Effect of Hypoxemia in the Determination of Short-Term Prognosis of Coronary Artery Bypass Graft Patients: A Prospective Study

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Abstract

Background: Respiratory failure and hypoxemia are the known complications of anesthesia and surgery. As a major surgery mainly at advanced ages, the coronary artery bypass graft (CABG) surgery could lead to hypoxemia in the early post-operative phase. Currently, the fraction of partial pressure of arterial oxygen to the fraction of inspired oxygen (PiO_2/FiO_2) is used to determine the severity of the respiratory assault.

Objectives: This study aimed to find the effect of hypoxemia measured by PaO_2/FiO_2 at the first hour following CABG in the determination of short-term prognosis of CABG.

Methods: Being approved by a local ethics committee, this observational cross-sectional study was conducted in 212 patients undergoing CABG on the cardiopulmonary pump, with no concurrent surgery or other cardiac pathologies. Factors like age, sex, weight, height, the duration of pump and cross-clamp, as well as other medical conditions including chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM), opioid use, ejection fraction (EF), and creatinine clearance (CrCl) before the surgery were brought into consideration as possible confounders. The ratio of PiO_2/FiO_2 in the first hour after the surgery was measured, and its effect on intubation time and intensive care unit (ICU) length of stay was evaluated as the primary outcomes. The *t*-test and chi-squared were used to compare quantitative and qualitative variables, respectively. The repeated measures ANOVA test was used to compare the means.

Results: There was no significant relationship between hypoxemia measured as the ratio of PaO_2/FiO_2 and the duration of ICU length of stay (P value = 0.220) and the total intubation time (P value = 0.661). Among the qualitative variables, just opium addiction in patients with $PaO_2/FiO_2 > 300$ was associated with significantly longer intubation time (P value = 0.016). Furthermore, in the quantitative variables, longer intubation time was associated with higher cross-clamp time (P value = 0.035) in hypoxemia in the range of ARDS patients.

Conclusions: Hypoxemia after the CABG surgery is common and does not affect the short-term prognosis of CABG patients.

Keywords: Hypoxemia, CABG, Oxygenation Dysfunction, Intubation Time, ICU, Length of Stay

1. Background

CABG is considered the most proper treatment for multiple coronary vessels occlusion (1). Several elements have been known to affect the final outcome of this surgery including the mortality and morbidity of the surgery, the complications of the surgery, the duration of ICU admission, and the patients' quality of life (2, 3). Two groups of factors can contribute to higher mortality and morbidity of this surgery. The first group consists of the patients' factors such as age, sex, BMI, left ventricular ejection fraction (EF), DM, smoking, and other concomitant medical conditions (e.g., COPD, renal diseases, and so on) (3, 4). The second group consists of environmental factors such as the surgical and anesthesia methods, quality of myocardial protection, the hemodynamic stability, cardiopulmonary bypass method, and the quality of ICU care (5, 6). Recently, there has been a considerable improvement in some surgical and anesthesia methods, as well as in myocardial protection quality, which has contributed to decreasing patients' intubation and hospital stay (7). At the same time, the patient's age and the concomitant diseases are increas-

ing, which lead to longer intubation and hospital stay ([7](), [8]()). According to the statistics, a fall in mortality and a rise in morbidity have been observed during recent decades ([9](), [10]()).

The respiratory complications are common, life-threatening morbidities of the CABG that can cause longer hospital stay and ICU care ([11]()). Considering the high cost and the use of resources for ICU patients, finding a practical algorithm to predict the length of ICU admission and a way to reduce it can decrease costs and the waste of resources ([12-16]()). In addition, due to various complications of mechanical ventilation, there is an attempt to minimize the ventilator time.

During the on-pump CABG, the activation of the inflammatory cascade could affect the function of all organs including the lungs ([17](), [18]()). The biochemical and histological effects of CPB on the provocation of the systemic inflammatory response syndrome are described in several studies, but off-pump CABG could not completely prevent the inflammatory cascade ([6](), [19]()).

This systemic inflammatory response syndrome increases pulmonary permeability and pulmonary vascular resistance and leads to variations in surfactant quantities ([20](), [21]()), which can lead to alveolar edema, congested alveolar capillary, and accumulation of erythrocytes and neutrophils ([22]()).

