



## Risk Factors for Postoperative Respiratory Mortality and Morbidity in Patients Undergoing Coronary Artery Bypass Grafting

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### ABSTRACT

Nowadays, coronary artery bypass grafting (CABG) is considered to be one of the most common surgical procedures. This procedure has been the main topic in many clinical research studies, which have assessed the effect of the procedure on patients' outcomes. Like other surgical procedures, this procedure is also accompanied by a number of unwanted complications, including those of the respiratory system. Since the respiratory system plays an integral role in defining the clinical outcome of patients, improvements in studies that can assess and predict clinical outcomes of the respiratory system, assume greater importance. There are a number of predictive models which can assess patients in the preoperative period and introduce a number of risk factors, which could be considered as prognostic factors for patients undergoing CABG. The respiratory system is among the clinical systems that are assessed in many prediction scoring systems. This review assesses the main studies which have evaluated the possible risk factors for postoperative respiratory mortality and morbidity, in patients undergoing CABG.

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#### ► Implication for health policy/practice/research/medical education:

The main issues considered in this review evaluate the possible risk factors for postoperative respiratory mortality and morbidity, in patients undergoing CABG.

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### 1. Introduction

Coronary artery bypass grafting (CABG) is currently a very common procedure. This major surgical procedure does, however, have a great impact on the majority of body or-

gans. In such patients, it would be useful to determine the perioperative risk factors, which can predict the possibilities for pulmonary morbidity and mortality after cardiac surgery. Risk factor identification and assessment would improve the quality of clinical management of these patients

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much more accurately (1, 2). The optimization of clinical conditions before the start of the surgical procedure might help to enhance the clinical outcomes for these patients (3, 4), and could also help clinicians in their clinical management, thus preventing untoward postoperative events and complications. In addition, cardiovascular surgical teams have to be aware of potential risk factors predisposing patients to unacceptable postoperative outcomes (5).

In CABG patients, there are a number of adverse stress responses imposed on them (6) due to the nature of the procedure; including the anesthesia and surgical procedures, superimposed by the stress of the cardiopulmonary bypass (CPB) surgery, itself. These unwanted factors affect all physiologic parts of the body, including the pulmonary endothelial beds in diseased or even normal pulmonary beds, and this leads to a number of side effects on the lungs (7). A number of these changes would normally be created after all types of anesthesia, when accompanied with muscle relaxation and mechanical ventilation (8). However, there are a number of effects that are mainly seen after CABG, such as; decreased vital capacity, decreased functional residual capacity, arterial hypoxemia, and reduced lung compliance with resultant breathing work, which could increase the total oxygen utilization by up to 20% in spontaneous ventilation. Finally, it would increase the burden imposed on the myocardium, while the myocardium is ischemic (9).

One of the most important organs affected in CABG patients, is the respiratory system. Moreover, pulmonary complications are among the main complications encountered after cardiac surgery (10), and there are a number of risk factors attributed to prolonged mechanical ventilation, although not all of them are definitive. CABG patients are usually extubated within a maximum of three days after CABG. Nevertheless, there are a number of preoperative risk factors that are predictive for the occurrence of postoperative respiratory complications, and hence could induce postoperative mortality and morbidity due to respiratory problems (11, 12).

## 2. Preexisting Chronic Obstructive Pulmonary Disease

One of the main factors that can predict a patient's risk factors for postoperative respiratory complications is the underlying lung status (1, 2). Therefore, patients with a preoperative forced expiratory volume of less than 70%, are at greater risk (3). Patients with preoperative ventilation problems also have increased risk factors for postoperative problems (12). Those patients who experience prolonged ventilation for more than hours have increased (2, 13). Preexisting chronic obstructive pulmonary disease (COPD) is considered to be a major risk for CABG patients in the postoperative period regarding respiratory morbidity and mortality. However, this risk factor is mainly seen in patients with severe COPD, especially in patients

aged 75 years or older (1-4).

## 3. Blood Transfusion and Volume Balance

Issues related to blood transfusion and volume status in the operating room, are among the most important intraoperative factors predicting the occurrence of postoperative respiratory problems (4, 10-15). In one study, it was demonstrated that these factors had a determining role in postoperative pulmonary morbidity and mortality, mainly through their effects on the occurrence of re-admission after cardiac surgery with fast-track recovery, in this study, the main reason for ICU readmission was respiratory distress. The study demonstrated that in readmitted patients (11-13, 15) and in patients receiving more than four units of packed cells and fresh frozen plasma, the mortality rate was significantly higher. (15-17). Chest tube drainage of more than 500 mL, is also considered to be one of the main independent risk factors for ICU re-admission in fast track CABG (12, 15), possibly because it may increase the chances of packed cell transfusion. The efforts performed by clinicians to reduce blood loss (and hence, the need for transfusion) are among the most important key factors for early tracheal extubation and preventing postoperative respiratory complications (17).

