

# The Risk Factors of Prolonged Mechanical Ventilation after Isolated Coronary Artery Bypass Graft Surgery

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## Abstract

**Background:** Failure to wean a patient from mechanical ventilation after cardiac surgery is associated with poor outcome.

**Aim:** The present study was performed aimed to investigate the risk factors of prolonged mechanical ventilation (PMV) following isolated coronary artery bypass graft (CABG) surgery.

**Method:** This retrospective cohort study was performed on 2155 consecutive adult patients undergoing isolated coronary artery bypass graft surgery (May 2012 to November 2016 at Imam Reza hospital, Mashhad, Iran). The subjects were assessed for duration of weaning from mechanical ventilation, predictive risk factors for prolonged mechanical ventilation and associated outcomes including intensive care unit (ICU) and hospital length of stay (LOS), and mortality. Data were analyzed by SPSS (version 22).  $P < 0.05$  was considered statistically significant.

**Results:** The median (25 -75 percentile) duration of mechanical ventilation was 360 (225-540) minutes. Also, 51.20%, 45.80% and 2.30% patients were weaned from mechanical ventilation in less than 6 hours, 7 to 24 hours, and more than 24 hours, respectively. Cerebral vascular accident was the most common cause of PMV (34.04%). After adjustment for confounder variables, on-pump CABG ( $P < 0.05$ ), duration of surgery ( $P < 0.01$ ), preoperative renal failure ( $P < 0.05$ ) and *New York Heart Association* (NYHA) class 4 were associated with PMV ( $P < 0.05$ ). PMV was associated with increased length of ICU and hospital stay ( $P < 0.01$ ). There was a higher mortality rates in patients with PMV ( $P < 0.001$ ).

**Implications for Practice:** Most patients are weaned from mechanical ventilation within 24 hours uneventfully after isolated CABG. Furthermore, on-pump CABG, prolonged surgery, preoperative renal insufficiency, and NYHA class 4 were independent predictors of prolonged mechanical ventilation. Identifying the risk factors causing PMV can prevent its adverse consequences.

**Keywords:** Coronary artery bypass graft surgery, Mechanical ventilation, Weaning

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## Introduction

Heart surgery is one of the most common surgeries in the world; more than 30,000 heart surgeries are performed in Iran every year (1,2). Patients are generally transferred to the intensive care unit (ICU) following cardiac surgery while intubated. They are weaned from mechanical ventilation when the effects of anesthetics subside and gain acceptable level of consciousness, with hemodynamic stability and no profound bleeding, as well as other necessary weaning requirements. Most of these patients are weaned uneventfully within a few hours postoperatively. However, some patients may require prolonged ventilator support which may increase the rate of mortality (3,4) and morbidity (5,6) including increased length of ICU and hospital stay (7), acute kidney injury (8), and health resource utilization and costs (9).

The frequency of prolonged mechanical ventilation (PMV) after cardiac surgery ranged from 2.9% to 8.6% depending on the nature of the surgery and definition of PMV (6, 10, 11). This may vary over time due to changes in patients' characteristics and surgical and anesthetic technique (12).

Some perioperative risk factors have been reported as predictors of PMV after cardiac surgery, these factors include female sex (3), pump time (13), cross clamp time (5), duration of surgery (14), cardiac dysfunction (13), combined surgery (5, 15), chronic kidney disease (5, 16), low ejection fraction (EF) (4, 7), chronic obstructive pulmonary disease (COPD) (4, 5), advanced age (5, 7, 14), need for dialysis (17) and blood transfusion (15, 16).

Early and timely removal of tracheal tube improves the functioning of the respiratory tract and mucous exchanges, and as a result, reduces the incidence of pneumonia, atelectasis and other pulmonary complications, and also increases the comfort level of patient and reduces the costs and duration of ICU hospitalization. Today, the need for high-quality, safe and cost-effective care for patients undergoing CABG surgery has led to many efforts to reduce the length of stay in intensive care units and hospitals (18). Therefore, specific protocols should be designed considering its consequences and complications to properly and safely manage patients and try to recover quickly after surgery.