The PaO_2/FiO_2 ratio is one of the most important indicators of respiratory complications and the main assessment tool for remarking pneumonia, lung atelectasis, intrapulmonary shunts, ARDS, ALI, and need for respiratory support including mechanical ventilation. However, the establishment of the diagnosis of major respiratory complications is difficult, misleading, or impossible in the early postoperative phase ([23](), [24]()). On the other hand, the majority of CABG patients experience transient hypoxemia as a result of the huge induced inflammatory response during cardiopulmonary bypass and/or direct lung trauma during surgery ([18](), [23]()).

2. Objectives

The purpose of this study was to assess the effect of low PaO_2/FiO_2 values -in the range of ALI and ARDS- one hour after the surgery, on the ICU length of stay and duration of mechanical ventilation as the primary outcomes. The second objectives of the study were to assess the effect of other quantitative and qualitative variables on the ICU length of stay and duration of mechanical ventilation.

3. Methods

This cross-sectional study was conducted on patients who underwent CABG with the extracorporeal cardiopulmonary pump in a specialized university-based hospital during a three-month period from Jul to Sep 2012. The study was approved by the institutional ethics committee. All patients signed an informed consent form to be included in the study. The inclusion criteria were as follows: (1) CABG surgery with no concurrent operation, (2) intubation in the operation room, (3) the absence of other cardiac pathologies including moderate to severe valvular heart disease, and (4) the ejection fraction of more than 30% in preoperative assessments. Patients with any of the following criteria were excluded from the study: Pneumonia or other infections, other pathologies requiring repairing operation -e.g., valvular heart disease-, hemodynamic instability before the surgery, history of aortic balloon pump use, respiratory distress or overt respiratory disease before the surgery, elective or emergent intubation within two months before the surgery, $PCO_2 > 45$ mmHg, $PaO_2 < 60$ mmHg before the surgery or in the beginning of the surgery, FEV1 < 60%, FEV1/FVC < 60%, VC < 50% before the surgery, EF < 30% before or during the study, reoperation for any reasons before extubation, any unwanted neurologic complications with a change at the conscious level or motor deficit, BMI $\geq$ 40, blood transfusion before surgery, severe renal insufficiency -e.g., a past medical history of dialysis or GFR $\leq$ 30 mL/min-, need to corticosteroid and inotrope therapy before the surgery, and infections before the surgery.

The data were recorded in a designed questionnaire by ICU trained nurses as research assistants. The ABG sample was obtained an hour after ICU admission. The intubation time and ICU length of stay were recorded.

Preoperative perpetration and anesthesia care were established based on the local evidence-based protocol and as similar as possible between the patients. All patients had a comprehensive preoperative training course. The evidence-based enhanced recovery after surgery (ERAS) was applied through the adjusted hospital protocols uniformly since they were governing the post-operative cases, too. Anesthesia medications for induction and maintenance were similar.

A cardioplegic solution containing 20 mEq/L potassium chloride (KCl) was given at 15 mL/kg loading dose and one-third of the primary volume was repeated every 20 min containing 10 mEq/L KCl. Except for anemic patients who had the blood in priming, others were primed with normal saline. Ventilation and extubation were based on "open lung concept" guidelines ([25]()), by considering the patients' hemodynamic status, level of consciousness, mus-

cular power, and so on. Data collection was performed by four cooperative experienced ICU nurses using a questionnaire.

Probable confounding factors of the study were patients' weight and height, the time on cross-clamp and CBP, Cr level, and concurrent disease.

Frequencies of qualitative variables and mean, range, and standard deviation of quantitative variables were determined by SPSS software (IBM Corp. Released 2011, IBM SPSS Statistics for Windows, version 20.0, Armonk, NY: IBM Corp.). The *t*-test and chi-squared were used to compare the quantitative and qualitative variables of the two groups, respectively. The confidence interval of 95% and P values of less than 0.05% were considered. To compare the means, the repeated measures ANOVA test was used.

4. Results

By considering restrictive inclusion and exclusion criteria of the study, 212 patients, in total, including 50 (23.6%) females and 162 (76.4%) males entered into the study. Table 1 shows the demographic and medical history characteristics of the patients.

