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ORIGINAL RESEARCH

Prolonged Mechanical Ventilation Following Coronary Artery Bypass Graft in Santiago De Cali, Colombia

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Purpose: The purpose of this study was to describe factors associated with prolonged ventilatory support in subjects undergoing coronary artery bypass graft.

Patients and Methods: This was an analytical retrospective case–control study. Cases were defined as subjects requiring prolonged mechanical ventilation (>48 hours) following isolated coronary artery bypass graft. Subjects older than 18 years who had undergone surgery were included, while subjects with missing clinical record data, subjects in coma or subjects with prior cardiac surgery were excluded. Variables were measured at the three time points surrounding surgery.

Results: A total of 204 cases and 408 controls were included. The final logistic model showed an association between prolonged mechanical ventilation and the following presurgical variables: chronic obstructive pulmonary disease (OR 1.85; 95% CI: 1.06–3.23, p = 0.03) and chronic kidney disease (OR 1.90; 95% CI: −3.31; p = 0.02). The associated transurgical variable was the use of intra-aortic balloon pump (OR 3.63; 95% CI: 1.73–7.61, p = 0.00), and associated postsurgical variables were venous oxygen saturation <60% (OR 2.00; 95% CI: 1.18–3.40, p = 0.01), mediastinitis (OR 18.51; 95% CI: 4.06–84.40, p = 0.00), inotrope use (OR 2.82; 95% CI: 1.77–4.48, p = 0.00), pleural effusion requiring drainage (OR 3.57; 95% CI: 2.02–6.32, p = 0.00) and delirium (OR 3.45; 95% CI: 1.91–6.25, p = 0.00).

Conclusion: This study identifies factors associated with prolonged mechanical ventilation in subjects subject to coronary artery bypass graft over the presurgical, transurgical and postsurgical periods, identifying a new factor, delirium, for this type of population.

Keywords: coronary bypass, prolonged ventilatory support, risk factor, cardiac surgery, epidemiology

Introduction

Mechanical ventilation (MV) support is a therapeutic option since it provides vital support for the maintenance or substitution of the ventilatory function in subjects with different conditions, such as respiratory failure, and subjects subject to surgical procedures, such as coronary bypass or coronary artery bypass graft (CABG).[1] The need for MV following this type of cardiovascular surgery results in subjects admission to intensive care units (ICUs). Respiratory support is generally removed within the first 24 hours, but some subjects may not recover immediately and may need prolonged mechanical ventilation (PMV), which is associated with different comorbidities or surgical and postsurgical complications.[2]

PMV is defined as any period in which patients require respiratory support for more than 21 days,[3–5] although the cut-off point is controversial, and there is substantial variation in terms of terminology and defining criteria, which is why standardization of criteria is needed.[6] According to the literature review, PMV in subjects subject to CABG can be defined by different ranges: >12 hours, >24 hours and >48 hours of ventilatory support.[1,7,8] The latter was used for this study. PMV is considered a significant complication following cardiovascular surgery; even though its incidence levels

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are low, ranging from 2.9% to 8.6%,[9–11] it is associated with higher morbidity and mortality rates, which is why it is still a relatively common issue.

Several studies have identified factors associated with PMV such as advanced age, left ventricular ejection fraction (LVEF) <30%, high score in the New York Heart Association (NYHA) functional classification, chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), procedure duration and the performance of an emergency surgery.[12–14] In addition, it is worth mentioning that PMV results in longer ICU stays, which increases the use of resources and health care costs.[15]

Identification of variables associated with PMV following CABG allows for the development of prevention and risk mitigation strategies aimed at reducing the adverse events of this condition and promoting early removal of the respiratory support. This results in a faster recovery and functional rehabilitation in a timelier manner.[16] This study is the only of its kind in Colombia and it was conducted in a cardiovascular surgery reference center located in the Southwest region of the country with a 10-year observation period. Hence, the purpose of this research was to identify risk factors associated with PMV following CABG in Santiago de Cali, Colombia.

Patients and Methods

Subjects and Study Design

A retrospective case-control study was conducted in a high complexity healthcare institution in the city of Cali, Colombia. Subjects older than 18 years who had undergone isolated CABG from January 1 2006 and December 31 2015 were included. Subjects with missing clinical record data, subjects in coma or with prior cardiac surgery were excluded.

