Original Article

Risk factors of prolonged mechanical ventilation following open heart surgery: what has changed over the last decade?

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Objective: To identify the risk factors for prolonged invasive mechanical ventilation after open heart surgery in Pakistan.

Design: This study is based on retrospective analysis of database.

Place and duration: We conducted study of all patients who underwent open heart surgery at CPE Institute of Cardiology, Multan from March 2009 to May 2011.

Patients & methods: The data was retrieved from the database in the form of electronic spreadsheet which was then analyzed using SPSS software. The patients with incomplete data entries were removed from the analysis resulting in a set of 1,617 patients The data of each patient consisted of 65 preoperative, operative and postoperative variables. The data was summarized as means, medians and standard deviations for numeric variables and frequencies and percentages or categoric variables. These risk factors were compared using Chi-sqaure test. Their ODDs ratios and 95% confidence intervals of ODD's Ratios and P values were calculated.

Results: Out of a total of 1,617 patients, 77 patients (4.76%) had prolonged ventilation for a cumulated duration of more than over 24 hours. Preoperative renal failure, emphysema, low EF (<30%), urgent operation, preoperative critical state, prolonged bypass time, prolonged cross clamp time, complex surgical procedures and peri-operative myocardial infarction were found to be risk factors for PIMV. Old age, female gender, advanced ASA class, advanced NYHA class, diabetes mellitus, smoking, history of COPD, redo surgery, left main stenosis, obesity and use of intra-aortic balloon pump were not found to have significant ODDs ratios for PIMV. The patients with prolonged ventilation had significantly high mortality i.e. 32.47% while the normal ventilation group had 0.32% overall mortality.

Conclusions: Many of the previously considered risk factors for prolonged ventilation after open heart study are no more significant risk factors. However, prolonged ventilation continues to be associated with very high mortality.

Key Words: Extracorporeal circulation induced lung injury; prolonged ventilation; open heart surgery; respiratory failure

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Introduction

Prolonged invasive mechanical ventilation (PIMV) is a well recognized complication of cardiovascular surgery and its incidence has been reported from 3% to 22% (1-3). This wide variability is largely due to the discrepant definitions of PIMV. Irrespective of the definition of PIMV, it has always been incriminated for increased morbidity, mortality and cost of hospital treatment (4). Over the last decade much has changed in the field of cardiac surgery and cardiac anesthesia. Crystalloid cardioplegia has been replaced with more physiological blood cardioplegia.

Surgeons, perfusionists and anesthetist have become much more sensitized to the concept of inflammatory response to cardiopulmonary bypass and are adopting strategies to obviate this problem. Invasive monitoring has achieved much higher levels of refinement. Newer and better inhalational agents have been adopted for anesthesia and long acting narcotics have been replaced with short acting alternatives. It is therefore time to re-evaluate the risk factors of PIMV.

Patients & methods

Institutional setting & study design

This study was conducted at CPE Institute of Cardiology (CPEIC) in Multan. The CPEIC is one of the largest cardiac institute in Pakistan. At present more than 1,000 open heart operations are performed annually in our unit. The institute has Ethical Review Committee which rigorously binds the research workers to follow the guidelines of Helsinki Conventions. The study had formal approval of the Ethical committee. The unit has a state of the art electronic database (CascadeDatabases v. 2007, Lahore). The database is well maintained and validated since early 2009.

This study is based on retrospective analysis of all patients who underwent open heart surgery from March 2009 to May 2011. The patient characteristics, operative variables, respiratory and hemodynamic condition on ICU admission and inotropic support were extracted from our database. The data was retrieved from the database in the form of electronic spreadsheet which was then analyzed using SPSS 10. The data was summarized as means, medians and standard deviations for numeric variables and frequencies and percentages or categoric variables. For the sake of comparison and calculation of odds ratios we converted important numeric variables into categoric variables by using the definitions given in the subsequent paragraph. These risk factors were compared using Chi-sqaure test. Their ODDs ratios and 95% confidence intervals of ODD's Ratios and P values were calculated. Only those variables were enlisted which had significant ODDs ratios. We attempted to perform multivariate analysis but abandoned the idea as the number of patients in some subcategories was too small and any inferences drawn from such data would have been misleading.