Table 1. The Demographic and Medical History Characteristics of Study Patients

Variable	Mean $\pm$ SD
Age, y	60.45 $\pm$ 9.51
Weight, kg	73.4 $\pm$ 11.80
Height, cm	164 $\pm$ 10.16
BMI (kg.m^{-2})	27.26 $\pm$ 3.95
EF%[a]	48.74 $\pm$ 8.44
Graft number	3.42 $\pm$ 0.83
Pump time, min	67.50 $\pm$ 24.24
Cross-clamp time, min	40.85 $\pm$ 14.77
FEV1%[b]	87.47 $\pm$ 15.82
FEV1/FVC[c]	86.68 $\pm$ 8.28
Creatinine[d]	1.27 $\pm$ 0.386

Abbreviations: BMI, body mass index; EF, ejection fraction; FEV1, forced expiratory volume in the first second; FVC, forced vital capacity; GFR, glomerular filtration rate.
[a] Only patients who had EF > 30% were included in the study.
[b] Only patients who had FEV1 > 60% were included in the study.
[c] Only patients who had FEV1/FVC > 60% were included in the study.
[d] All patients who had the past medical history of dialysis or GFR $\leq$ 30 mL/min were excluded from the study.

In this study, among the major qualitative risk factors that could affect the respiratory outcome, 80 people (37.9%) had a history of smoking, seven people (3.3%) were labeled or treated for COPD formerly, 65 cases (30.8%) had

diabetes mellitus (DM), and 32 cases (15.2%) reported opium dependence or were in withdrawal.

Table 2 shows the ABG findings one hour after the surgery in the study population.

Table 2. The Variables Extracted from ABG (Measured One Hour After ICU Admission)

Variables	Mean $\pm$ SD
pH	7.37 $\pm$ 0.78
PaO$_2$, mmHg	133.61 $\pm$ 38.52
PaCO$_2$, mmHg	33.59 $\pm$ 5.96
BE	- 4.92 $\pm$ 3.3
SpO$_2$, %	98.04 $\pm$ 1.44
PaO$_2$/FiO$_2$, mmHg	264.89 $\pm$ 78.11

Abbreviations: ABG, arterial blood gas; BE, base excess; ICU, intensive care unit; PaCO$_2$, partial pressures of arterial carbon dioxide; PaO$_2$/FiO$_2$, the fraction of partial pressure of arterial oxygen to fraction of inspired oxygen; PaO$_2$, partial pressure arterial oxygen; pH, the potential of hydrogen; SpO$_2$, blood oxygen saturation.

It can be seen that the mean ratio of PaO$_2$/FiO$_2$ presents hypoxemia in the range of acute lung injury (ALI) one hour after surgery. However, the cardiac reasons for hypoxia should be rolled out to label patients as ALI. The patients were classified into four groups based on their PaO$_2$/FiO$_2$ ratio: (1) PaO$_2$/FiO$_2$ > 300: No hypoxemia or within the normal ranges, (2) 300 > PaO$_2$/FiO$_2$ > 200: Hypoxemia in the range of ALI, (3) 200 > PaO$_2$ > 150: Hypoxemia in the range of acute respiratory distress syndrome (ARDS), and (4) PaO$_2$/FiO$_2$ < 150: Hypoxemia in the range of severe ARDS. Table 3 shows the frequency of these four respiratory conditions among our patients.

Table 3. The Frequencies of Different Levels of Hypoxemia (One Hour After CABG)

	Frequency (%)
No hypoxemia or within the normal range: PaO$_2$/FiO$_2$ > 300	69 (32.5)
Hypoxemia in the range of ALI: 300 > PaO$_2$/FiO$_2$ > 200	98 (46.2)
Hypoxemia in the range of ARDS: 200 > PaO$_2$ > 150	33 (15.5)
Hypoxemia in the range of severe ARDS: PaO$_2$/FiO$_2$ < 150	12 (5.6)
Total	212 (100.0)

Abbreviations: ALI, acute lung injury; ARDS, acute respiratory distress syndrome; PaO$_2$/FiO$_2$, the fraction of partial pressure of arterial oxygen to fraction of inspired oxygen.

Table 4 presents the relationship between PaO$_2$/FiO$_2$ one hour after the surgery and the intubation time and ICU length of stay as the primary outcomes of the study.

