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**PREDICTORS OF PROLONGED MECHANICAL VENTILATION AFTER ISOLATED
CORONARY ARTERY BYPASS GRAFT SURGERY**

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ABSTRACT

A retrospective study was carried out in a Cardiosurgical Intensive Care Unit (ICU) in order to evaluate the incidence of prolonged mechanical ventilation after coronary artery bypass graft surgery and identify its predictors.

The study enrolled 1344 consecutive patients undergoing coronary artery bypass graft surgery. Baseline variables including age, sex, obesity, history of smoking, preoperative renal failure, left-ventricular ejection fraction, emergency surgery, history of MI, history of unstable angina, chronic obstructive pulmonary disease and diabetes mellitus were collected. Intraoperative variables were: cardiopulmonary bypass duration and cross clamp time. The measured postoperative variables were: reoperation for bleeding or other complications.

1344 patients underwent Coronary Artery Bypass Graft surgery. 69 patients needed mechanical ventilation more than 24 hours postoperatively (5.1%). Cardiopulmonary bypass duration (P-value=0.000), Cross clamp time (P-value=0.000), female gender (P-value=0.03), diabetes mellitus (P-value=0.025), LVEF (P-value=0.038) and reoperation (P-value=0.000) were independently associated with prolonged mechanical ventilation.

Cardiopulmonary bypass duration, Cross Clamp Time, female gender, diabetes mellitus, LVEF and reoperation were associated with prolonged mechanical ventilation, longer ICU stay and longer hospitalization.

The ability to identify patients with increased risk for prolonged ventilation may allow the development of pre-operative strategies and appropriate resource allocation.

Keywords: Prolonged mechanical ventilation, Coronary Artery Bypass Surgery, Predictors

INTRODUCTION

The prevalence of ischemic heart disease (IHD) is progressively increasing as a result of relative illnesses, increased consumption of fatty foods and city life in general.

The main course of treatment in patients suffering from IHD is usually medical, although some may need revascularization technics such as Coronary Artery Bypass Graft (CABG) surgery. This operation, if performed by an expert team of surgeons, on a patient with no underlying disease and agreeable left-ventricle functionality, is quite safe and mortality is less than 1% (1).

Care and support for IHD patients has developed considerably over the years, resulting in longer life expectancy for the patients. Therefore many coexisting medical conditions may be present at the time CABG is demanded. However survival has increased despite the increasing coexisting risk factors (2).

Patient care, before, whilst and after CABG is considerably dependent on advanced and expensive equipment components. Meanwhile common financial policies call for shorter hospitalization and less expenses (3, 4). In order to obtain this financial goal

many programs have been presented, resulting in shorter ICU and hospital stay and generally less expenses in the post-CABG treatment (2).

Respiratory system incidents like pneumonia and respiratory failure are the main causes of prolonged mechanical ventilation after surgery (5). Incidence of such situations differ from less than 3% in patients with no risk factors, to more than 32% in patients with multiple risk factors (6). Studies have estimated the need for prolonged mechanical ventilation in first-time CABG surgeries 5.5%, and in second-time CABG surgeries 10.5% of cases (7).

Prolonged mechanical ventilation is a known factor in elongated ICU stay, higher expenses and decreased hospital bed vacancy. Also due to atelectasis and pulmonary shunts, prolonged mechanical ventilation presents troublesome situations after extubation (6). Prolonged mechanical ventilation in post-CABG patients is closely associated with higher mortality rates compared to post-operation conditions with early extubation possible (6). This however does not necessarily indicate that long term

mechanical ventilation means higher mortality rate, but suggests that CABG patients under these conditions are facing higher mortality and morbidity risks. Evidently earlier extubation has many benefits specially for the respiratory and cardiovascular systems (8, 9).

Prolonged mechanical ventilation can be attributable to many conditions such as hematologic causes like post-operative hemorrhage, neurologic causes like cerebrovascular accidents, respiratory causes like ARDS and cardiovascular causes (7).

Few studies have explored predicting factors present in CABG candidates that result in requiring long term mechanical ventilation (1, 6, 9).

This study aims to evaluate the incidence and outcome of prolonged mechanical ventilation in a large number of CABG patients in Imam Khomeini Hospital, Tehran. The results of this study may be beneficial in future allocation of resources and develop strategies to eliminate prolonged mechanical ventilation thus eliminating morbidity and mortality rates in CABG patients.