Cases were defined as adult subjects that had undergone CAGB and received invasive ventilatory support for more than 48 hours following surgery. Exposure variables were measured at the presurgical, transurgical and postsurgical time points. Data was collected from clinical records, clinical laboratory results, diagnostic imaging reports and perfusion and postsurgical follow-up records made by cardiovascular surgeons of the institution.

Sample size was estimated with a 95% safety level, α=0.05, and a 90% statistical potency, β=0.1, with a ratio of two controls per each PMV case. Sample sizes were estimated based on exposure values taking the study made by the US Society of Thoracic Surgeons (STS) as a reference.[17] The exposure factor "being older than 75 years" resulted in a bigger sample size, with 204 cases and 408 controls, which were randomly selected from the database built by researchers, for which a simple random sampling was carried out using the EPIDAT 3.1 software; for this purpose included a total of 812 subjects. All the information about the people was processed during the period of time evaluated and included in this study for both the cases and the controls.

This study was conducted pursuant to the international recommendations for clinical research included in the Declaration of Helsinki. According to Resolution 8430 of 1993 issued by Ministerio de Salud de Colombia (Ministry of Health of Colombia), this study was classified as a risk-free research, since data was collected from secondary sources. Informed consent was not required as it was a retrospective study. This project was approved by the Research and Ethics and Bioethics Committee of the Faculty of Health "CEB-USC" (Minutes No. 01–2017) of the institution in which the study was conducted.

In this case-control study, biases were minimized as follows: The population at risk is often not defined. This situation in the study was handled properly since the population is framed in a surgical act. In this investigation, the cases and controls were selected from the cardiovascular surgery database of the reference institution, during the 10 years. It is difficult to ensure the comparability of rare risk factors. In the exploratory data analysis, the frequency of these factors was identified and exposed in the analysis of the information and results. They can frequently generate information biases, because the exposure in most cases is measured, reconstructed or quantified, after the development of the disease. In this study, when constituting the cases, the event of prolonged mechanical ventilation, this disadvantage was not presented, in addition to considering that they are incident cases. On the other hand, in the registry of the existence, dose, and time of exposure of the risk factors, a special study was made in the different sources of the clinical history to confirm the data, sources such as the daily registry of evolution, laboratory report, clinical records in physical and

digitized media, and post-surgical control, which it had been observed that the institution had adequate content and quality of information.

Statistical Analysis

Concordance and statistical validation of the database, where data had been entered twice, were estimated, which allowed for the organization of data into a master database. This was followed by a descriptive analysis of the risk factors for the general population, as well as for cases and controls. This description was performed for qualitative data by distributing relative frequencies and ratios. For quantitative data, a numerical analysis of central tendency and dispersion measures was conducted.

Subsequently, the independent effect of exposure variables on the likelihood that predicted cases becoming actual cases was determined, with its respective 95% confidence interval. Bivariate case associations were then estimated, and each of the exposures of interest was calculated with a Chi² test.

A variance analysis and a correlation coefficient were used for quantitative variables. After verifying the normality of the data through the Shapiro Wilk test, student's *t*-test was used to test the hypothesis of differences between sample means. Variables for the construction of the final model were identified during this step. Strength of association was measured with odds ratio (OR), with a 0.05 significance level and a 95% confidence level. The criterion used to assign a non-exposure category was based on the literature review about factors associated with the study event and/or the categories of variables with lower PMV case occurrence (Figure 1).

A multiple analysis was then conducted, which consisted of conditional logistic regression modeling. Based on statistical criteria, only independent variables with $p \leq 0.25$ in univariate models were introduced in the initial logistic model, through a stepwise-backward elimination procedure with a <0.10 entry probability and a >0.25 removal probability, resulting in the final explanatory model.