Concerning the secondary outcomes, the effect of qualitative variables, i.e., gender, DM, COPD, smoking, and opium addiction, on intubation time and ICU length of

Table 4. The Relationship Between PaO_2/FiO_2 (One Hour After Surgery) and the Intubation Time and ICU Length of Stay

Hypoxemia Range	Variable, hours	Mean $\pm$ SD	Pearson Correlation	P Value
No hypoxemia or within the normal range: $PaO_2/FiO_2 > 300$	Intubation time	13.17 $\pm$ 17.82	- 0.144	0.286
	ICU length of Stay	35.6 $\pm$ 28.41	- 0.044	0.727
Hypoxemia in the range of ALI: $300 > PaO_2/FiO_2 > 200$	Intubation time	12.75 $\pm$ 14.85	- 0.053	0.624
	ICU length of stay	42.91 $\pm$ 33.05	0.049	0.641
Hypoxemia in the range of ARDS: $200 > PaO_2 > 150$	Intubation time	9.33 $\pm$ 3.41	0.094	0.628
	ICU length of stay	37.31 $\pm$ 25.71	0.320	0.079
Hypoxemia in the range of severe ARDS: $PaO_2/FiO_2 < 150$	Intubation time	8.33 $\pm$ 2.56	- 0.179	0.598
	ICU length of stay	55.72 $\pm$ 46.76	0.076	0.825
Total	Intubation time	11.94 $\pm$ 14.08	0.033	0.661
	ICU length of stay	41.12 $\pm$ 32.42	- 0.089	0.220

Abbreviations: ALI, acute lung injury; ARDS, acute respiratory distress syndrome; ICU, intensive care unit; PaO_2/FiO_2, the fraction of partial pressure of arterial oxygen to fraction of inspired oxygen; SD, standard deviation.

stay was examined by *t*-test among the four different levels of PaO_2/FiO_2. The results showed that just opium addiction in patients with normal values of PaO_2/FiO_2 (> 300) was associated with significantly longer intubation time (P value = 0.016). Other variables in different oxygenation subgroups did not show a significant effect on the intubation time or ICU length of stay.

Furthermore, among the quantitative variables, longer intubation time was associated with higher cross-clamp (P value= 0.035) in hypoxemia in the range of ARDS patients.

Nevertheless, a longer ICU stay was associated with longer values of pump time (P value = 0.000) and cross-clamp time (P value = 0.031) in patients without hypoxemia, as well as with longer pump time (P value = 0.001) and cross-clamp time (P value = 0.014) in hypoxemia in the range of ALI patients, and higher pump time (P value = 0.040) in hypoxemia in the range of severe ARDS subgroups. None of the other quantitative confounders showed a statistically meaningful correlation.

Table 5 shows the effect of confounding factors on intubation time and ICU length of stay based on the P values of the Pearson Correlation test.

None of the patients participated in the study passed away during their ICU stay.

5. Discussion

CABG with cardiopulmonary bypass usually leads to degrees of respiratory injuries that could be due to primary cardiac or pulmonary complications or both. These injuries could prolong the recovery period and length of hospital and ICU stay in 5% to 22% of patients in various studies (26) and consequently increase mortality and morbidity among patients. We conducted this study to assess

Table 5. The P Values of the Effect of Confounding Factors on Intubation Time and ICU Length of Stay Analyzed by the Pearson Correlation Test[a]

	Pearson Correlation	
	Intubation Time	**ICU Length of Stay**
Age, y	0.381	0.035
Graft number	0.765	0.258
Pump time, min	0.035	0.000
Cross-clamp time, min	0.425	0.001
Weight, kg	0.073	0.289
Height, cm	0.358	0.719
BMI, kg.m^{-2}	0.215	0.408
EF, %	0.278	0.739
Creatinine	0.215	0.954
FEV1, %	0.228	0.205
FEV1/FVC, %	0.983	0.340
pH	0.257	0.945
PaO_2, mmHg	0.995	0.071
$PaCO_2$, mmHg	0.964	0.334
BE	0.072	0.507
SpO_2, %	0.412	0.213
Previous surgery	0.520	0.000

Abbreviations: BE, Base Excess; EF, Ejection Fraction; FEV1, forced expiratory volume in the first second; FVC, Forced Vital Capacity; ICU, Intensive Care Unit; BMI, Body Mass Index; $PaCO_2$, partial pressures of arterial carbon dioxide; PaO_2, partial pressure of arterial oxygen; pH, potential of hydrogen; SpO_2, blood oxygen saturation.
[a] P values of < 0.05 considered statistically meaningful.

the effect of the PaO_2/FiO_2 ratio in the first hour after the surgery in predicting the short outcome of CABG patients

measured by intubation time and ICU length of stay. In this study, 212 patients undergoing CABG with cardiopulmonary pump were included and the impacts of different values of the PaO_2/FiO_2 ratio one hour after CABG and other risk factors on short-term outcomes (intubation time and ICU length of stay) were evaluated.