The present study was performed aimed to determine the risk factors of prolonged mechanical ventilation after isolated CABG in order to decrease the associated mortality and morbidity.

## Methods

This retrospective cohort study was performed on 2155 consecutive adults undergoing elective isolated CABG including off-pump, on-pump, and on-pump beating surgeries from May 2012 to November 2016 at Imam Reza hospital, Mashhad, Iran. Data were extracted from the paper file of the patient and the hospital information system (HIS). Patients had given informed consent to the anonymous use of their information for educational and research purposes. The inclusion criteria were the patients undergoing coronary artery surgery, no chronic lung disease, and no dependent on inotrope, vasopressor, or severe sedative drugs. The patients were excluded if they were under mechanical ventilation preoperatively, extubated on arrival, expired within 24 hours postoperatively, or data regarding weaning was missing.

Patients received oral lorazepam 1 mg, intravenous morphine 0.05 mg/Kg, and intravenous promethazine 25-50 mg as premedication. Anesthesia was induced with fentanyl 10-15 µg/Kg, midazolam 0.1 mg/Kg, and propofol 1.5-2 mg/Kg, and then atracurium 0.15 mg/Kg was given to facilitate tracheal intubation. A central venous line was fixed in either jugular vein. Fluid therapy was performed during surgery by isotonic crystalloid solution to maintain urine output more than 1 mL/kg/hour, lactate less than 2 meq/L, and mean atrial pressure (MAP) in 70-80 mmHg range. Propofol 50-100 µg/Kg/min and fentanyl 2-10 µg/Kg/hour, and atracurium 3 µg/Kg/min were infused to maintain the anesthetic state. If the hemoglobin dropped to less than 10 mg/dL during operation, a cross match test was performed and a unit of red blood cell (RBC) was transfused to maintain hemoglobin level higher than 10 mg/dL. Epinephrine/norepinephrine 0.01-0.02 mic/kg/minute or dobutamin 2-20 mic/kg/minute were used to maintain MAP in 70-80 mmHg range fluid therapy was not effective.

Upon ICU admission, all patients received mechanical ventilation initially with synchronized intermittent mandatory ventilation (SIMV), tidal volume 8 ml/kg ideal body weight (IBW), frequency 10 to 15 rate per minute (to keep PaCO<sub>2</sub>: 35-45 mmHg), positive end-expiratory pressure (PEEP): 5 cmH<sub>2</sub>O, inspiratory time: 1.5 second, fraction of inspired oxygen (FiO<sub>2</sub>) 40%, and pressure support (PS) 10 cmH<sub>2</sub>O. Once the patient began spontaneous breaths and gained appropriate level of

consciousness and presented satisfactory clinical conditions including hemodynamic stability, absence or minimal bleeding (less than 50 ml per hour), acceptable oxygenation ( $\text{PaO}_2:\text{FiO}_2 > 200$ ) and ventilation ( $\text{PaCO}_2$  30-50mmHg), absence of severe acidosis or alkalemia (pH 7.25-7.50), and no life threatening arrhythmia, respiratory frequency was decreased to 4 breaths per minute. The mode was then switched to pressure support ventilation (PSV) with a pressure support (PS) level to achieve a spontaneous tidal volume of 6-8 ml/kg ideal body weight and respiratory rate less than 30 breaths per minute. Patients were extubated if they were fully conscious, without copious secretions and with minimum tidal volume 6 ml/kg with a PS of 8 cmH<sub>2</sub>O. They were reintubated if developed hypoxic or hypercapnic respiratory failure, loss of consciousness, cardiopulmonary arrest, severe hemodynamic instability, or massive bleeding requiring reexploration for surgical reasons.

Patients were monitored for vital signs, invasive blood pressure, SpO<sub>2</sub>, electrocardiography, level of consciousness, urine output, bleeding, and meticulous attention by critical care team including an intensivist, critical care fellow, or anesthesia residents per shift.

Weaning patterns were defined as fast track (weaning in less than 6 hours), dysfunctional ventilator weaning response (DVWR) (7-24 hours) and PMV (more than 24 hours).

