Monaldi Arch Chest Dis
2010; 74: 22-27

ORIGINAL ARTICLE

Predictors and Early Outcome of Prolonged Mechanical Ventilation in Contemporary Heart valve Surgery

Predittori ed outcome della ventilazione meccanica prolungata nella chirurgia valvolare contemporanea

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ABSTRACT: ***Predictors and Early Outcome of Prolonged Mechanical Ventilation in Contemporary Heart valve Surgery. M. Shirzad, A. Karimi, S.H. Ahmadi, M. Marzban, M. Tazik, H. Aramin.***

Background: During last decades mechanical ventilation has been an important support in the postoperative management of patients undergoing cardiac surgery. This study was designed to determine the predictors of prolonged mechanical ventilation (PMV) in patients undergoing heart valve surgery.

Methods: This retrospective study considered of 1056 patients who underwent isolated valve surgery at Tehran Heart Center from March 2002 to March 2009. PMV is considered as mechanical ventilation period of ≥24 hours at postoperative hospital stay in this study.

Results: PMV occurred in 6.6% of patients. Initial ventilation hours, atrial fibrillation, cardiac arrest and reintubation were the most prevalent postoperative complications. Preoperative renal failure, postoperative stroke, intra aortic balloon pump insertion, emergent operation, complete heart block, longer perfusion time were independent predictors of PMV in our patients.

Conclusion: PMV is associated with significant comorbidities and increased hospital mortality. Strategies to delineate the patients at risk and to modify these risk factors by prophylactic measures should probably lead to a lower incidence of prolonged mechanical ventilation for patients undergoing isolated valve surgery.

Keywords: CABG, prolonged mechanical ventilation, mortality, morbidity.

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Introduction

During the last decades mechanical ventilation has been an important support in the postoperative management of patients undergoing heart valve surgeries, coronary artery bypass graft (CABG), and other cardiac surgery procedures. Most of the patients are extubated within 6 to 8 hours after operation [1]; however, a considerable number of patients need mechanical ventilation for a prolonged period after cardiac surgery, and this is associated with increased mortality and morbidity [2, 3]. Previous studies described predictors of PMV in patients undergoing coronary artery revascularization [4-6]. In addition a great number of patients presenting with an aggravating risk profile due to increased multiple preoperative comorbidities most likely would experience this complication [7]. Thus, we aimed to understanding the epidemiology of PMV in a contemporary cohort of valvular surgery patients and to determine predictors and early outcomes following this complication. Such preliminary study may be a key element to design prevention strategies for preoperative evaluation.

Material & Methods

This retrospective study considered 1056 patients who underwent isolated valve surgery at Tehran

Heart Center from March 2002 to March 2009. We excluded patients who had concomitant cardiac surgery, preoperative cardiogenic shock, recent myocardial infarction (< 7days), pulmonary edema and ventricular assist device implantation. PMV as a postoperative complication is our main variable and it is considered as mechanical ventilation period of ≥24 hours from the time of arrival to ICU to the time of extubation as define by the Society of Thoracic Surgeons (STS) guideline [7]. In each analysis, we grouped the patients by those who needed PMV and those who did not. For all patients, data recorded consisted of information on patient characteristics and their preoperative comorbidities, operative and postoperative variables. All data were prospectively entered into the database. The definitions of STS were used for all entries in the database [8]. The protocol was approved by the institutional review board ethical committee of our center.