It was seen that the most frequent range of PaO_2/FiO_2 was hypoxemia in the range of ALI (46.2%). Based on the PaO_2/FiO_2 ratio, only 32.5% of the patients had a normal respiratory condition and the rest of them were classified under hypoxemia in the range of ALI or even more severe forms of hypoxemia. Although these conditions are expected to be associated with high morbidity and mortality rates, in this study, there were no statistical differences in the intubation time and ICU length of stay between patients with different values of PaO_2/FiO_2 and the mortality rate was zero. This is the main finding of the study.

Among the subgroups, just the pump time and cross-clamp time were associated frequently with longer ICU stay with distinct values. However, this relationship and the effect of age or addiction on the intubation time or ICU length of stay, in some subgroups, could be due to problems other than hypoxemia.

In a study by Suematsu et al., it was proposed that the PaO_2/FiO_2 ratio is a reliable predictor of pulmonary function after surgery and an appropriate sign for weaning from mechanical ventilation. In their retrospective study, the PaO_2/FiO_2 ratio was classified into two groups of more than 350 and less than 350. Their findings showed that the predictive factors of low PaO_2/FiO_2 were low weight, low PaO_2 before and after the surgery, prolonged surgery time, history of hypertension and smoking, and high FiO_2 after the surgery. The study concluded that patients with high blood pressure and/or low PaO_2 before the surgery may need better care during and after the surgery, as these two are closely related to the PaO_2/FiO_2 ratio (27). Considering the methodological differences with this study, our findings showed no meaningful relationship between the PaO_2/FiO_2 ratio an hour after the surgery and ICU length of stay and intubation time (27).

Nozawa et al. indicated that factors that contribute to prolonged mechanical ventilation (more than 10 days) after CABG are low EF, dialysis, and pneumonia. Although they accepted PaO_2/FiO_2 as an oxygenation index to wean patients from the ventilator, it was not recognized as a predictor of intubation time (28). The findings of the mentioned study are concordant with the results of our study.

In a study by Guizilini et al., pulmonary function after CABG was compared between the two groups of 15 patients with and without cardiopulmonary bypass. The pulmonary function in terms of FVC, FEV1, and ABG was measured before the surgery and on the 1st, 3rd, and 5th days

after the surgery. Both groups experienced a considerable drop in their FEV1 and FVC until the 5th day. This drop was more significant among those with cardiopulmonary bypass. Similarly, PaO_2 and PaO_2/FiO_2 dropped in both groups although more severe in the bypass group. The results of our study showed that pump time is also an important factor in increasing the risk of respiratory failure.

Abrahamyan et al. conducted a retrospective study on 391 patients undergoing CABG to assess mortality and morbidity and the length of ICU stay. Their findings showed that patients with a past medical history of cardiac surgery, medicine allergy, low EF, DM, and left main coronary artery involvement had a higher risk of more severe morbidities. The risk factors for the prolongation of ICU stay were advanced age, the absence of sinus heart rate, high blood pressure, and previous cardiac surgery (29). Likewise, in our study, there was a significant relationship between advanced age and ICU stay; however, we considered EF values of less than 30 as an exclusion criterion.

Canver and Chanda studied 8802 patients and could recognize the risk factors contributing to respiratory failure following CABG. The only variable during the surgery that could increase the risk of respiratory failure was CBT time (30). Our findings showed a meaningful relationship between the length of ICU stay and the duration of the cardiopulmonary pump, as well.

In another study, Weiss et al. evaluated the efficacy of low PaO_2/FiO_2 as an indicator of hypoxemia shortly after CABG with CPB and assessed factors that could cause hypoxemia 24 h after the surgery. They measured the PaO_2/FiO_2 ratio at 1st, 6th, and 12th hours after the surgery. They introduced age, weight, cardiac insufficiency, past history of MI, emergent surgery, high Cr, alveolar edema In X-ray, prolonged CPB, and dropped PaO_2/FiO_2 ratio as risk factors for developing hypoxemia. Interestingly, their findings showed that only the drop of PaO_2/FiO_2 at 6th hour after the surgery had a meaningful relationship with the length of intubation and pulmonary injury. However, unlike their findings, our findings did not show a relationship between obesity, high Cr, and low EF, and the length of ICU stay and intubation duration (31). Instead, we found a similar relationship between CPB time and age, and the length of ICU stay.