The patients were assessed for the causes of DVWR and PMV, the need for reintubation and its causes, ICU and hospital LOS, and in hospital mortality. The duration of the tracheal tube remain was calculated from the moment that the patient entered the ICU until when the tracheal tube was removed and the person was able to breathe spontaneously. According to the protocol in the department, the mechanical ventilation for more than 6 hours was considered as PMV.

The association of PMV and perioperative variables was explored. These variables included: age, sex, body mass index (BMI), history of myocardial infarction (MI) within the past 90 days, chronic obstructive pulmonary disease (COPD), cerebrovascular accidents (CVA), diabetes, opium abuse, smoking, anemia, renal insufficiency (defined as creatinine more than 1.3 mg/dL), EF, NYHA class, Euro II score, type of surgery, operation time, use of cardiopulmonary bypass (CPB), and intraoperative bleeding requiring more than one unit of red blood cells.

### **Statistical analysis**

Means and standard deviation were used for normal distribution variables and median and interquartile range for otherwise. Frequency and percentage were used for categorical variables. Normal distribution of data was assessed by Kolmo-grove Smirnov test. Chi-square test or Fisher's exact test was used for categorical variables. Mann-Whitney test was used to compare non-parametric variables between the groups. Univariate and multivariate logistic regression model was used to determine the variables associated with PMV. Variables with P value less than 0.1 in univariate analysis were included in multivariate model. Forward method was used for entering variables in the model.  $P < 0.05$  was considered statistically significant. Data were analyzed using SPSS 22 (IBM SPSS, Chicago, IL).

### **Results**

During the study period, a total of 2155 patients were explored for the inclusion criteria and 2074 individuals were included in the study. The ratio of male to female was 1.88: 1 and the mean age of patients was  $60.24 \pm 10.57$  years. Demographic characteristics and surgical data of patients were displayed in Table 1. In this study, 15 (0.7%) patients expired in less than 24 hours. The results showed that 1062 (51.2%), 950 (45.8%) and 47 (2.3%) patients were weaned from mechanical ventilation in less than 6 hours (fast track), 7 to 24 hours (DVWR), and more than 24 hours (PMV), respectively. Also, 20, 28, and 3 patients were reintubated in the fast track, DVWR, and PMV groups, respectively. The most common causes of re-intubation were loss of consciousness and hemodynamic instability.

Among patients who required PMV, 20 cases underwent tracheostomy and 2 were transferred to general ICU in order to accomplish their weaning process because of bed shortage. Patients undergoing on-pump CABG had longer duration of mechanical ventilation compared to off-pump and on-pump beating heart patients ( $P < 0.001$ ). Distribution of frequency of weaning type based on surgical technique was presented in Table 2. Failure to gain consciousness was the most common cause of DVWR and PMV (Table 3). Ischemic cerebral vascular accident (CVA) was the most common cause of delayed awakening in patients requiring PMV. Before adjustment, prolonged

**Table 1. Patient's demographic characteristics and surgical data**

Sex	Male	1354 (37.71)
	Female	720 (62.29)
NYHA class	I	309 (14.90)
	II	1085 (50.20)
	III	626 (36.00)
	IV	54 (2.30)
Social history	Smoking	268 (12.90)
	Drug abuse	413 (19.90)
Perioperative risk factors	Use of CPB	476 (22.98)
	EF Median	50 (2.41)
	HLP	749 (36.16)
	None	799 (38.45)
Underlying disease	COPD	53 (2.55)
	HTN	1076 (51.95)
	Recent MI	130 (6.27)
	CVA	35 (1.68)
	Diabetes	618 (29.79)
	Renal insufficiency	128 (6.17)
	Age (years)	60.24±10.57
	Duration of surgery (min)	152.73± 44.80
	Weight (kg)	70.50 ± 13.11
	Height (Cm)	164.48 ± 9.93
	BMI (%)	26.11 ± 4.49

Data are presented as frequency (percentage) or mean ± standard deviation

mechanical ventilation was associated with use of cardiopulmonary pump, duration of surgery, EF<40%, preoperative anemia and renal insufficiency, NYHA>2, and Euro score (Table 4). After adjustment for other confounders, on-pump CABG, duration of surgery, preoperative renal insufficiency, and NYHA class 4 were the independent factors for PMV (Table 4).