Anesthetic and Surgical Technique

All patients received 1-2 mg lorazepam (Chemidarou, Tehran, Iran) the night before their surgery. Preoperative sedation consisted of 0.1 mg/kg morphine sulphate (Darou Pakhsh, Tehran, Iran) and 0.5 mg/kg promethasin (Tehran Chemie, Tehran, Iran), both administered one hour before surgery. Anaesthesia was induced with 5-10 μg/ kg fentanyl (Fentanyl-Janssen®, Janssen-Cilag, Beerse, Belgium), with sodium thiopental (Thiopental®, Sandoz, Kundl, Austria) 250 mg IV. As neuromuscular blocker these patients received pancuronium bromide (Darou Pakhsh, Tehran, Iran) with the following details: 80 μg/kg for intubation and 40 μg/kg every hour as maintenance. Before CPB, these patients received no halothane (Nicholas Piramal India, Chennai, India), or < 0.5 minimal alveolar concentration (MAC). Propofol (Propofol-Lipuro®, B Braun Melsengen, Melsengen, Germany) infusion was used for maintaining anaesthesia at 20-50 μg/kg/min until the end of surgery [9]. Briefly, heparin was given intravenously at a dose of 300 IU/kg, with additional intravenous doses of 3000 IU to maintain the activated clotting time more than 480 seconds throughout cardiopulmonary bypass (CPB). A standard CPB performed by use of a roller pump (flow rate, 1.8-2.4 L/min/m2) and membrane oxygenator. Mean arterial pressure was maintained at 50 to 60 mm Hg during CPB. For all operations, myocardial protection was predominantly done by a combination of intermittent antegrade and retrograde cold blood cardioplegia, with moderate systemic hypothermia to 28°C to 32°C. On aortic surgery, where deep hypothermic circulatory arrest was required, the target cooling temperature was 18°C.

ICU Management

At the end of the operation, patients were transferred to the ICU. The lungs were ventilated with 60% oxygen using volume controlled ventilation. Adjustments in FIO2 and respiratory rate were made according to routine blood gas analysis, to maintain PaO2 between 80 and 100 mm Hg, and PaCO2 between 35 and 40 mm Hg. Forced air warming was used until a stable nasopharyngeal temperature of 37°C had been reached. The decision to extubate a patient was at the independent discretion of the consultant anesthetist and followed a predefined protocol, aiming at early extubation. Once the patient was warmed to 36°C, weaning from the ventilator was performed in the presence of hemodynamic and respiratory stability (no or decreasing use of cardioactive drugs), absence of significant bleeding (< 100 ml/hour), absence of significant arrhythmias, and oxygen saturation> 95% with FiO2< 0.50. Before extubation the patient had to be neurologically alert and orientated with equal movement throughout all limbs, initiating adequate respiration and obeying commands. Decisions about transfers from the ICU to the post ICU and from the post ICU to the ward, and vice versa, were made by anesthesiologist and cardiac surgeons. Extubated patients who required continuous monitoring of either blood pressure or urine output, or prolonged chest physiotherapy were moved to the post ICU.

Statistical method: Numerical variables were presented as mean ± SD, while categorical variables were summarized by absolute frequencies and percentages. Continuous variables were compared using the Student's t test or nonparametric Mann-Whitney U test whenever the data did not appear to have normal distributions, and categorical variables were compared using chi-square test. Multivariable stepwise logistic regression model for risk factors of prolonged mechanical ventilation was constructed. Variables were included into the Multivariable model if the p value was found to be less than or equal to 0.15 in the univariate analysis. The associations of independent predictors with PMV in the final model were expressed as odds ratios (OR) with 95% CIs. Model discrimination was measured using the c statistic, which is equal to the area under the ROC (Receiver Operating Characteristic) curve. Model calibration was estimated using the Hosmer-Lemeshow (HL) goodness-of-fit statistic (higher p values imply that the model fit the observed data better). For the statistical analysis, the statistical software SPSS version 13.0 for windows (SPSS Inc., Chicago, IL) and the statistical package SAS version 9.1 for windows (SAS Institute Inc., Cary, NC, USA) were used. All p values were 2-tailed, with statistical significance defined by p≤0.05.

Result

Patient characteristic

Of the 1056 patients undergoing isolated valve surgery 500 (47.3%) were females, and average age of all patients was 48.43 ± 13.7 years. There were significant differences in both groups with respect to mean age (P=0.009). More than 14% of patients with PMV were diabetic and 15.7% of them had previous history of cerebro vascular accident (CVA). Ten percents of them had history of renal failure (preoperative serum creatinin ≥2 mg/dl) and endocarditis. Redo valve surgery was found in 24.3% of this patients. Combined valve surgery was found in 37.1% of patients. Patients with PMV had longer perfusion time and total ICU stay. Baseline patient characteristics, preoperative and operative risk factors are presented in Table 1.

