and more efficient in high-volume cardiac centres. This would be the future of health care based efficient cost and better quality of life outcomes after cardiac surgery. With accurate failure prediction model for fast-track care in cardiac surgery, there would be expected increase in bed utilization from 23-67% even after adding risk for unplanned ICU admission.<sup>2</sup>

The first and foremost concern is the safety of early extubation in cardiac surgery. A previous study showed that early extubation was associated with shorter CICU length of stays and lower re-intubation rates, this lower intubation rate shows that FTE is considered safe to be done in patients with open heart surgery without increased risk of postoperative mortality or major complication.<sup>1,2,6,7</sup>

Although safe and effective, multiple studies showed FTE failure rate at 11-16% depending on the patient population, one of the studies has a failure rate of 48%.<sup>1</sup> Multiple factors contributed to the high failure rate including hemodynamic instability, drowsiness found in elderly patients, and significant bleeding which

will contribute as some major contributing factors for FTE failure. This review aims to profile the preoperative factors to predict the successfulness of FTE in CABG patients.

### Age

The mean age profile of the successful FTE patients in some studies was 56.3±10.5 years, 55.2±13.6 years and younger than 65 years.<sup>3-5</sup> Elderly patients associated with drowsiness (difficulty to arouse) and poor cough/gag reflexes which found in 39.2% of all major reasons for fast-track failure.<sup>1</sup> As explained by Sebekos et al. and Lemaire et al. that age has become one of the determinants of the outcome of a surgery, with increasing age, the prevalence of a patient's comorbidities increases, decreased physiological function and stress due to surgery than in younger patients.<sup>8-10</sup>

The structural alterations in the chest wall, leading to reduced flexibility, can be attributed to conditions like osteoporosis, which can shrink the size of the thoracic vertebrae, stiffening of the chest wall by osteoporosis further hinders chest expansion during inhalation. This reduced chest wall flexibility accounts for around 31% of the aging effect.<sup>11</sup>

Regarding gas exchange and ventilation, the gap between oxygen levels in the alveoli and arteries widens with age due to various

factors, including alterations in alveoli structure and size, changes in pulmonary blood vessel patterns, and shifts in blood distribution. The overinflation of the lungs also contributes to aging, potentially resulting from damage to the lung tissue or the supportive framework. Furthermore, muscle wasting impacts the strength of the diaphragm, which is crucial for effective breathing, potentially leading to respiratory difficulties during heightened ventilation. The decline in lung function is suggested to commence around the age of 35.<sup>11</sup>

### Renal Function

The perioperative renal insufficiency was low in the success group of FTE.<sup>1</sup> In Toraman study, creatinine >2mmol/L and in Akhtar study preoperative renal dysfunction which defined as serum-creatinine >1.5mg/dl and post operative Acute Renal Injury defined as 50% increases in Serum-Creatinine above preoperative normal value. Preoperative and post-operative renal dysfunction was a significant co-morbid contributing factor for the failure of FTE (5.0 vs. 16.2%, p=0.003) and (28.6 vs 49.2%; p=0.001).<sup>1,3</sup>

There are various ways in which compromised kidney function can lead to detrimental effects on patients undergoing mechanical ventilation. One such factor is the challenge in safeguarding lung ventilation with limited air volumes,

particularly in individuals with kidney issues who struggle to counter respiratory acidosis effectively. Additionally, excessive fluid retention in patients experiencing reduced urine output can hinder the respiratory system's flexibility, placing undue strain on the lungs in their efforts to facilitate optimal gas exchange during pulmonary diffusion.<sup>12</sup>

Patients who have undergone cardiac surgery with the use of CPB machines experience a decline in renal function due to elevated inflammatory factors and ischemia-reperfusion injury.<sup>13</sup>

### Diabetes Mellitus

Diabetes mellitus (DM) increased the length of ICU stays but not significantly affect TFE success.<sup>1</sup> The prevalence of DM among patients undergoing CABG is on the rise. Currently, about 30-40% of CABG patients are affected by diabetes mellitus, which is considered one of the metabolic syndrome disorders. Patients with both CABG and diabetes tend to experience poorer outcomes compared to those without diabetes. This includes higher mortality rates and an increased likelihood of complications such as renal impairment, stroke, sternal wound infections, and a greater need for inotropic support.<sup>14</sup>

Recent focus on the impact of diabetes mellitus has revealed a reduction in pulmonary function. Although the precise mechanisms behind these effects are not entirely understood, they are thought to involve factors like elevated blood sugar levels, excessive insulin production, autonomic nerve damage, heightened oxidative stress, both micro- and macroangiopathy in the capillaries and arterioles of the lungs, protein glycosylation in tissues, alterations in collagen and elastin, surfactant dysfunction, and disorders in respiratory muscle function.<sup>15</sup>