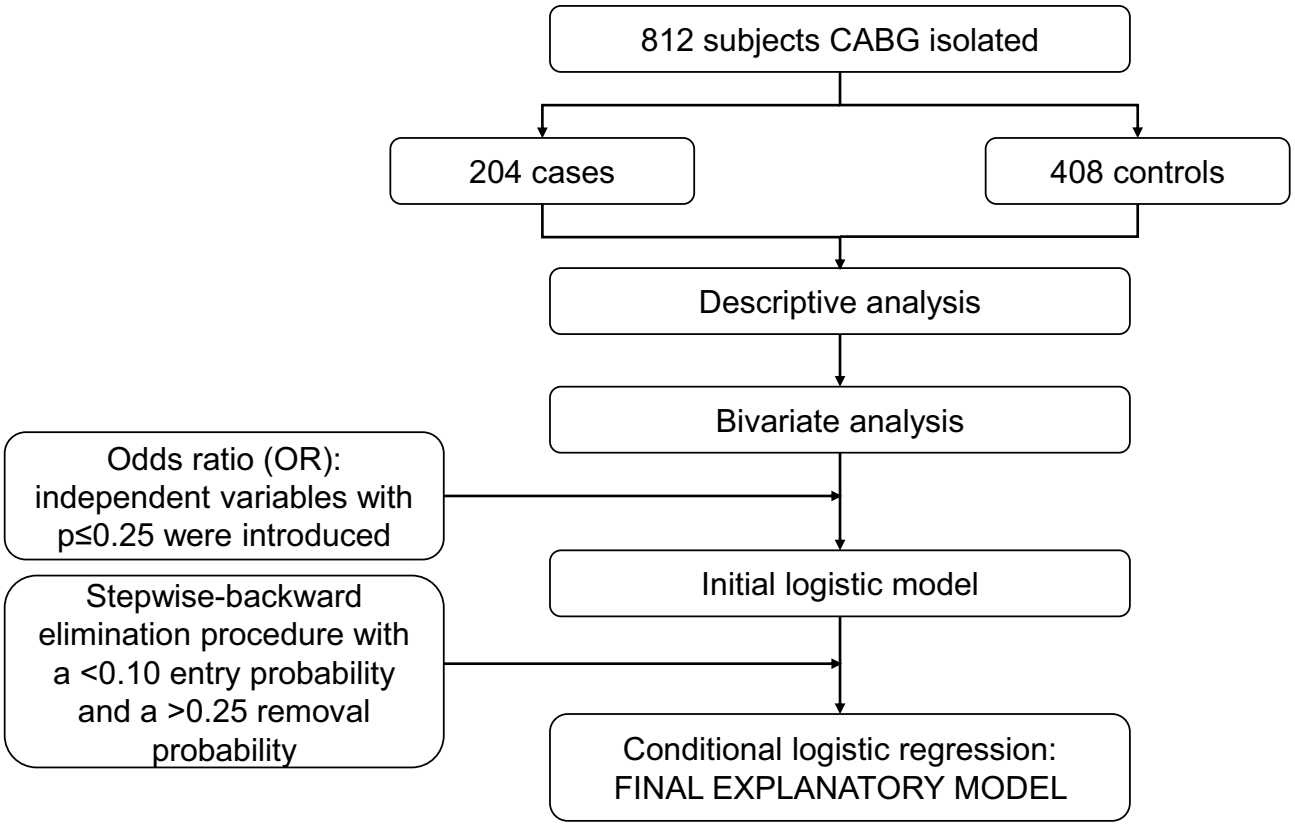

Figure 1 Statistical model.

Confusion and interaction tests were conducted with variables from the adjusted model. The model was validated with the Hosmer-Lemeshow goodness of fit test and the likelihood ratio test. Data analysis was processed using STATA 16.0® statistical software.

Results

When comparing the exposure frequencies of the variables from the presurgical period (Table 1), a trend could be observed towards a higher average age, history of heart failure (with preserved or reduced ejection fraction), COPD, CKD, peripheral vascular disease (PVD), pulmonary hypertension, vasodilator use and ventilatory support, as well as LVEF ≤35%, kidney function with creatinine ≥2.3 mg/dL and hemoglobin ≤12 g/dL and emergency surgery. Heart valve stenoses were not considered because they were only found in 5 subjects, and they were not severe.