Definitions

The prolonged mechanical ventilation PIMV was defined as cumulative duration of 24 hours or more of post operative endotracheal intubation starting from transfer of the patient to cardiac intensive care unit after completion of the index operation. This implies that it included patients who were not extubated within 24 hours as well as those who had one or more unsuccessful extubation attempts resulting in an accumulated duration of at least 24 hours of endotracheal intubation.

Advanced age was defined as documented age of more than 60 years. Pre-operative renal failure was defined as preoperative serum creatinine level of 2.0 or more. The history of chronic obstructive pulmonary disease (COPD) was defined as history of Emphysema or chronic bronchitis necessitating the use of bronchodilator inhaler or steroids or previous spirometery report revealing COPD. Similarly hypertension was defined as patients receiving treatment for hypertension or high blood pressure (i.e. >140 mmHg systolic or >90 mm diastolic) noted during preoperative stay. Perioperaitive myocardial infarction was defined as any patient having fresh ECG changes including new q-waves in two precordial leads, new bundle branch block, haemodynamic compromise with new segmental wall motion dysfunction or elevation of CK MB over 100 after undergoing open heart surgery.

The surgical operations were divided into two groups as simple and complex procedures. The simple open heart procedures included isolated CABG, isolated single valve surgery, repair of secondum atrial spetal defect and repair of simple ventricular septal defects. Combined CABG and Valve operations, multiple valve surgeries, CABG requiring coronary endarterectomies, and combination of any other operation with a CABG or valve replacement were defined as complex procedures.

As a standard policy of the unit all patients were explained the details of surgery and informed consent was taken. The patients were made fully aware of the fact that their clinical details might be used for academic purposes while maintaining full secrecy of the patient identity. The study was conducted in strict compliance of the rules established by the revised Helsinki convention and had approval from the Ethical Review Committee of the institute.

The protocols of anesthesia, surgery and intensive care

The operations were carried out by three consultant surgeons themselves or by senior registrars under direct supervision of consultants. Primary responsibility for ventilator management, including timing of extubation and re-intubation was assumed by consultant cardiothoracic anesthetist.

Patients were premedicated with tablet of 3 mg bromazepam the night before surgery. Anesthetic induction was done with morphine (0.1 mg/kg), midazolam (0.05-0.1 mg/kg), and propofol (1.0-2.5 mg/kg) given intravenously. Atracuronium (1 mg/kg) was given before endotracheal intubation. The anesthesia was maintained with sevoflorane/isoflurane. Additional doses of analgesics or paralyzing agents were given as required. The cardiopulmonary bypass (CPB) was established with aortic and 2-stage right atrial cannulae. The CPB circuit was primed with crystalloid Ringer's solution. The Heparin was administered in a dose of 300 U/Kg. Mild to moderate systemic hypothermia (30-32 ℃) was employed. The local cooling was done with ice cold saline or local ice slush according to the preference of operating surgeons. Cold antegrade blood cardioplegia was given through aorta and was repeated every 20 minutes. The first dose of cardioplegia was 10-15 mL/kg and further doses were given as 5-7 mL/kg. The haematocrit was maintained between 20% to 27% and haemofilteration was used in patients whose haematocrit dropped below the desired level.

During ICU stay all patients had invasive and non-invasive hemodynamic monitoring. All patients underwent elective mechanical ventilation on SIMV mode and were gradually shifted to CPAP once they regained spontaneous breathing. We actively followed a policy of extubation as early as possible. The assessment for extubation was made by the resident anesthetist. The patients were considered for extubation once they were fully conscious, hemodynamically stable, chest drainage was 50 mL/hour or less and body temperature was >36.5 ℃. The pulmonary criteria for extubation included PO_2 of 80 to 100 mmHg on FIO_2 of 45% or less, breathing rate of 11-25/min and PCO_2 of 35-45 mmHg. The patients were shifted to high dependency unit on the morning of first postoperative day unless they required extended monitoring or respiratory support. Those patients who could not be extubated in 76 hours and were expected to need PIMV underwent surgical tracheostomy.

Results

We found records of 1,617 patients in our database in the study period. They underwent different types of open heart surgeries which included 747 isolated conventional CABG, 55 OPCAB operations, 414 isolated single or multiple valve replacements, 359 operations for congenital heart disease and 42 various combined or miscellaneous procedures. Out of the total 1,617 patients, 1,540 were extubated within 24 hours of operation while 77 (4.76%) had prolonged ventilation for more than 24 hours.