Diabetic patients undergoing CABG surgery typically exhibit more severe clinical and anatomical characteristics compared to non-diabetic patients. Additionally, diabetes is associated with larger blood vessels and a higher occurrence of lesions. These patients may also experience a decrease in right ventricular function. According to Wendler et al., the

prevalence of diabetes mellitus in patients undergoing this procedure was notably higher, at 93%, in contrast to 83% for those without diabetes. Moreover, diabetic patients tend to have a greater incidence of coronary heart stenosis and a lower ejection fraction rate compared to their non-diabetic counterparts.<sup>15</sup>

Diabetes Mellitus has long been linked to increased mortality in patients undergoing surgery with CPB. A prospective study by Herlitz et al. revealed that diabetic patients had a significantly higher in-hospital mortality rate (6.7%) compared to non-diabetic patients (3.0%). The authors attributed this difference to additional conditions often present in diabetic patients, such as a history of acute myocardial infarction, obesity, symptoms of coronary heart disease, and peripheral vascular disease, all of which elevate the risk in coronary artery surgery. However, in larger multicentre studies, when the influence of these factors was accounted for through multivariate analysis, diabetes was found to be a weaker or even non-significant predictor of early mortality.<sup>16</sup>

Certain postoperative complications, fatal or not, are more prevalent in patients with diabetes. Hyperglycaemia, for instance, renders the body more susceptible to infections. Studies have demonstrated that elevated blood sugar levels accelerate glycosylation and deactivation of immunoglobulins and complement component C3. Similarly, hyperglycemia results in the glycosylation of newly synthesized collagen, collagenase activation, and collagen reduction in surgical wounds. Additionally, leukocytes exhibit impaired adhesion, phagocytosis, chemotaxis, and reduced bactericidal capacity in the presence of high sugar levels. Various studies have shown that elevated sugar levels during the initial postoperative days elevate the risk of infectious complications, particularly mediastinitis.<sup>17</sup>

Respiratory failure is a notable issue in post-surgical patients, particularly in those who have undergone cardiac surgery and have diabetes mellitus. While this is an indirect factor, it may explain why DM patients are more susceptible to extended stays in the intensive care unit.<sup>18</sup>

### Ejection Fraction

One of the predictors of delayed extubation was preoperative congestive heart failure and ejection fraction less than 0.40.<sup>3</sup> Akhtar study showed multiple factors that detected for the failure of FTE including hemodynamic instability which caused by hypotension secondary to low cardiac output or vasodilation, leading to higher dose of inotropes and vasopressor which lead to delaying the extubation beyond 6 hours.

Heart failure stands as a primary contributor to heightened respiratory exertion in patients. Individuals with heart failure and a diminished ejection fraction often display a less effective response to cardiac output during physical activity. Additionally, they commonly experience compromised respiratory function, including challenges with gas exchange, obstructive-restrictive lung conditions, and reduced lung flexibility. The escalated respiratory effort necessitates increased oxygen intake by the respiratory muscles. However, this may potentially divert oxygen supply from the locomotor muscles, thereby disrupting the patient's capacity for muscular movement.<sup>19</sup>

### Atrial Fibrillation

Postoperative atrial fibrillation (POAF), defined as atrial fibrillation occurs between 24 to 96 hours after surgery. Atrial fibrillation potentially leads to complications including stroke and longer hospital length of stay. The etiology of POAF after CABG is still unclear, it may be affected by multifactorial such as older age, history of atrial fibrillation, and low blood magnesium concentration.<sup>8</sup> The incidence of POAF after surgery can be reduced by 36% with intravenous magnesium treatment. Akhtar, et al. study result showed that Atrial Fibrillation as one of the significant arrhythmias would affect the anesthesia and surgical team decision-making and contribute to delay in early extubation in CICU.

While the exact mechanism behind atrial fibrillation remains partially understood, a pathophysiological theory suggests that it arises from re-entry and focal ectopic activity. Three key factors influence this re-entry. First, a shorter refractory period aids cardiomyocytes



in returning from depolarization and maintaining activity. Second, slow conduction, brought about by factors like fibrosis, abnormal connexins, or reduced Na<sup>+</sup> current (I<sub>Na</sub>), contributes to circuit formation by either forming a barrier or re-establishing re-entry. Third, structural remodeling of the heart, such as atrial dilation, leads to a lengthening of the conduction pathway or the presence of a more complex circuit. Diastolic dysfunction is also seen in most of patients with coronary heart disease, increased atrial afterload, stretched atrial wall and increased in atrial pressure contributed to occurrence of atrial fibrillation. Atrial fibrillation results in irregular, small contractions of the atrium, leading to increased oxygen demand in the atria. This, coupled with a rapid elevation in ventricular rhythm, leads to heightened oxygen demand in the heart and a reduction in cardiac output. Ultimately, this results in hemodynamic disruptions for the patient.<sup>20,21</sup>