## 4. Anticoagulants and Hemostatic Drugs

Clopidogrel (Plavix) when administered before an operation may increase postoperative bleeding and its complications following CABG. Aprotinin is a high molecular weight, nonspecific serine protease inhibitor which could significantly reduce the amount of blood transfusion required (18, 19), however, critics claim that it might not benefit patients in regard to their clinical outcomes in reducing morbidity or mortality (20-24). On the other hand, a low postoperative dose of aprotinin in patients receiving clopidogrel is safe, and has comparable effects regarding postoperative bleeding complications, as a high dose (25).

## 5. Cardiopulmonary Bypass and Perfusion Status

More than half of a century has passed since the introduction of total CPB for cardiac surgery and nowadays it is used thousands of times each day all around the world (26). One of the main untoward effects of CPB is systemic inflammation, which affects various endothelial beds all over the body. The CPB is composed of a multitude of elements, so due to the great number of resulting interactions between these varying components with the blood components, this creates a significant inflammatory reaction, which is due to humoral and cellular reactions of the immune system, and part of this inflammatory response involves the pulmonary system. The inflammatory effects of CPB on the lungs and the untoward effects of

the surgery itself, mandates the use of anti-inflammatory strategies in order to decrease the severity of pulmonary micro-injuries and inflammation (27-29), although many of these anti-inflammatory approaches have not been as successful as expected (28, 29).

It has been demonstrated that cardiopulmonary bypass with longer durations (eg, in one study, surgery took more than 77 minutes), increases the risk for postoperative complications including respiratory complications (3, 15, 30, 31). There are also studies which demonstrate that in patients undergoing CABG without cardiopulmonary bypass (off-pump CABG), that the time needed for tracheal extubation is shorter than on-pump CABG patients (17). This means that earlier tracheal extubation may be performed in patients receiving off-pump CABG. However, this finding has not always been confirmed (1-3, 17, 32-34).

## 6. Preexisting Arrhythmias

Postoperative atrial fibrillation (AF) has been shown to be a risk factor for prediction of post-operative long-term mortality, therefore, using warfarin as an anticoagulant could improve survival (3, 31). The main reason why underlying AF could aggravate the respiratory outcome relies on a number of factors, including; increased pulmonary arterial pressure due to impaired contraction of the left atrium, increased risk for production of atrial clots, especially in the left atrial appendage (LAA), lack of effective contractile force of the LAA and a multitude of other proposed mechanisms (31-33, 35).

## 7. Underlying Function of the Left Ventricle

The underlying functioning of the myocardium is a major predictive factor for postoperative clinical outcomes. It has been shown that patients with preexisting low ejection fraction (EF) are at a higher risk of developing respiratory problems than patients with normal EF (11, 12, 32-36). Impaired left ventricular ejection fraction (LVEF) of less than 30%, history of previous myocardial infarction (36, 37), and preexisting congestive heart failure, age, diabetes mellitus and arterial hypertension, have all been shown to be independent, significant predictors for developing these respiratory problems (30, 31, 35). Low EF especially, has a determining role in patients with a pre-existing cardiac problem, mainly valvular heart diseases, such as low gradient aortic stenosis (AS). In such cases, a low EF would be a predictor of postoperative morbidity after aortic valve replacement. This factor affects patient outcomes in such a way that it greatly influences the process of clinical decision making, in order to use or discard surgical methods for treating the diseased valve. Postoperative renal and respiratory complications are among the other important factors in these patients (33, 34, 36). It has also been demonstrated that in patients undergoing CABG combined with valve disease, there is

an increased possibility that the patients would require readmission to the ICU. In such patients, post-operative respiratory complications are the most common reasons for readmission (32-34, 36-38). In addition, a history of myocardial infarction during the last 90 days and a previous history of cardiac surgery, are both considered to be important predictors of postoperative respiratory problems (36-40).

## 8. Peripheral Arterial Disease

Peripheral vascular diseases, mainly in the category of peripheral arterial disease, are considered to be one of the main independent risk factors for ICU readmission in fast track CABG. In these patients, underlying peripheral vascular disease has high rates of adverse outcomes (5, 11-13, 37-40).

## 9. Preexisting Endocrine Disorders

Diabetes mellitus is one of the most important endocrine disorders. It is also, considered to be a major risk factor for patients undergoing CABG, which could predict the possibility of postoperative mortality and morbidity in these patients, especially for diabetic patients with respiratory problems (30-38). On the other hand, there is a great amount of current evidence that demonstrates a very clear difference between, well controlled and poorly controlled diabetes mellitus, in predicting respiratory problems, hence, controlling the level of blood glucose in diabetics (at least below 200 mg/dL blood levels) would greatly affect the overall clinical outcome, including respiratory outcomes, in patients undergoing cardiac surgery, especially CABG, compared with poorly controlled diabetics (35-37).

Subclinical hypothyroidism could increase the chances for postoperative complications, including postoperative respiratory complications, however, it is still unproven that preoperative administration thyroxin can prevent this risk factor (41, 42).