Regarding exposure factors during surgery (Table 2), subjects needing PMV showed significant differences between the average pump and ischemia times in extracorporeal circulation, higher rates of blood transfusion with ≥3 units of red

Table 1 Description of Presurgical Variables

Variable	Cases PMV n=204		Controls No PMV n=408		Total		*P* value
	n (%)		n (%)		n (%)		
Age (years):							
<55	13	(6.4)	54	(13.2)	67	(10.9)	0.427
55–64	54	(26.5)	129	(31.6)	183	(29.9)	
65–74	83	(40.7)	151	(37.0)	234	(38.2)	
≥75	54	(26.5)	74	(18.1)	128	(20.9)	
Average ± SD*	68.2 ± 9.2		65.4 ± 9.3		66.3 ± 9.4		<0.001
BMI (kg/m²):							
<25	96	(47.1)	172	(42.2)	268	(43.8)	0.931
25–29	77	(37.7)	192	(47.1)	269	(44.0)	
30–34	24	(11.8)	39	(9.6)	63	(10.3)	
≥35	7	(3.4)	5	(1.2)	12	(2.0)	
Average ± SD*	25.8 ± 3.9		25.9 ± 3.4		25.8 ± 3.6		0.755
Body surface (m²)							
<1.5	14	(6.9)	26	(6.4)	40	(6.5)	0.239
1.5–1.74	85	(41.7)	155	(38.0)	240	(39.2)	
1.75–1.99	84	(41.2)	192	(47.1)	276	(45.1)	
≥2.0	21	(10.3)	35	(8.6)	56	(9.2)	
Average ± SD*	1.8 ± 0.2		1.8 ± 0.2		1.8 ± 0.2		1.000
Sex:							
Female	64	(31.4)	114	(27.9)	178	(29.1)	0.431
Male	140	(68.6)	294	(72.1)	434	(70.9)	
Socioeconomic stratum:							
High	21	(10.3)	30	(7.4)	51	(8.3)	0.326
Medium	124	(60.8)	266	(65.2)	390	(63.7)	
Low	59	(28.9)	112	(27.5)	171	(27.9)	
Smoking:							
No	102	(50.0)	189	(46.3)	291	(47.5)	0.439
Yes**	102	(50.0)	219	(53.7)	321	(52.5)	

(*Continued*)

Table 1 (Continued).

Variable	Cases PMV n=204		Controls No PMV n=408		Total		*P* value
	n (%)		n (%)		n (%)		
Diabetes Mellitus:							
No	115	(56.4)	257	(63.0)	372	(60.8)	0.135
Yes	89	(43.6)	151	(37.0)	240	(39.2)	
Dyslipidemia:							
No	88	(43.1)	160	(39.2)	248	(40.5)	0.398
Yes	116	(56.9)	248	(60.8)	364	(59.5)	
Heart failure:							
No	127	(62.3)	312	(76.5)	439	(71.7)	<0.001
Yes	77	(37.7)	96	(23.5)	173	(28.3)	
LVEF:							
<35%	16	(7.8)	15	(3.7)	31	(5.1)	0.043
≥35%	188	(92.2)	393	(96.3)	581	(94.9)	0.011
Average ± SD*	52.0 ± 10.4		49.7 ± 10.9		51.3 ± 10.7		
Arterial hypertension:							
No	13	(6.4)	46	(11.3)	59	(9.6)	0.073
Yes	191	(93.6)	362	(88.7)	553	(90.4)	
COPD:							
No	165	(80.9)	366	(89.7)	531	(86.8)	0.003
Yes	39	(19.1)	42	(10.3)	81	(13.2)	
Sepsis:							
No	184	(90.2)	381	(93.4)	565	(92.3)	0.217
Yes	20	(9.8)	27	(6.6)	47	(7.7)	
Chronic kidney failure:							
No	165	(80.9)	371	(90.9)	536	(87.6)	<0.001
Yes	39	(19.1)	37	(9.1)	76	(12.4)	
Kidney function:							
Creatinine <2.3 mg/dL	188	(92.2)	396	(97.1)	584	(95.4)	0.011
Creatinine ≥2.3 mg/dL	16	(7.8)	12	(2.9)	28	(4.6)	0.001
Average ± SD*	1.1 ± 1.0		1.4 ± 1.3		1.2 ± 1.1		
Peripheral vascular disease:							
No	144	(70.6)	353	(86.5)	497	(81.2)	<0.001
Yes	38	(18.6)	33	(8.1)	71	(11.6)	
Not reported	22	(10.8)	22	(5.4)	44	(7.2)	
Pulmonary hypertension:							
No PH	164	(80.4)	354	(86.8)	518	(84.6)	0.052
Mild PH	15	(7.4)	29	(7.1)	44	(7.2)	
Moderate PH	14	(6.9)	19	(4.7)	33	(5.4)	
Severe PH	11	(5.4)	6	(1.5)	17	(2.8)	
Cerebrovascular accident:							
No	191	(93.6)	393	(96.3)	584	(95.4)	0.193
Yes	13	(6.4)	15	(3.7)	28	(4.6)	

(*Continued*)

Table 1 (Continued).