The *Table 1,2* have summarized the numeric and categoric variables. It is obvious that both groups had similar demographic profile. Although the prolonged ventilation group had relatively more female and slightly older patients which had relative more predicted risk of mortality evident from Parsonnet Score. However these difference were not statistically significant. Similarly, the patients in prolonged ventilation group were more frequently in NYHA class III & IV and also in ASA Class III or above.

The *Table 3* shows the factors which were found to be significant in risk analysis. Amongst the preoperative variables uncontrolled hypertension, congestive cardiac failure, presence of emphysema, chronic renal failure, pre operative critical state and need for urgent surgery had significantly high ODD's ratios. Amongst the operative variables, prolonged cardiopulmonary bypass time (>120 min), prolonged cross clamp time (>80 min), perioperaitive MI and complexity of operation had significantly high ODD's ratios for prolonged ventilation.

Discussion

The prevalence of PIMV after cardiac surgery in this study was 4.76%. This is on the lower side of the range reported in the published literature (1-3). Currently, the patients are generally extubated within 6 hours after cardiovascular surgery recognizing the benefits of early extubation (5). We defined PIMV as cumulative ventilation time of more than 24 hours believing that 24 hours is a sufficiently long time for hemodynamic stabilization and to off-set the deleterious effects of surgery and cardiopulmonary bypass if used. Moreover 24-hours cut-off limit for prolonged ventilation is also used in the STS database.

Early in 1996 Habib *et al*. examined the role of 48 variables in determining the duration of mechanical ventilator support required after coronary bypass surgery in a group of 507 (6). Their study provided interesting insight in this field. They found that NYHA Class IV, intra-operative fluid retention, use of Intra-aortic balloon pump, transfusion of banked blood, lower body mass index and larger number of bypass grafts were predictors of PIMV. While obesity has been a controversial risk factor the low body mass index has always been noted as risk factors. This scenario is mostly observed in chronically ill patients who

Table 1 Summary statistics: categoric variables

Variable		Normal ventilation (n=1,540)		Prolonged ventilation (n=77)	
Name	Description	n	%	n	%
Pre-operative					
Gender	Female	436	28.31	29	37.66
	Male	1,104	71.69	48	62.34
ASA class	I-II	1,064	69.09	48	62.34
	III-V	467	30.32	29	37.66
NYHA class	I-II	713	46.30	31	40.26
	II-IV	827	53.70	46	59.74
Congestive cardiac failure		34	2.21	8	10.39
Uncontrolled hypertension		8	0.52	3	3.90
Pulmonary hypertension		191	12.40	13	16.88
Diabetes mellitus		284	18.44	12	15.58
Smoking	Non-smoker	1,172	76.10	63	81.82
	Ex-smoker	299	19.42	10	12.99
	Smoker	69	4.48	4	5.19
Asthma		7	0.45	3	3.90
COPD		28	1.82	3	3.90
Renal failure		1	0.06	2	2.60
Left main stenosis		200	12.99	10	12.99
Critical state		16	1.04	6	7.79
Urgent surgery		13	0.84	5	6.49
Redo operation		4	0.26	0	0.00
Post-operative			0.00		0.00
Superficial sternal infection		14	0.91	3	3.90
Mediastinitis		4	0.26	3	3.90
Peri-operative MI		3	0.19	2	2.60
Renal failure		22	1.43	20	25.97
Neurological deficit		14	0.91	21	27.27
Pleural effusion		47	3.05	18	23.38
Pneumothorax		14	0.91	1	1.30
Pulmonary edema		0	0.00	12	15.58
ARDS		1	0.06	2	2.60
Death		6	0.39	25	32.47