**Table 2. Weaning pattern by types of CABG**

Variable	Off-pump	On-pump	On-pump beating	P value*	$\chi^2$
Frequency	1660(80.62)	273(13.1)	126 (6.1)		
Fast track	902 (54.3)	103 (37.7)	57 (45.2)	<0.001*	1.64
DVWR	732 (44.10)	156(57.1)	62(49.2)		
PMV	26 (1.61)	14(5.1)	7(5.6)		

\* Chi square test

**Table 3. Etiologies of DVWR and PMV**

Variable	DVWR	PMV
	Frequency (percentage)	Frequency (percentage)
Delayed awakening	620(65.3)	2(4.25)
CVA	0(0)	18(38.29)
Bleeding	112(11.8)	4(8.5)
Hemodynamic instability	60(6.3)	14(29.78)
Rexploration	25(2.6)	2(4.3)
Metabolic acidosis	72(7.5)	0(0)
Agitation	35(3.7)	0(0)
Respiratory acidosis	14(1.5)	2(4.25)
Hypoxemia	8(0.8)	5(10.63)
Arrhythmia	2(0.2)	0(0)
Pulmonary edema	2(0.2)	0(0)

**Table 4. Risk factors associated with PMV**

Variable	OR*( 95%CI)	P-value
Age (yr)	1.01(0.98-1.04)	0.29
Sex (Male)	0.84 ( 0.46-1.53)	0.58
BMI	1.01 (0.94-1.08)	0.79
Recent MI	1.89 (0.87-4.12)	0.105
History of DM	1.01 (0.55-1.85)	0.97
Smoking	0.79 (0.31-2.02)	0.62
Surgery type (on pump)	3.39 (1.75-6.60)	<0.001
Surgery type (on pump beating)	3.70 (1.57-8.69)	0.003
Duration surgery(min)	1.006 (1.003-1.01)	<0.001
Univariate analysis		
Left main	1.07(0.41-2.81)	0.876
3 vessels	0.96 (0.33-2.80)	0.95
40<EF	3.01 (1.62-5.58)	0.001
Anemia	0.99 (0.98-1.01)	0.93
Renal failure	2.38 (1.17-4.86)	0.17
COPD	0.90 (0.12-6.63)	0.91
Drug abuse	0.69 (0.32-1.56)	0.38
NIHA(2)	6.39 (0.85-47.64)	0.07
NIHA (3)	9.19 (1.22-69.19)	0.03
NIHA(4)	38.37(4.52-324.75)	0.001
Euro score	1.17 (1.02-1.33)	0.017
Multivariate analysis		
Surgery type (on pump)	2.96 (1.10-6.57)	0.029
Surgery type (on pump beating)	1.29(0.28-5.93)	0.74
Duration surgery(min)	1.01 (1.003-1.014)	0.002
40<EF	1.61 (0.62 -4.20)	0.32
Renal failure	2.57(1.09-6.07)	0.03
NIHA(4)	13.10(1.28-133.18)	0.03

\*Odds ratio (OR) was estimated by binary logistic regression

Patients with prolonged mechanical ventilation had longer ICU stay [median (IQR); 6(7) days versus 2(1) days; ( $P < 0.01$ )]. The median hospital LOS were 11(11) and 7(2) days in PMV and no PMV groups, respectively ( $P < 0.001$ ). The mortality rate was higher in the PMV (21 [35%] cases) than no PMV (26 [1.3%] cases) group ( $P < 0.001$ ).