## 10. Operating Room Management Factors

The weekly schedule of the operation has been studied as a determinant of outcomes, since elective surgery is usually scheduled for weekdays during 'normal' working hours (43-46). Regarding the preoperative risk factors for postoperative pulmonary functions, this factor was not a main determinant of postoperative risk status. The particular time of the surgery; during the day, during the week or during the year, was not related to poor respiratory outcomes in elective CABG (3-5). So, this would not be considered as a risk factor for CABG patients.

On the other hand, the efforts performed by the clinicians to reduce the operation time are among the most important key factors for early tracheal extubation and the prevention of postoperative respiratory complica-

tions (16).

## 11. Age

Old age is considered to be an independent risk factor predicting postoperative complications in many studies (2-4, 11-13, 16). Older aged patients (age  $\geq$  70 years old) is among the most important factors which could impose a greater risk on the CABG patients, as they need to be able to tolerate severely decreased levels of systemic oxygenation and systemic hypoxemia after myocardial revascularization (29, 30). Therefore, clinicians should administer effective treatments for such patients in order to prevent postoperative respiratory problems, of these, pulmonary recruitment strategies (including positive end expiratory pressure or PEEP) need to be mentioned as the top choice of such strategies (1, 29-34, 36-41). In another study, it was demonstrated that one of the main independent risk factors for ICU readmission in fast track CABG, is a patient's age of more than 65 years (11-13). All of the above findings should be tempered with the fact that the more age increases above 65 years, there is an increased risk for postoperative complications (36-40).

## 12. Ethnic Factors

There are studies that demonstrate ethnic lifestyles may be a strong risk factor for the prediction of postoperative clinical status, including respiratory complications. However, this has not yet been fully elucidated and needs larger confirmatory studies to verify the value of ethnicity regarding perioperative complications (47-49).

### 12.1. Gender

Female patients seem to be at a slightly higher risk of postoperative respiratory complications (1-3, 44-48).

### 12.2. Obesity

Obesity is a major risk factor in predicting the chances of postoperative respiratory failure (3, 12, 13, 15). This effect is both due to the direct effects of obesity on the respiratory system and also, due to the effects of obesity on other organ systems, which could in turn affect the respiratory system (48-52). Although the definite margin for body mass index (BMI) considered as the index of obesity and its role in increasing the risk of respiratory problems has been identified, the effect of this factor is of such importance that even at lower ranges, an increased BMI figure may affect pulmonary outcomes.

### 12.3. History of Smoking

Patients, who are current smokers, are at increased risk for postoperative respiratory problems. This is directly due to the effects of smoking and indirectly due to the effects of smoking on other systems, like the cardiovas-

cular system and the respiratory system, as well as in its role of increasing the risk of pulmonary infections (1, 40, 41, 53). Moreover, a number of smokers also have a history of abuse of other compounds (13). Even though a current and active history of smoking is important, a previous history of smoking, which has not continued up to the time of the operation, should also not be neglected (53).

### 12.4. Preexisting Renal Failure

Increased blood urea nitrogen (BUN) levels or the serum creatinine level in the preoperative period, are independent and potent risk factors, which elevate the chances of postoperative respiratory complications (1-3, 13, 16, 53). Though this is a well-known fact, the exact preoperative levels involved of blood BUN and/or creatinine are still controversial.

### 12.5. Preexisting Arterial Hypertension

Underlying arterial hypertension is considered to be a definitive risk factor, which could predict postoperative pulmonary complications (28, 30).

### 12.6. Condition of the Operation

There are a considerable number of studies which have demonstrated that re-do operations (re-do CABG) and emergency CABG may increase the risk for postoperative pulmonary morbidity and mortality (3, 12, 13, 15). Urgent surgery and emergency surgery are both considered as risk factors for postoperative pulmonary complications. Emergency surgery in particular, is considered to be a risk factor, which is usually associated with an underlying coexisting disease (2, 5).

## 13. Administration of Preoperative Inotropic Agents

Administration of preoperative inotropic agents could increase the risk of postoperative pulmonary morbidity and mortality (3, 11-13, 15).

## 14. Patient Risk Classification Status

These patient classes are at increased risk for postoperative mortality and morbidity (3, 11-13, 54-60):

Higher classes of the New York Heart Association, above class II (3, 12, 13) higher classes of the Canadian Cardiovascular Society, above class II (12, 13); higher classes of the Society for Thoracic Surgeons cardiac risk model, above class II (13), higher classes of the ASA classification (3, 12), and higher classes of European cardiac surgical patients, namely Euroscore (11, 54-56).

## 15. Conclusions

Previous studies have demonstrated that preexisting

conditions can affect postoperative clinical outcomes. Therefore, an assessment of the following factors could help clinicians improve the outcomes of their patients.

Preexisting chronic obstructive pulmonary disease, blood transfusion and volume balance, anticoagulant and hemostatic drugs, cardiopulmonary bypass and perfusion status, preexisting arrhythmias, underlying function of the left ventricle, peripheral arterial disease, preexisting endocrine disorders, operating room management factors, age, ethnic factors, female gender, obesity, history of smoking, preexisting renal failure, preexisting arterial hypertension, condition of the operation, administration of preoperative inotropic agents, and patient risk classification status.

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