Table 1. - Demographic, preoperative and operative characteristics of patients undergoing isolated valve surgery*

p-value	Without PMV 986 (93.4%)	With PMV 70 (6.6%)	Variables
			Preoperative risk factors
0.972			Gender
	519 (52.6%)	37 (52.9%)	Male
	467(47.4%)	33(47.1%)	Female
0.009	48.25±13.66	53.93±12.84	Age
0.183	25.24±4.77	24.46±4.56	BMI (kg/m^2)
0.997	197 (20%)	14(20%)	Smoke
0.087	82 (8.3%)	10 (14.3%)	Diabetes
0.088	244(24.7%)	11(15.7%)	Dyslipidemia
0.458	8(0.8%)	1(1.4%)	Peripheral vascular disease(PVD)
0.531	235(23.8%)	19(27.1%)	Hypertension
0.090	93(9.5%)	11(15.7%)	Cerebrovascular accident (CVA)
<0.001	16(1.6%)	7(10.0%)	Renal failure (RF)
0.063	2(0.2%)	1(1.4%)	Chronic lung disease (severe)
0.017	39(4.0%)	7(10.0%)	Active Endocarditis
			Previous cardiovascular Surgery
0.008	4 (0.4%)	3 (4.3%)	CABG
<0.001	66 (6.7%)	17 (24.3%)	Valve
0.144	27(2.7%)	4(5.7%)	Previous myocardial infarction (MI)
0.002	682(69.2%)	36(51.4%)	NYHA ≥ III
0.730	36(3.7%)	2(2.9%)	Ejection Fraction <30%
0.126	50.15±10.51	48.14±11.67	Mean ejection fraction (%)
0.115	7 (7%)	2 (2.9%)	Number of diseased vessel ≥3
			Operative Risk factors
0.445			Aortic valve surgery
	23 (2.3%)	0(0%)	Repair
	467(47.4%)	40 (57.1%)	replacement
0.428			Mitral valve surgery
	24(2.4%)	2(2.9%)	Repair
	694(70.4%)	52(74.3%)	replacement
0.048	250(25.4%)	26 (37.1%)	Mitral and Aortic valve surgery
			Operative risk factors
<0.001	4 (0.4%)	5 (7.1%)	Emergent surgery
<0.001	18(1.8%)	19(27.1%)	Intra aortic balloon pump insertion (IABP)
<0.001	108.27±5.60	170.90±7.55	Perfusion time (min)
<0.001	52.68±7.33	216.69±22.87	Total hours of ICU stay
0.895	16.79±10.52	18.48±5.26	Hospital length of stay (HLOS)

* Data are expressed as absolute frequencies (percentages) or mean ± SD
CABG: Coronary Artery Bypass Grafting, EF: Ejection Fraction
PMV: Prolonged Mechanical Ventilation

Patient outcome

Out of 1056 valve procedures performed there were 52 in hospital death (4.9%), of which 2.08% were cardiac related. Seventy patients required ventilation for more than 24 hours (6.6%) after surgery with a mortality rate of 42.9% (p<0.001). Patients ventilated for more than 24 hours were ventilated for an average of 70.55±9.48 hours (range 25-255 hours) (Table 2). The overall median length of hospitalization was 18.48±5.26 days with a range of 3-177 days in patients with PMV (Table 1). The use of intra-aortic balloon pump

Table 2. - Postoperative complications in patients undergoing isolated valve surgery*

p-value	Without PMV 986(93.4%)	With PMV 70(6.6%)	Variables
<0.001	9.37±0.13	70.55±9.48	Initial ventilation hours
<0.001	44(4.5%)	13(18.6%)	Reoperation for bleeding
0.008	326(33.1%)	34(48.6%)	Atrial fibrillation
0.055	4(0.4%)	2(2.9%)	Valve dysfunction
<0.001	1(0.1%)	3(4.3%)	Tamponade
<0.001	10(1.01%)	15(21.4%)	Blood product transfusion
<0.001	3(0.3%)	11(15.7%)	Inotrops
<0.001	3(0.3%)	6(8.6%)	Continuous coma >24hr
<0.001	18(1.8%)	8(11.4%)	Complete heart block
<0.001	26(2.6%)	29(41.4%)	Cardiac arrest
0.291	4(0.4%)	1(1.4%)	Pulmonary emboli
<0.001	3(0.3%)	18 (12.9%)	Stroke
<0.001	15(1.5%)	14(20%)	Renal failure
<0.001	18(1.8%)	32(45.7%)	Re intubations
<0.001	4(0.4%)	4(5.7%)	Septicemia
<0.001	22(2.2%)	30(42.9%)	Mortality
<0.001	10(1.0%)	12(17.1%)	Cardiac Mortality
<0.001	12(1.2%)	22(31.4%)	Non-Cardiac Mortality