Variable	Cases PMV n=204		Controls No PMV n=408		Total		*P* value
	n (%)		n (%)		n (%)		
Arrhythmia:							
No	191	(93.6)	383	(93.9)	574	(93.8)	0.952
Yes	13	(6.4)	25	(6.1)	38	(6.2)	
Type of arrhythmia:							
Atrial fibrillation	6	(2.9)	14	(3.4)	20	(3.3)	0.935
Supraventricular tachycardia	4	(2.0)	5	(1.2)	9	(1.5)	0.721
Ventricular tachycardia	0	(0.0)	4	(0.98)	4	(0.65)	0.375
Ventricular fibrillation	1	(0.5)	2	(0.5)	3	(0.5)	0.539
Extrasystole	2	(1.0)	4	(1.0)	6	(1.0)	0.663
AMI:							
No	107	(52.5)	216	(52.9)	323	(52.8)	0.977
>21 days	37	(18.1)	70	(17.2)	107	(17.5)	
8–21 days	43	(21.1)	87	(21.3)	130	(21.2)	
1–7 days	17	(8.3)	35	(8.6)	52	(8.5)	
Prior percutaneous intervention:							
No	160	(78.4)	330	(80.9)	490	(80.1)	0.543
>6 hours	44	(21.6)	78	(19.1)	122	(19.9)	
IABP use:							
No	198	(97.1)	402	(98.5)	600	(98.0)	0.353
Yes	6	(2.9)	6	(1.5)	12	(2.0)	
Angina:							
No	103	(50.5)	242	(59.3)	345	(56.4)	0.050
Yes	101	(49.5)	166	(40.7)	267	(43.6)	
Hospital stay:							
≤7 days	134	(65.7)	280	(68.6)	414	(67.6)	0.521
8–14 days	54	(26.5)	107	(26.2)	161	(26.3)	0.352
≥15 days	16	(7.8)	21	(5.1)	37	(6.0)	
Average ± SD*	6.8 ± 6.2		6.3 ± 6.4		6.5 ± 6.3		
Number of injured vessels:							
1 vessel	7	(3.4)	26	(6.4)	33	(5.4)	0.504
2 vessels	32	(15.7)	63	(15.4)	95	(15.5)	
≥3 vessels	165	(80.9)	319	(78.2)	484	(79.1)	
Left main artery injury:							
No	154	(75.5)	323	(79.2)	477	(77.9)	0.352
Yes	50	(24.5)	85	(20.8)	135	(22.1)	
Hemoglobin:							
<12 g/dL	66	(32.4)	90	(22.1)	156	(25.5)	0.007
≥12 g/dL	138	(67.6)	318	(77.9)	456	(74.5)	1.000
Average ± SD*	13 ± 2		13 ± 2		13 ± 2		
Blood transfusion: ***							
No	193	(94.6)	396	(97.1)	589	(96.2)	0.201
Yes	11	(5.4)	12	(2.9)	23	(3.8)	

(*Continued*)

Table 1 (Continued).