The frequency of PaO_2/FiO_2 compromise in patients with cardiac surgery is significantly high. The mean PaO_2/FiO_2 of patients was in the range of ALI. However, it was a benign form of hypoxemia and was not associated with a higher mortality rate or even significant rise in the length of ICU stay and intubation time.

Considering the facts that we were not able to exclude ALI and ARDS due to not using cardiac monitoring (e.g. Swan Gas) and we excluded patients with heart failure or

valvular disease and patients who needed inotropes or cardiac pump following the surgery and due to the low rate of metabolic acidosis in this study, we can conclude that overall, hemodynamic and cardiac state of patients in this study were stable; thus, the majority of cases with low PaO_2/FiO_2 could be attributed to pulmonary dysfunction and the majority of this form of benign hypoxemia could be a special benign subtype of ARDS and ALI. However, to prove it, the exclusion of cardiogenic hypoxemia is needed in a clinical trial.

In the end, it could be concluded that hypoxemia is very common after on-pump CABG. There was no significant relationship between hypoxemia measured by the quantity of PaO_2/FiO_2 and the ICU length of stay and the total intubation time.

5.1. Limitation

This was a cross-sectional and single center study. The effect of confounders was diminished by the restricting inclusion and exclusion criteria. However, due to the complexity of hypoxemia risk factors, it is impossible to completely abolish the effect of confounders. Furthermore, some probable confounders with minimal and indirect effects, e.g., electrolytes, were not considered in this study. Nevertheless, while the possibilities of cardiogenic hypoxemias and mix pathologies were low in this study, they were still possible. The follow-up time was limited to the ICU length of stay. The duration of ICU stay and medical care during and after surgery could be different in other cardiac surgery units, and this could affect the prevalence and effects of hypoxemia.

Footnotes

Conflict of Inrerests: There is no conflict of interests for authors in this study.

Ethical Considerations: The authors declare that the research reported in the paper was undertaken in compliance with the Helsinki Declaration. The study was approved by the institutional ethics committee.

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Patient Consent: All patients signed informed consent forms to be included in the study.

References

1. Gupta V, Grover V. Risk assessment and outcome after CABG. *Ann Card Anaesth*. 2002;**5**(2):156–8. [PubMed: 17827606].

2. Peterson ED, Coombs LP, Ferguson TB, Shroyer AL, DeLong ER, Grover FL, et al. Hospital variability in length of stay after coronary artery bypass surgery: Results from the Society of Thoracic Surgeon's National Cardiac Database. *Ann Thorac Surg*. 2002;**74**(2):464–73. doi: 10.1016/S0003-4975(02)03694-9. [PubMed: 12173830].

3. Ferguson TB Jr, Hammill BG, Peterson ED, DeLong ER, Grover FL, S. T. S. National Database Committee . A decade of change-risk profiles and outcomes for isolated coronary artery bypass grafting procedures, 1990-1999: A report from the STS National Database Committee and the Duke Clinical Research Institute. Society of Thoracic Surgeons. *Ann Thorac Surg*. 2002;**73**(2):480–9. discussion 489-90. doi: 10.1016/S0003-4975(01)03339-2. [PubMed: 11845863].

4. Tu JV, Sykora K, Naylor CD. Assessing the outcomes of coronary artery bypass graft surgery: How many risk factors are enough? Steering Committee of the Cardiac Care Network of Ontario. *J Am Coll Cardiol*. 1997;**30**(5):1317–23. doi: 10.1016/S0735-1097(97)00295-7. [PubMed: 9350934].

5. Higgins TL, Estafanous FG, Loop FD, Beck GJ, Lee JC, Starr NJ, et al. ICU admission score for predicting morbidity and mortality risk after coronary artery bypass grafting. *Ann Thorac Surg*. 1997;**64**(4):1050–8. doi: 10.1016/S0003-4975(97)00553-5. [PubMed: 9354526].