MATERIALS AND METHODS

Patients:

This was a retrospective study on 1344 patients who had exclusively undergone CABG surgery. Participants were randomly

enrolled from patients referring to the imam Khomeini hospital for CABG surgery dating from April 2008 to march 2012 who matched the criteria. Patients simultaneously undergoing other heart surgeries (e.g. valvular, aneurysmal,...) and/or suffering from other heart conditions (e.g. valvular, congenital,...) were excluded from the study.

Data collection and definitions:

Baseline variables such as age, sex, Chronic Obstructive Pulmonary Disease, history of smoking and myocardial infarction history, were retrieved from patient's history files. Diabetes is decided by a repeated fasting blood sugar of 126mg/dl and higher. Obesity is defined as Body Mass Index of 30 and higher. Impaired renal function is defined as creatinin levels exceeding 1.4mg/dl. Left Ventricular Ejection Fraction was calculated by cardiologists via echocardiography. Necessity of surgical operation within 24 hours of symptom unset is considered as emergency surgery. Cardiopulmonary bypass time (CBT), Cross Clamp Time and other intraoperative data is retrieved from the surgical reports filled by the operating surgeons.

Prolonged mechanical ventilation is described as ventilator dependency for over 24 hours after CABG. The decision to extubate patients, vary from one patient to

another and is decided by the cardiothoracic surgeon, anesthesiologist and nursing staff. Patients in danger of lower oxygen delivery are extubated with more delay. Such a condition is manifested by impaired tissue perfusion resulting in rising lactate levels, decreasing blood oxygen saturation, low renal output and distinct hemodynamic instability.

STATISTICAL ANALYSIS

Independent sample t-test has been used to compare the averages of the quantitative values. Chi-square method has been used to analyze the qualitative values. Collected data from all variables was inserted in the SPSS software and final analysis was performed by SPSS 13 (Chicago Package)

RESULTS

In this study 1344 patients were investigated, and 69 patients (5.1%) underwent prolonged mechanical ventilation after CABG.

29.7% of participants in our study were female patients. The effect of sexual gender on prolonged mechanical ventilation was explored. In the prolonged ventilation group 58% were male and 42% were female subjects, were as in the early extubated patients 70.9% were male and 29.1% were female (figure 1) . The prevalence of prolonged ventilation was 4.2% in the male

and 7.3% in the female patients which has significant difference (P-value=0.03).

The prevalence of prolonged ventilation post CABG surgery in account to qualitative values is presented in table 1.

As can be seen in table 1, the highest prevalence rate of prolonged post-CABG ventilation is associated with re-operated patients (15%) and COPD patients (14.2%). In other words, COPD and re-operation, as possible predictors, are 3 time more common in the prolonged ventilation group than in the early extubated group.

In order to explore the effect of each predictor on the prolonged ventilation rates, each variable was analyzed by the Chi-square equation and the results are shown in table 2.

COPD, Chronic Obstructive Pulmonary Disease

In the univariate analysis performed on dichotomous data in this study, female gender, diabetes mellitus and re-operation significantly (P-value<0.05) increase the risk of post-CABG prolonged ventilation. Alternatively other factors such as smoking, COPD, renal impairment prior to the surgery obesity, history of myocardial infarction and unstable angina were not significantly effective.

In contrast to other study reports, although the prevalence of COPD in prolonged

ventilation patients was considerably (3 times) greater than in patients who were extubated earlier than 24 hours, it was not statistically significant. This could be explained by difference of sample sizes.

The mean age in patients receiving prolonged ventilation was 61.23 years and in early extubated patients this average was 59.61 years. This mean age difference was evaluated via independent T-Test analysis and with the P-value=0.208 was considered not significant. Mean age diagram with 95% confidence interval (CI) for both groups of ventilation duration is shown in figure 2.

The average value of each quantitative variable along with related standard deviation

was calculated in the group of early extubated patients and in those with longer than 24 hours ventilation. The results are presented in table 3. To assess the significance (P-value<0.05) difference between the mentioned two groups, independent sample t-test analysis method was used.

As observable in table 3 predictors such as LVEF, increased Cross Clamp Time and CPB time result in the prolongation of mechanical ventilation (P-value<0.05) while age does not seem to have a significant effect on the ventilation duration.