* Data are expressed as absolute frequencies (percentages) or mean ± SD
PMV: Prolonged Mechanical Ventilation

(IABP) was defined as any IABP use perioperatively and was required in 27.1% of patients. Inotropes were utilized in 15.7% of patients and were defined as any inotrope used post-operatively. Blood product use included: fresh frozen plasma, cryoprecipitate, platelets or packed red blood cells, and was limited to 21.4% of patients with 13 (18.6%) patients reoperated for bleeding. Permanent stroke (12.9%), renal failure (20.0%), complete heart blocks (11.4%) were significantly higher in patients with PMV. Details of surgical outcome are summarized in Table 2. Multivariate stepwise logistic regression analysis regarding preoperative and postoperative variables as independent predictors of PMV are shown in Table 3.

Discussion

In our study, we tried to discuss our finding in patients with isolated valve surgery who had PMV and compare their outcomes to those with ventilation time less than 24 hours after isolated valve procedure. The incidence of PMV after first CABG operation and after redo CABG was 5.5% and 10.5%, respectively [10]. This incidence in our population was approximately 6.6% which was associated with significant mortality rate as compared to patients with isolated valve surgery who did not had PMV (42.9% vs. 2.2%,p<0.001, respectively). Most of studies were attempted to assess preoperative predictors of PMV in patients undergoing CABG

Table 3. - Multivariate independent predictors of prolonged mechanical ventilation in patients undergoing valve surgery obtained by logistic regression

p-value	95% CI	OR	
0.014	1.424-22.484	5.657	Preoperative renal failure
<0.001	5.508-18.832	12.164	Postoperative stroke
<0.001	6.887-12.565	3.478	Intra aortic balloon pump insertion (IABP)
0.002	2.686-21.201	15.906	Emergent procedure
0.015	1.376-20.657	5.331	Complete heart block
0.012	1.118- 12.157	3.452	Perfusion time (min)

* CI: Confidence Interval, OR: Odds Ratio

surgery [11-14]. In a previous study it has been suggested that, female gender, age >70 years, diabetes, renal failure, active endocarditis, EF <30%, congestive heart failure, myocardial infarction, emergent procedure, reoperation, double aortic and mitral valve procedure and CBP time >180 min were predictors of respiratory failure after valve surgery [15]. In our study preoperative renal failure, IABP insertion, emergent procedures, longer perfusion time, postoperative stroke and complete heart block were independent factors associated with PMV. The result of one study described renal failure as a strong predictor of postoperative PMV in patients undergoing CABG and valve surgery [16]. Renal failure predisposes patients to adverse outcome and has been seen to be associated with pulmonary edema, sepsis and metabolic dysfunction which may require prolonged intubations [17]. It has been proved that renal failure can effectively influence a worse outcomes of cardiac surgery resulting in prolonged mechanical ventilation and prolonged ICU stay [18]. This study showed that emergent procedure was a predictor of PMV. In accordance with other reports it seems that emergent procedures has been associated with major postoperative complication in addition to increasing mortality and morbidity rate [19]. Our study also identified that IABP insertion was associated with PMV. In a trial study IABP insertion was an independent predictor of PMV in patients undergoing CABG [20]. In contrast other studies showed that IABP was not a major risk of PMV in patients who underwent either valve surgery or CABG [21, 22]. In our study a longer perfusion time was a significant predictor of PMV after isolated valve surgery. We believe that decreased functional residual capacity, reduced static dynamic compliance, increased alveolar-arterial oxygen gradient, atelectasis, metabolic and hemodynamic changes partially related to systemic inflammatory response syndrome (SIRS) might be the reasons for PMV [23, 24].