6. Chiarenza F, Tsoutsouras T, Cassisi C, Santonocito C, Gerry S, Astuto M, et al. The effects of on-pump and off-pump coronary artery bypass surgery on respiratory function in the early postoperative period. *J Intensive Care Med*. 2017:8.8506661769685E+14. doi: 10.1177/0885066617696852. [PubMed: 29112468].

7. Cohen AJ, Katz MG, Frenkel G, Medalion B, Geva D, Schachner A. Morbid results of prolonged intubation after coronary artery bypass surgery. *Chest*. 2000;**118**(6):1724–31. doi: 10.1378/chest.118.6.1724. [PubMed: 11115465].

8. Gluck EH. Predicting eventual success or failure to wean in patients receiving long-term mechanical ventilation. *Chest*. 1996;**110**(4):1018–24. doi: 10.1378/chest.110.4.1018. [PubMed: 8874263].

9. Northrup WF 3rd, Emery RW, Nicoloff DM, Lillehei TJ, Holter AR, Blake DP. Opposite trends in coronary artery and valve surgery in a large multisurgeon practice, 1979-1999. *Ann Thorac Surg*. 2004;**77**(2):488–95. doi: 10.1016/S0003-4975(03)01359-6. [PubMed: 14759424].

10. Ghotkar SV, Grayson AD, Fabri BM, Dihmis WC, Pullan DM. Preoperative calculation of risk for prolonged intensive care unit stay following coronary artery bypass grafting. *J Cardiothorac Surg*. 2006;**1**:14. doi: 10.1186/1749-8090-1-14. [PubMed: 16737548]. [PubMed Central: PMC1526720].

11. Kaul TK, Fields BL, Riggins LS, Wyatt DA, Jones CR, Nagle D. Adult respiratory distress syndrome following cardiopulmonary bypass: Incidence, prophylaxis and management. *J Cardiovasc Surg (Torino)*. 1998;**39**(6):777–81. [PubMed: 9972899].

12. Bucerius J, Gummert JF, Walther T, Doll N, Falk V, Schmitt DV, et al. Predictors of prolonged ICU stay after on-pump versus off-pump coronary artery bypass grafting. *Intensive Care Med*. 2004;**30**(1):88–95. doi: 10.1007/s00134-003-1950-5. [PubMed: 14504725].

13. Hsieh CH, Peng SK, Tsai TC, Shih YR, Peng SY. Prediction for major adverse outcomes in cardiac surgery: Comparison of three prediction models. *J Formos Med Assoc*. 2007;**106**(9):759–67. doi: 10.1016/S0929-6646(08)60037-6. [PubMed: 17908665].

14. Salamonsen MR, Bailey MJ, Salamonsen RF. Can ICU stay be predicted accurately enough for fast-tracking cardiac surgical patients? *Crit Care Resusc*. 2008;**10**(3):194–201. [PubMed: 18798717].

15. Rosenfeld R, Smith JM, Woods SE, Engel AM. Predictors and outcomes of extended intensive care unit length of stay in patients undergoing coronary artery bypass graft surgery. *J Card Surg*. 2006;**21**(2):146–50. doi: 10.1111/j.1540-8191.2006.00196.x. [PubMed: 16492273].

16. Hein OV, Birnbaum J, Wernecke K, England M, Konertz W, Spies C. Prolonged intensive care unit stay in cardiac surgery: Risk factors and long-term-survival. *Ann Thorac Surg*. 2006;**81**(3):880–5. doi: 10.1016/j.athoracsur.2005.09.077. [PubMed: 16488688].

17. Yousefshahi F, Bashirzadeh M, Abdollahi M, Mojtahedzadeh M, Salehiomran A, Jalali A, et al. Effect of hypertonic saline infusion versus normal saline on serum ngal and cystatin C levels in patients undergoing coronary artery bypass graft. *J Tehran Heart Cent*. 2013;**8**(1):21–7. [PubMed: 23646044]. [PubMed Central: PMC3587670].

18. Mazandarani M, Yousefshahi F, Abdollahi M, Hamishehkar H, Barkhordari K, Boroomand MA, et al. Comparison of hypertonic saline versus normal saline on cytokine profile during CABG. *Daru*. 2012;**20**(1):49. doi: 10.1186/2008-2231-20-49. [PubMed: 23351427]. [PubMed Central: PMC3555740].