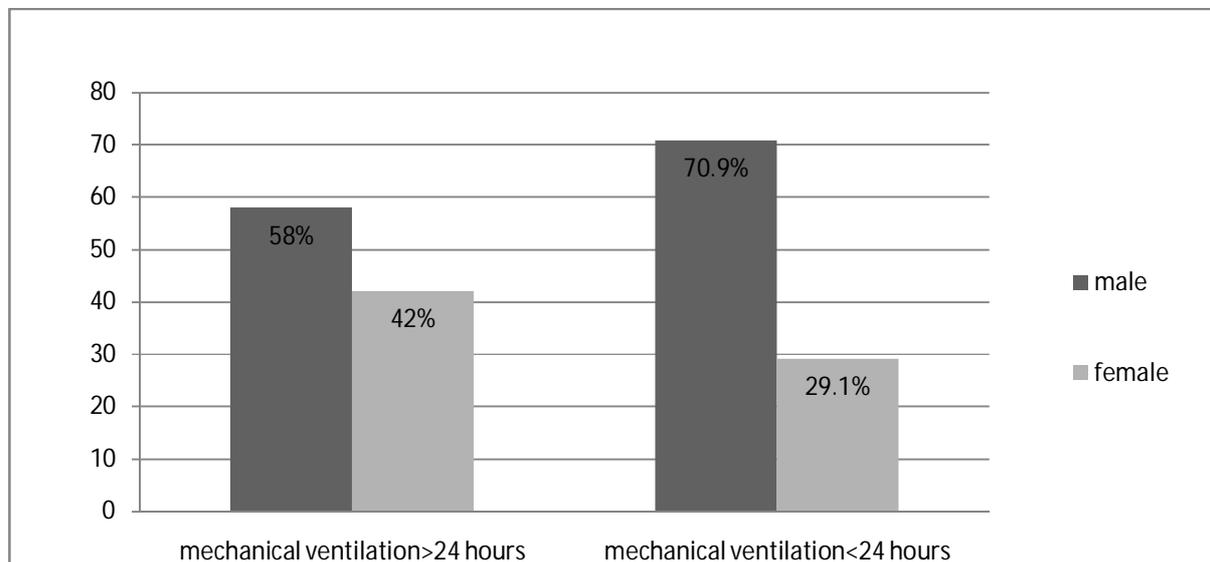


Figure 1: Gender distribution according to prolonged ventilation (n=1344)

Table 1: Qualitative variables, Prevalence of Prolonged Ventilation in Subgroups of Predictors (n=1344)

Predictor	Prevalence of prolonged ventilation	Ventilation>24 hours	Ventilation<24 hours
Sex			
Male	4.2%	58%	70.9%
Female	7.3%	42%	29.1%
Smoking			
Yes	4.2%	27.5%	33.7%

No	5.5%	72.5%	66.3%
Diabetes Mellitus			
Yes	7.1%	46.4%	32.7%
No	4.1%	53.6%	67.3%
Renal Dysfunction			
Yes	8%	15.9%	9.9%
No	4.8%	84.1%	90.1%
COPD			
Yes	14.2%	2.9%	0.9%
No	5%	97.1%	99.1%
Obesity			
Yes	5.2%	21.7%	21.3%
No	5.1%	78.3%	78.7%
Reoperation			
Yes	15%	17.4%	5.3%
No	4.5%	82.6%	94.7%
Emergent Surgery			
Yes	4.1%	49.3%	62%
No	6.7%	50.7%	38%
Previous myocardial infarction			
Yes	5.5%	21.7%	20.2%
No	5%	78.3%	79.8%
Unstable Angina			
Yes	5.7%	4.3%	3.8%
No	5.1%	95.7%	96.2%

COPD, Chronic Obstructive Pulmonary Disease

Table2. Qualitative variables, Univariate Analysis for Risk Factors of Prolonged Mechanical Ventilation (n=1344)

Predictor	P-value
Female Gender	0.030
Smoking history	0.359
Diabetes Mellitus	0.025
Renal Dysfunction	0.105
COPD	0.159
Obesity	0.881
Reoperation	0.001
Emergent Surgery	0.104
Previous myocardial infarction	0.795
Unstable Angina	0.747