Table 2 Summary statistics: numeric variables

Variable		Normal ventilation (n=1,540)			Prolonged ventilation (n=77)		
Name	Units	Mean	Median	S.D.	Mean	Median	S.D.
Pre-operative							
Age	years	30.29	27.00	13.95	39.50	41.00	21.28
Height	cm	156.69	158.00	15.83	161.10	160.00	90.99
Weight	kg	48.94	48.00	14.83	55.90	52.50	16.62
Body mass index		19.61	18.39	4.61	21.63	19.53	6.88
Hemoglobin	mg/dL	12.09	12.00	1.82	10.85	10.50	1.95
Serum creatinine	mg/dL	0.90	0.80	0.74	1.12	1.00	0.28
Ejection fraction	%	58.89	60.00	8.77	55.10	60.00	13.92
LVIDD	mm	49.57	48.00	17.62	52.30	50.00	11.16
LVIDS	mm	34.54	33.50	10.84	36.70	37.00	7.69
Parsonnet score		5.99	6.00	4.79	14.20	8.80	16.42
Log-EuroScore		3.13	3.13	1.99	5.59	3.30	5.40
Operative							
Bypass time	min	86.87	81.50	33.62	119.40	101.50	41.75
Cross clamp time	min	61.35	58.00	28.95	68.20	70.50	37.38
Post-operative							
Ventilation time	hours	5.36	4.00	4.01	143.40	91.00	147.37
ICU stay	hours	36.84	30.00	22.31	227.00	120.00	250.04
Inotropic support	hours	15.38	6.00	24.13	141.90	107.00	124.57
Chest drainage	mL	642.35	500.00	485.33	1121.00	905.00	767.22

Table 3 ODDs ratios for significant risk factors of Prolonged Ventilation after open heart surgery

Variables	ODDS ratio	95% Confience interval	P
Pre-operative			
CCF	5.14	2.29-11.51	<0.0001
HTN	7.76	2.02-29.87	<0.0001
Emphysema	20.25	1.26-326.85	0.003
Renal failures	41.04	3.68-457.68	<0.0001
EF <30%	2.75	1.39-5.45	0.002
Raised S. Creatinine	5.97	2.50-14.28	<0.0001
Critical state	8.05	3.06-21.19	<0.0001
Urgent priority	8.16	2.83-23.50	<0.0001
Operative			
Complex procedure	2.60	1.62-4.15	<0.0001
Bypass time >120min	2.50	1.56-4.01	<0.0001
Cross clamp time >80min	2.33	1.35-4.02	0.002
Post-operative			
Perioperaitive MI	13.66	2.25-82.99	<0.0001
Pleural effusion	9.70	5.31-17.7	<0.0001
Pulmonary edema			<0.0001
ARDS	41.04	3.70-457.68	<0.0001

undergo multiple valve replacements. They commonly suffer from right ventricular dysfunction resulting in severe derangement of liver functions. Most of them loose their respiratory muscle mass due poor nutrition. Rodrigues *et al.* (2011) have reported association of preoperative respiratory muscle dysfunction with PIMV (7). They observed this feature in 6% of the patients undergoing valve surgery. Very high mortality (60%) was seen in this particular subset of patient. Despite the modern developments in critical care, prolonged invasive mechanical ventilation continues to have strong repercussions on mortality, morbidity and cost of treatment. Rajakaruna *et al*. (2005) have shown that amongst 7,553 patients included in their study, the mortality in PIMV was 22.2% while it was 1.0% in non PIMV group. The mean cost of bed occupancy in PIMV was $ 14,286 whereas it was only $ 2,761 in patients who did not need PIMV (4). We also observed similar pattern of very high mortality rates of 32.46% in prolonged ventilation group as compared to 0.39% in normal ventilation group. One plausible explanation is that prolonged ventilation increases the risk of mortality. Howevere, it might as well suggest that in the current practice of cardiac surgery the operative mortality is generally delayed as the moribund patients continue lingering on mechanical ventilation due to aggressive intensive care management.

Georghiou *et al*. (2006) suggested that optimizing early extubation after coronary bypass surgery is possible and should be aimed for as extubation within 6-hours did not have much difference in their preoperative characteristics (8). Moreover patients extubated earlier had faster overall recovery.

Durand *et al*. noted that decreased vital capacity, low FEV1, and low PaO_2 before cardiac surgery predict prolonged duration of mechanical ventilation after surgery (9).

We observed that history of emphysema, hypertension, congestive heart failure, preoperative renal failure, low ejection fraction (<30%), urgent need for surgery and preoperative critical state were associated with PIMV. Similarly, prolonged CPB time (≥120 minutes), long cross clamp time (>80 minutes), complex surgical procedures and perioperaitive MI were significantly associated with PIMV. Interestingly many of the previously documented risk factors like obesity, asthma, aortic root replacement, and redo operations did not have significant P value in our study. This might be the result of improved understanding of the disease process, judicious perioperative medical management and better intraoperative organ protection. It is also interesting to note that in our study perioperaitive use of IABP was not associated with PIMV. This might have happened due to our policy of using IABP sooner than later which avoids bad effects high doses of vasoconstricting inotropic agents of low cardiac output itself.