## Discussion

The present study was performed with aim to investigate ventilator weaning process and etiology of prolonged mechanical ventilation after isolated CABG. According to the results of the present study, most patients were successfully weaned within 24 hours after surgery. Furthermore, on-pump CABG, duration of surgery, preoperative renal insufficiency, and NYHA class 4 were the predictors of prolonged mechanical ventilation which led to increased ICU and hospital LOS as well as mortality. Since there is increased number of old sicker patients with more comorbidities, longer ventilation time is expected after cardiac surgery (19). Hsu et al. reported that age is considered as one of the background factors before the operation, which leads to increasing days of intubation and long-term mechanical ventilation (20). Also, Imanipour et al. indicated that age was the only variable related to the length of the endotracheal tube remained (21). But in the present study, no correlation was observed between age and PMV, which could be due to the high average age of participating patients (60 years), but the preoperative renal insufficiency, and NYHA class 4 as underlying disease were the predictors of prolonged mechanical ventilation. Also, Jubran et al. showed that age and gender do not affect the duration of ventilation, but underlying diseases can affect the duration of mechanical ventilation and increases the duration of ICU hospitalization (22).

Perioperative factors such as low static pulmonary compliance due to sternotomy, pleural drains, trauma to chest wall during dissection, decreased intercostal blood supply after removal of internal thoracic artery, use of CPB, reduced vital capacity and functional residual capacity may lead to postoperative pulmonary dysfunction and further mitigate weaning process (9). Vargas and colleagues demonstrated that pleural effusion and atelectasis due to postoperative pleuro-pulmonary changes

might delay weaning process (23). The results of duration of mechanical ventilation and hospital stay in the present study can be explained by the inclusion criteria, because patients with COPD and other conditions that could cause respiratory complications were excluded from the present study.

There is no general agreement on definition of prolonged mechanical ventilation after cardiac surgery and the duration ranges from 1 to 10 days (3, 11, 13, 16). In the present study, PMV was considered as ventilation time more than 24 hours. It has been reported that even ventilation longer than 24 hours has been associated with adverse outcomes (4, 10).

Failure to wean patients from mechanical ventilation after cardiac surgery has been associated with adverse early outcomes (5, 11, 15). Some of these patients are transferred to other specialized facility to speed the process of weaning (24).

The incidence of PMV was 2% in the present study that is less than other reports in the literature (10, 11, 16, 25). This can be attributed to inclusion of only isolated CABG, use of a protocolized weaning plan, trained nurses, and different characteristics of the patients. Totunchi et al. (16) reported several perioperative factors as the predictors of PMV including gender, history of COPD, chronic kidney disease and endocarditis, type of surgery, operation time, pump time, transfusion in operating room, postoperative bleeding and inotrope dependency. However, multivariate analysis was not performed in their study and it is not known if these factors are independent predictors for PMV. Papplardo and colleagues demonstrated that dialysis, low cardiac output, emergency surgery, redo surgery, preoperative renal failure, and female sex were associated with increased risk of PMV and related mortality and morbidity (3). They suggested that PMV longer than 7 days can even influence long term patients' outcomes and quality of life (3). However, in the present study, the patients were not followed after discharge and it was not possible to assess the long term outcomes.

Despite different surgical population in the present study, the results were in consistent with the results of the study by Gumus et al. (10) which showed that renal dysfunction was an independent risk factor for PMV. Severe cardiac dysfunction has been reported as a predictor for patients requiring PMV (13, 17). Similarly, that the results of the present study showed that advanced NYHA class was a strong predictor of PMV indicating inability of these patients to tolerate early weaning owing to their poor cardiovascular reserve.

Failure to gain consciousness has been suggested as the leading cause of failure to early extubation after cardiac surgery (26). In line with the findings of the present study, Yende et al. reported that depressed level of consciousness is the leading cause of failure to wean within 8 hours and hypoxemia is the most common cause of PMV (27). In contrast, the present study demonstrated that delayed awakening was the most common cause of PMV. This discrepancy may be attributed to the difference in demographic characteristics of the patients and comorbidities and surgical anesthetic techniques.

### **Implications for practice**

Most patients are weaned from mechanical ventilation within 24 hours uneventfully after isolated CABG. Nevertheless, those requiring prolonged mechanical ventilation have increased ICU and hospital LOS and mortality. Furthermore, on-pump CABG, prolonged surgery, preoperative renal insufficiency, and NYHA class 4 were independent predictors of prolonged mechanical ventilation.

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### **Conflicts of interest**

The authors declared no conflict of interest.

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