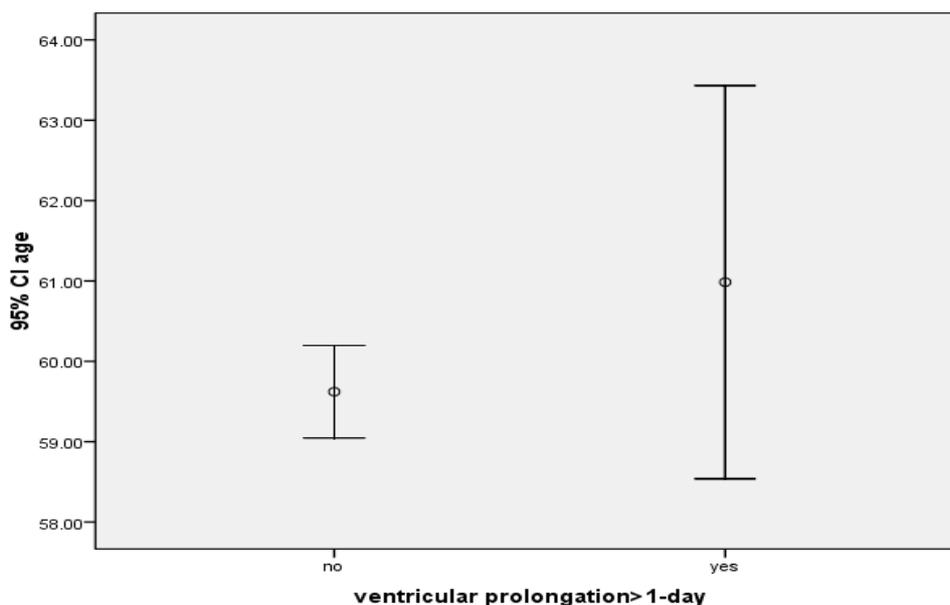


Figure 2: Mean age of patients according to mechanical ventilation subgroups (95% CI)

Table 3. Quantitative variables, comparison between patients with prolonged ventilation and patients with ventilation <24 hours (n=1344)

Predictor	Mean±SD (Ventilation>24 hrs)	Mean±SD (Ventilation<24 hrs)	P-value
Age	61.2±10.1	59.6±10.4	0.208
LVEF	41%±11.6	46.6%±19.5	0.038
Cross Clamp Time	78.5±38.7 min	60.7±31.4 min	0.001
CPB time	138.1±61.1 min	106.7±35.4 min	0.001

LVEF: Left Ventricular Ejection Fraction; CPB time: Cardiopulmonary Bypass time

DISCUSSION

The CABG surgery is a common procedure worldwide in the course of treating IHD patients. If performed by a team of expert surgeons on patients with no serious underlying medical condition and a normal left ventricle function, it is considered safe and has a mortality rate of less than 1%.

One of the more grave complications of this surgery is respiratory failure and requires long term mechanical ventilation and is closely associated to the mortality and morbidity rates of the CABG surgery.

This study was intended to assess the prevalence of prolonged mechanical ventilation in post-CABG patients and identify the predicting factors for this complication.

In the study executed by Légaré JF et al and in other researches too, the risk of prolonged ventilation after CABG is evaluated and stated in the range of 3-32% (6, 7, 10 , 11). In the present study 1344 patients were observed and 69 of the patients required longer ventilation after surgery, thus resulting in a prevalence of 5.1% which is compatible with other studies.

It was observed that in patients who required prolonged ventilation the cardiopulmonary bypass time (CPB time) and the cross-clamp time had been longer, comparing to those who could be extubated in 24 hours or less. This finding is also supported by previous studies such as the study of Y. Suematsu et al. performed throughout 1994 to 1998 (10).

Elongated CPB time increases the polymorphonuclear (PMN) and complement system activity (12). PMN mediators play a major role in the inflammation of pulmonary endothelium and ischemic endocardium tissue during the CABG operation (13-15). these mediators also account for systemic complications like increased permeability in the sarcolemma membrane which in turn results in undesirable weight gain and delays rapid recovery after surgery (16).

Prolonged CPB time and extensive aortic clamp can lead to cardiac failure and hypothermia during the surgery. Hypothermia can alter the distribution and decrease the metabolism of the administered anesthetics and muscle relaxant drugs. These all lead to delay in recovery thus prolonged mechanical ventilation (17).

The female gender was another factor which significantly affected the extubation time for the worst and was recognized as a predicting risk factor. This result was also reported in

previous studies (6, 11, 18). Smaller physiques in women and smaller coronary artery diameter in comparison to men, could explain this effect (19). Another explanation could be that women develop coronary artery disease at a later age than men, and therefore CABG surgery is needed at higher age. Although this was the case in our study too, but gender was an affective factor independent of other variables.