In congenital heart surgery, younger age (<30 days), greater severity of illness at admission, hospital acquired infections, noninfectious pulmonary complications, and the need for re intervention are associated with prolonged mechanical ventilation (10). Our unit at present is not dealing primarily with surgery of neonates and infants. We prefer not to perform open heart surgery in patients, whose weight is less than ten kilogram. It is therefore not appropriate to draw any parallels for another study in this regard.

One of the aims of studying the risk factors for PIMV is to develop a system for identifying high risk patients so that preoperative planning could be done to modify the risk factors. Dunning *et al*. (2003) designed a system for prediction of patient at risk of PIMV. In their analysis of 3,070 patient, 201 patients (%) required PIMV (11). The variables used in their formula included Parsonnet Score over 7, ejection fraction, urgency of operation, age and pulmonary artery pressure. Their formula gave a specificity of over 90%. A more recent and much more robust attempt has been made in this direction by Reddy *et al*. (2007), who have developed a predictor of risk model for PIMV after adult cardiac surgery (12). They defined PIMV as ventilation for greater than 48 hours and used logistic regression analysis of data collected from 12,662 patients. Their prediction formula showed very good discriminatory power. They have also developed a simplified additive scoring system which also had excellent discriminatory power.

We used the Parsonnet Score and EuroScore for stratification of the risk of mortality. The use these scoring systems was not by choice as these are incorporated in our electronic database. Nevertheless, these scoring systems especially the Euroscore are widely used by the cardiac surgeons. However, these scores only predict the risk of mortality and provide no information about the risk of prolonged ventilation. The STS scoring systems however is much more comprehensive in this regards as it also predicts the risk of various morbidities including prolonged ventilation. According to the STS risk scoring system, CABG in a male patient of 60 years or less with no other comorbidities carries 2.4% risk of prolonged ventilation. This risk increases to 3.3% with mild chronic lung disease and becomes 4.0% and 5.6% in moderate and severe chronic lung disease. The chronic lung disease has been defined on the basis of FEV1 and the need of steroid therapy. The Mild disease therefore defined as FEV1 60% to 75% of predicted, and/or on chronic inhaled or oral bronchodilator therapy. The Moderate Disease is defined as FEV1 50% to 59% of predicted, and/or on chronic steroid therapy aimed at lung disease while the disease is classified as Severe when FEV1 is <50% predicted, and/or Room Air pO_2 <60 or Room Air pCO_2 >50 (http://209.220.160.181/STSWebRiskCalc261/de.aspx). Ad N *et al*. have highlighted that the use of spirometry for defining chronic lung disease is not regulated for the participating centers in STS database. The use of patient history for symptoms, medication, and/or oxygen use as the only method to define chronic lung disease has led to underreporting of chronic lung disease and underestimation of the risk for adverse outcomes. Therefore, they believe that the data submission to STS database needs improvement as the use of spirometry prior to cardiac surgery may impact the STS risk prediction score (13). Despite these critical remarks it is well established that the database is perhaps the largest of its type, the *risk* prediction model based on it has good predictive value. It is established from the STS database that PIMV is associated with high mortality (14).

Lastly, it is satisfying to note that the old tradition of over-night ventilation has completely vanished over last 10 years. In current practice of cardiac surgery there is growing trend towards extubation as early as possible. This has occurred in the face of increasing complexity and acuity of illness. Perhaps strategies developed to preserve myocardial functions and minimize hemodynamic instability help explain this. Intra operative myocardial protection has become more sophisticated and CPB has been refined. In addition management of heart failure has improved tremendously due to judicious use of intra aortic balloon pump, newer pharmacologic agents and monitoring of cardiac output for selection of inotropes and adjusting their dosage.

Conclusions

This study shows that preoperative renal failure, emphysema, low EF (<30%), urgent need for surgery, preoperative critical state prolonged bypass time, prolonged cross clamp time, complex surgical procedures and peri-operative myocardial infarction continue to be risk factors for PIMV.

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