### Chronic Obstructive Pulmonary Disease

COPD has no significance in affecting the success of TFE, but COPD patients associated with increased length of ICU stays (p=0.04; OR=2.9; 95% CI 1.5-8.7).<sup>3</sup> COPD, or Chronic Obstructive Pulmonary Disease, is a term applied to individuals with an extended smoking history and diminished respiratory function, which can be diagnosed through pulmonary function tests, particularly spirometry. This condition is characterized by persistent inflammation of the airways and lung tissues, marked by heightened activity of macrophage cells. These cells are instrumental in recruiting other inflammatory elements like neutrophils and in releasing mediators, proteases, and activating specific types of T-lymphocytes (Tc1 cells and Th1 cells). The release of various inflammatory mediators brings about the inflammatory alterations seen in COPD. Macrophages and neutrophils release elastolytic enzymes, such as neutrophil elastase and matrix metalloproteinase-9 (MMP-9), contributing to emphysema. This process also leads to constriction of the smaller airways due to inflammation and fibrosis,

ultimately causing progressive airflow limitation and air trapping.<sup>22,23</sup>

While several studies suggest that COPD doesn't directly lead to respiratory failure or increased mortality post-coronary bypass surgery, it does heighten the risk of complications like pneumonia, prolonged mechanical ventilation, heart rhythm irregularities (such as atrial fibrillation), and extended hospital stays. This tendency is notably exacerbated in elderly patients and those on long-term steroid treatments.<sup>22</sup>

### CPB time

In patients treated with successful fast-track recovery, they showed a shorter CBP time profile (<100 minutes).<sup>5</sup> In Akhtar study, there was statistically significant lower median bypass time (100 minutes) in patients who were extubated before 6 hours (p=0.009).<sup>1</sup>

Cardiopulmonary Bypass (CPB) involves a tubing circuit made from polyvinylchloride and polycarbonate connections. When blood comes into contact with this CPB tubing circuit, it triggers the activation of various systems including the complement system, leukocytes, and platelets. This leads to the release of inflammatory mediators, as well as the activation of the coagulation system resulting in the formation of factor Xa and thrombin. These processes can collectively lead to a systemic inflammatory response and ischemic injury during reperfusion.<sup>22</sup>

CPB exerts post-operative effects on vital organs. In the blood, it diminishes coagulation function and reduces platelet count, resulting in increased post-operative bleeding. In the brain, CPB can lead to psychological changes or neurological disorders induced by embolism from fibrin fragments, air, antifoam, or endogenous sources, as well as decreased perfusion. Lung complications range from temporary hypoxemia to acute respiratory distress syndrome (ARDS) and may also include pulmonary edema, pulmonary interstitial bleeding, atelectasis, or haemothorax, collectively referred to as post-perfusion lung syndrome. These issues may necessitate prolonged use of mechanical ventilation. Kidney function may see a decrease in glomerular filtration rate and

renal plasma rate. In the heart, myocardial distension can lead to myocardial edema, subsequently reducing heart contractility and ultimately causing low cardiac output syndrome. This can extend the duration of post-operative care in the intensive care unit and necessitate increased medication use.<sup>24,25</sup>

### Aortic Cross-Clamped Time

In Akhtar et al. study there is no significant difference of cross clamped time in patients who were extubated after 6 hours compared to those who extubated within 6 hours. The average cross-clamped time was 62.5(50-84) minutes in success group and 68 (55-95) minutes in failure group with p value=0.135.

A study by Nissinen et al. assessed the impact of aortic cross-clamping time and cardiac bypass duration. They found that cardiac surgical procedures with CPB times less than 240 minutes and aortic cross-clamping times less than 150 minutes were associated with a lower risk of postoperative complications.<sup>26</sup>

### Post Operative Bleeding

The overall success rate of fast-track extubation was 51,9% and failure rate was 48,1%. Multiple factors were detected for the failure, and one major reason for FTE failure was post-operative bleeding (21,5%).<sup>1</sup>

### CONCLUSION

This study analyzed perioperative profile in patients undergoing CABG surgery to determine the preliminary success of FTE. The study advocated that FTE is safe to be implemented.<sup>7</sup> The perioperative profile in successful FTE showed patients aged between 45 to 65 years. Diabetes mellitus contributed to increasing ICU length of stay but not significantly affect the success of FTE. Patients with preoperative ejection fraction >0.4 have significantly has better chance for successful FTE. Atrial fibrillation patients showed delays in extubation decision-making in CICU that will lead to delayed extubation. While preoperative and postoperative renal function dysfunction yield higher comorbidity leading to failure of FTE.

## AUTHOR'S CONTRIBUTION

Siddiq Wiratama was primarily responsible for writing the manuscript and co-coordinated study design, data analysis, data interpretation and data collection. Yan Efrata Sembiring contributed to data analysis, data interpretation, critical revision of the article for intellectual purposes and final approval of the article. Philia Setiawan contributed to providing the article's material, expertise and writing for important intellectual content. All authors have reviewed and approved the final version of the manuscript for submission.

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## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This review of published literature did not require ethical review.

## COMPETING INTEREST

The authors declare that they have no competing interests.

## AUTHOR CONTRIBUTION

All author had contributed in manuscript writing and agreed for the final version of manuscript for publication.

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