Our study showed that emergent operation was one of predictors of PMV after isolated valve surgery. Emergent operations usually are performed when a patient is in unstable condition; therefore, it is expected that the operative morbidity and mortality are increased. Patients undergoing emergent procedures necessarily have higher degrees of preoperative instability, and may not have had an opportunity for preoperative evaluation and risk factor modification. In our population, patients undergoing valve surgery had a significant and independent elevation of risk for prolonged mechanical ventilation. Our multivariate analyses emphasizes that postoperative stroke was a predictor of PMV. It has also been demonstrated by others that stroke is an independent predictor for PMV after CABG [25]. Moreover, the association of early stroke with prolonged mechanical ventilation may be explained by hypotension and subsequent cerebral hypoperfusion [26]. We also found that complete heart block occurred more frequently in patients with PMV. In a study by Chen et al, they identified the presence of a preoperative left bundle branch block (LBBB), and of concomitant left ventricular (LV) aneurysmectomy as reasons of bradycardia or complete heart block that may cause hypoxemia [27]; other studies showed that persistent hypoxemia was the most common cause for PMV [28]. In our patients without PMV the mean ± SD (standard deviation) hours of early intubation was 9.37±0.13 hours (Table 2). Recent advances in surgical and anesthetic techniques have facilitated early hospital discharge following cardiac surgery such as fast-track protocols. In the fast-track protocols early extubation has been shown to accelerate the ICU discharge [29-31]. However, the timing of early extubation (4 hours, 8hours) has varied among different reports and its precise definition has not been established [32]. There are several potential benefits of early extubation such as accelerating the return of pulmonary function and improving respiratory dynamics [33]. In some study intrapulmonary shunt fraction significantly improved among patients extubated early. In addition, mechanical ventilation itself can impair venous return and decrease cardiac output thus [34]. Although this study has not demonstrated the safety of early extubation, serious adverse effects were observed less frequents in patients without PMV.

Limitation

This was a retrospective observational study and therefore conclusions are necessarily limited in their application. This study included a cohort of patients who underwent adult cardiac valve procedures without discrimination between repair and replacement, thus our findings are therefore applicable cautiously to most valve surgery patients. There were important preoperative imbalances between groups. Regression modeling can never entirely account for these imbalances, and the adjusted estimates may still be subject to some residual confounding. Furthermore, clinical outcome analysis focused on postoperative mortality and morbidity and we were not able to provide information on late complications, quality of life, and cause of death following discharge. Noteworthy, several variables were not found to be independent risk factors for prolonged mechanical ventilation despite many of them often being considered markers of disease severity.

Conclusion

PMV is associated with significant comorbidities and increased hospital mortality. Strategies to delineate the patients at risk and to modify these risk factors by prophylactic measures should probably lead to a lower incidence of prolonged mechanical ventilation in patients undergoing isolated valve surgery.

Riassunto

Background: Negli ultimi decenni, la ventilazione meccanica si è dimostrata un fondamentale supporto nella gestione postoperatoria dei pazienti sottoposti a cardiochirurgia. Il presente studio è stato disegnato per valutare i fattori predittivi di ventilazione meccanica prolungata (PMV) in pazienti sottoposti a chirurgia valvolare.

Metodi: Questo studio retrospettivo ha considerato 1056 pazienti sottoposti a chirurgia valvolare isolata al Tehran Heart Center nel periodo marzo

2002-2009. PMV è stata considerata una ventilazione meccanica per un periodo ≥24 ore nel decorso post operatorio.

Risultati: PMV si è verificata nel 6.6% dei pazienti. Complicazioni post operatorie prevalenti sono state l'inizio di una ventilazione precoce, fibrillazione atriale, arresto cardiaco e reintubazione. In questa popolazione di pazienti, fattori predittivi indipendenti di PMV sono rappresentati da insufficienza renale preoperatoria, ictus nel periodo post operatorio, inserimento di pompa intraortica, operazione in emergenza, blocco cardiaco completo ed un più lungo tempo di perfusione.

Conclusioni: La PMV è associata a comorbidità significative e ad aumentata mortalità ospedaliera. Strategie volte ad identificare pazienti a rischio e la modifica di tali fattori di rischio mediante misure profilattiche può verosimilmente risultare in una riduzione della incidenza di ventilazione meccanica prolungata nei pazienti sottoposti a chirurgia valvolare isolata.

Parole chiave: by-pass aorto-coronarico, ventilazione meccanica prolungata, mortalità, morbidità.

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