Variable	Cases PMV n=204		Controls No PMV n=408		Total		*P* value
	n (%)		n (%)		n (%)		
Type of surgery:							
Elective	185	(90.7)	390	(95.6)	575	(94.0)	0.026
Urgent	17	(8.3)	13	(3.2)	30	(4.9)	
Emergency	2	(1.0)	5	(1.2)	7	(1.1)	
Vasodilator use:							
No	148	(72.5)	327	(80.1)	475	(77.6)	0.043
Yes	56	(27.5)	81	(19.9)	137	(22.4)	
Ventilatory support:							
No	187	(91.7)	394	(96.6)	581	(94.9)	0.015
Yes	17	(8.3)	14	(3.4)	31	(5.1)	
Valvular insufficiency:							
Aortic valve							
No	174	(85.3)	364	(89.2)	538	(87.9)	0.203
Mild	26	(12.7)	31	(7.6)	57	(9.3)	
Moderate	3	(1.5)	11	(2.7)	14	(2.3)	
Severe	1	(0.5)	2	(0.5)	3	(0.5)	
Tricuspid valve							
No	173	(84.8)	363	(89.0)	536	(87.6)	0.179
Mild	26	(12.7)	38	(9.3)	64	(10.5)	
Moderate	3	(1.5)	4	(1.0)	7	(1.1)	
Severe	2	(1.0)	3	(0.7)	5	(0.8)	
Mitral valve							
No	119	(58.3)	271	(66.4)	390	(63.7)	0.061
Mild	58	(28.4)	115	(28.2)	173	(28.3)	
Moderate	25	(12.3)	19	(4.7)	44	(7.2)	
Severe	2	(1.0)	3	(0.7)	5	(0.8)	
Pulmonary valve							
No	201	(98.5)	406	(99.5)	607	(99.2)	0.427
Mild	2	(1.0)	0	(0.0)	2	(0.3)	
Moderate	1	(0.5)	2	(0.5)	3	(0.5)	

Notes: *Standard deviation. **Currently smokes or used to smoke. ***Red blood cells, plasma, platelets or cryoprecipitate.
Abbreviations: PMV, Prolonged Mechanical Ventilation; BMI, Body mass index; LVEF, Left ventricular ejection fraction; COPD, Chronic obstructive pulmonary disease; AMI, Acute myocardial infarction; IABP, Intra-aortic balloon pump.

blood cells, ≥2 units of plasma and ≥6 units of platelets, intra-aortic balloon pump (IABP) use, cardiogenic shock and need for vasopressor and inotropic agents.

In the postsurgical period (Table 3), cases showed a higher frequency of ICU stays of >3 days, a higher need for blood transfusion with ≥3 units of red blood cells, ≥2 units of plasma, ≥6 units of platelets and ≥10 units of cryoprecipitate, need for vasopressor and inotropic agents, IABP use, presence of cardiogenic shock; arrhythmias such as atrial fibrillation and supraventricular tachycardia and venous oxygen saturation (SvO_2) <60%. The majority of complications included surgical reintervention, pleural effusion requiring drainage, postsurgical bleeding, atelectasis, tracheal reintubation, pulmonary edema, delirium, bowel bleeding, sepsis, mediastinitis, coagulopathy, and acute kidney failure (definition of AKI Network) with and without dialysis ($p<0.05$).

Regarding hospital mortality (<30 days), it was more frequent among subjects receiving PMV as opposed to subjects in which ventilation was removed promptly (22.6% vs 6.1%). The main causes of death in the 46 subjects who died with PMV were sepsis (43.5%), cardiogenic shock (41.3%) and postsurgical bleeding (13%).