19. Taggart DP. Respiratory dysfunction after cardiac surgery: Effects of avoiding cardiopulmonary bypass and the use of bilateral internal mammary arteries. *Eur J Cardiothorac Surg*. 2000;**18**(1):31–7. doi: 10.1016/S1010-7940(00)00438-3. [PubMed: 10869938].

20. Royston D, Minty BD, Higenbottam TW, Wallwork J, Jones GJ. The effect of surgery with cardiopulmonary bypass on alveolar-capillary barrier function in human beings. *Ann Thorac Surg*. 1985;**40**(2):139–43. doi: 10.1016/S0003-4975(10)60006-9. [PubMed: 3896173].

21. Haslam PL, Baker CS, Hughes DA, MacNaughton PD, Moat NE, Dewar A, et al. Pulmonary surfactant composition early in development of acute lung injury after cardiopulmonary bypass: Prophylactic use of surfactant therapy. *Int J Exp Pathol*. 1997;**78**(4):277–89. doi: 10.1046/j.1365-2613.1997.330364.x. [PubMed: 9505939]. [PubMed Central: PMC2694537].

22. Wasowicz M, Sobczynski P, Biczysko W, Szulc R. Ultrastructural changes in the lung alveoli after cardiac surgical operations with the use of cardiopulmonary bypass (CPB). *Pol J Pathol*. 1999;**50**(3):189–96. [PubMed: 10624121].

23. Vakili M, Shirani S, Paknejad O, Yousefshahi F. Acute respiratory distress syndrome diagnosis after coronary artery bypass: comparison between diagnostic criteria and clinical picture. *Acta Med Iran*. 2015;**53**(1):51–6. [PubMed: 25597606].

24. Baghban M, Paknejad O, Yousefshahi F, Gohari Moghadam K, Bina P, Samimi Sadeh S. Hospital-acquired pneumonia in patients undergoing coronary artery bypass graft; comparison of the center for disease control clinical criteria with physicians' judgment. *Anesth Pain Med*. 2014;**4**(3). e20733. doi: 10.5812/aapm.20733. [PubMed: 25289379]. [PubMed Central: PMC4183076].

25. Yousefshahi F, Barkhordari K, Movafegh A, Tavakoli V, Paknejad O, Bina P, et al. A New Method for Extubation: Comparison between Conventional and New Methods. *J Tehran Heart Cent*. 2012;**7**(3):121–7. [PubMed: 23304181]. [PubMed Central: PMC3524325].

26. Kollef MH, Wragge T, Pasque C. Determinants of mortality and multiorgan dysfunction in cardiac surgery patients requiring prolonged mechanical ventilation. *Chest*. 1995;**107**(5):1395–401. doi: 10.1378/chest.107.5.1395. [PubMed: 7750337].

27. Suematsu Y, Sato H, Ohtsuka T, Kotsuka Y, Araki S, Takamoto S. Predictive risk factors for pulmonary oxygen transfer in patients undergoing coronary artery bypass grafting. *Jpn Heart J*. 2001;**42**(2):143–53. doi: 10.1536/jhj.42.143. [PubMed: 11384075].

28. Nozawa E, Azeka E, Ignez ZM, Feltrim Z, Auler Junior JO. Factors associated with failure of weaning from long-term mechanical ventilation after cardiac surgery. *Int Heart J*. 2005;**46**(5):819–31. doi: 10.1536/ihj.46.819. [PubMed: 16272773].

29. Abrahamyan L, Demirchyan A, Thompson ME, Hovaguimian H. Determinants of morbidity and intensive care unit stay after coronary surgery. *Asian Cardiovasc Thorac Ann*. 2006;**14**(2):114–8. doi: 10.1177/021849230601400207. [PubMed: 16551817].

30. Canver CC, Chanda J. Intraoperative and postoperative risk factors for respiratory failure after coronary bypass. *Ann Thorac Surg*. 2003;**75**(3):853–7. discussion 857-8. doi: 10.1016/S0003-4975(02)04493-4. [PubMed: 12645706].

31. Weiss YG, Merin G, Koganov E, Ribo A, Oppenheim-Eden A, Medalion B, et al. Postcardiopulmonary bypass hypoxemia: A prospective study on incidence, risk factors, and clinical significance. *J Cardiothorac Vasc Anesth*. 2000;**14**(5):506–13. doi: 10.1053/jcan.2000.9488. [PubMed: 11052429].