The prevalence of elongated ventilation was higher in patients who were re-operated and this was statistically significant. Previous studies such as Sachin et al had also reported the same results (7). Re-operation is because of hemorrhage or other complications of the first CABG surgery, and could cause prolonged ventilation because of unstable hemodynamics, pulmonary edema and non-cardiogenic pulmonary edema due to excessive transfusion of blood supplementary and volume over load (8). Also the excess of anesthetics required for a second surgery to locate and stop the source of bleeding, is another possible explanation for prolonged ventilation (8).

Prolonged ventilation was required more in patients diagnosed with diabetes mellitus than in those without and this was statistically significant. Oxygen transfer, before and after CABG, alters in diabetes

patients in contrast to non-diabetes (20). High plasma glucose levels affect neutrophil-endothelium behavior in multiple ways: altering the metabolism of arachidonic acid, increasing protein kinase C activity, increasing diacylglycerol activity and decreasing nitric oxide activity in the endothelial cell (20-23). also through increasing the formation of free radicals , high glucose levels cause cell dysfunction and therefore delay the extubation (24).Spivak et al also reached this result in their study (25).

Left ventricle ejection fraction was lower in patients who developed prolonged need for mechanical ventilation, than in those who were successfully extubated earlier. This difference was significant in our study results as it had been in other researches. Légaré JF et al and P.Branca et al both explained that LVEF before the surgery has a definite effect on ventilation duration after the surgery. This could be due to decreased tissue perfusion and dysfunctional oxygen exchange which will lead to prolonged ventilation (6, 11).

In this study other variable factors were also evaluated such as age, obesity, smoking history, COPD, underlying renal failure, emergence surgery, unstable angina and history of myocardial infarction. None of these had a statistically significant effect on

the outcome and possibly need further evaluation on more patients.

However this study was a retrospective research and upon the patients' medical data files, thus there could be unintentional errors in the data entry, concerning the profiles, baseline variable and complications (mainly clinical manifestations) or the complicated conditions might be understated. This said, as the patients with less than standard files were excluded from the study, it is not likely that entry errors should have compromised the results.

Also in some previous studies, the effect of possible predictors such as unstable angina, COPD history and age have been inspected and while some studies stated the above factors to be affective others argued not so. For instance, regarding the effect of COPD on ventilation duration, Spivack et al and Manganas et al, like this study, did not find statistical significance regarding the effect of these factors on ventilation (25, 26).

In the study N.W. Salomon et al performed on 698 post-CABG patients, from 1990 to 1994 , it was stated that prolonged mechanical ventilation , long and short term mortality and hospitalization time, all had higher rates in patients older than 75 years comparing to younger patients, but the difference had not been significant and was

dependent on other additional variables (27). In our study, too, age was not identified as an affective predictor.

What is important is to identify at-risk-patients who are candidate for CABG. Then, risk predictors may be reduced or corrected with appropriate management, for instance performing surgery in shorter time, adjusting the plasma glucose levels before the surgery, careful prevention of hemorrhage after surgery and possibly LVEF improvement.

Identifying at-risk-patients and minimizing the risk factors can lead to reduced prevalence rate of elongated mechanical ventilation and therefore reduced expenses and better allocation of resources.

One distinguishing property of this study is that it was carried out on coronary artery bypass patients exclusively, whereas in other studies, heart surgery patients in general were inspected. This article recommends more assessments on CABG patients to inspect the risk predictors in more detail and present prevention strategies for these factors that would eliminate the mortality and morbidity rates and lower hospital costs.

CONCLUSION

CABG is a common operational procedure worldwide in the treatment of IHD. One of the grave complications of CABG is respiratory failure and consequently long

term ventilation which increases the mortality and morbidity rates of the surgery. One manifestation of respiratory failure is prolonged need for mechanical ventilation. Identifying the predictor factors of prolonged requirement of ventilation after surgery, can assist to prevent it. In this study presumptive predictors were assessed so to identify at risk patients, eliminate the risks as much as possible, decrease mortality and reduce hospital expenses. Further studies on CABG patients to inspect the risk factors in more detail and presentation of strategies for these factors is recommended.

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CONFLICT OF INTEREST

There is no conflict of interest in this study.

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