Table 2 Description of Transurgical Variables

Variable	Cases PMV n=204		Controls No PMV n=408		Total		*P* value
	n (%)		n (%)		n (%)		
No. of revascularized vessels:							
<3 vessels	27	(13.2)	74	(18.1)	101	(16.5)	0.154
≥3 vessels	177	(86.8)	334	(81.9)	511	(83.5)	
Extracorporeal circulation:							
No	3	(1.5)	10	(2.5)	13	(2.1)	0.620
Yes	201	(98.5)	398	(97.5)	599	(97.9)	
Pump time:							
<90 minutes	151	(74.0)	346	(84.8)	497	(81.2)	0.001
≥90 minutes	53	(26.0)	62	(15.2)	115	(18.8)	
Average ± SD*	78.5 ± 24.4		70.2 ± 21.4		72.9 ± 22.8		<0.001
Ischemia time:							
<60 minutes	165	(80.9)	361	(88.5)	526	(85.9)	0.015
≥60 minutes	39	(19.1)	47	(11.5)	86	(14.1)	
Average ± SD*	49 ± 16		44 ± 14		46 ± 15		<0.001
Blood transfusion:**							
No	48	(23.5)	191	(46.8)	239	(39.1)	<0.001
Yes	156	(76.5)	217	(53.2)	373	(60.9)	
Type of blood product:							
Red blood cells							
<3 units	139	(68.1)	323	(79.2)	462	(75.5)	0.003
≥ 3 units	65	(31.9)	85	(20.8)	150	(24.5)	
Plasma							
<2 units	65	(31.9)	231	(56.6)	296	(48.4)	<0.001
≥ 2 units	139	(68.1)	177	(43.4)	316	(51.6)	
Platelets							
<6 units	174	(85.3)	374	(91.7)	548	(89.5)	0.022
≥ 6 units	30	(14.7)	34	(8.3)	64	(10.5)	
Cryoprecipitate							
<10 units	201	(98.5)	404	(99.0)	605	(98.9)	0.893
≥10 units	3	(1.5)	4	(1.0)	7	(1.1)	
IABP use:							
No	172	(84.3)	395	(96.8)	567	(92.6	<0.001
Yes	32	(15.7)	13	(3.2)	45	(7.4)	
Cardiogenic shock:							
No	185	(90.7)	396	(97.1)	581	(94.9)	0.001
Yes	19	(9.3)	12	(2.9)	31	(5.1)	
Arrhythmia:							
No	190	(93.1)	391	(95.8)	581	(94.9)	0.215
Yes	14	(6.9)	17	(4.2)	31	(5.1)	
Type of arrhythmia:							
Atrial fibrillation	3	(1.5)	6	(1.5)	9	(1.5)	0.721
Ventricular fibrillation	7	(3.4)	7	(1.7)	14	(2.3)	0.293
Ventricular tachycardia	2	(1.0)	5	(1.2)	7	(1.1)	0.893
Supraventricular tachycardia	3	(1.5)	0	(0.0)	3	(0.5)	0.065

(*Continued*)

Table 2 (Continued).

Variable	Cases PMV n=204		Controls No PMV n=408		Total		*P* value
	n (%)		n (%)		n (%)		
Use of vasopressor agents:							
No	137	(67.2)	323	(79.2)	460	(75.2)	0.001
Yes	67	(32.8)	85	(20.8)	152	(24.8)	
Inotrope use:							
No	76	(37.3)	205	(50.2)	281	(45.9)	0.004
Yes	128	(62.7)	203	(49.8)	331	(54.1)	
Vasodilator use:							
No	148	(72.5)	267	(65.4)	415	(67.8)	0.092
Yes	56	(27.5)	141	(34.6)	197	(32.2)	

Notes: *Standard deviation. **Red blood cells, plasma, platelets or cryoprecipitate.
Abbreviations: PMV, Prolonged Mechanical Ventilation; IABP, Intra-aortic balloon pump.

Table 3 Description of Postsurgical Variables

Variable	Cases PMV n=204		Controls No PMV n=408		Total		*P* value
	n (%)		n (%)		n (%)		
Intensive care unit stay:							
≤2 days	15	(7.4)	86	(21.1)	101	(16.5)	<0.001
>3 days	189	(92.6)	322	(78.9)	511	(83.5)	
Hospital stay:							
≤2 days	74	(36.3)	110	(27.0)	184	(30.1)	0.022
>3 days	130	(63.7)	298	(73.0)	428	(69.9)	
Blood transfusion:**							
No	70	(34.3)	307	(75.2)	377	(61.6)	0.016
Yes	134	(65.7)	101	(24.8)	235	(38.4)	
Type of blood product:							
Red blood cells							
<3 units	134	(65.7)	392	(96.1)	526	(85.9)	<0.001
≥ 3 units	70	(34.3)	16	(3.9)	86	(14.1)	
Plasma							
<2 units	142	(69.6)	390	(95.6)	532	(86.9)	<0.001
≥ 2 units	62	(30.4)	18	(4.4)	80	(13.1)	
Platelets							
<6 units	177	(86.8)	400	(98.0)	577	(94.3)	<0.001
≥ 6 units	27	(13.2)	8	(2.0)	35	(5.7)	
Cryoprecipitate							
<10 units	193	(94.6)	408	(100.0)	601	(98.2)	<0.001
≥10 units	11	(5.4)	0	(0.0)	11	(1.8)	
Use of vasopressor agents:							
No	67	(32.8)	323	(79.2)	390	(63.7)	<0.001
Yes	137	(67.2)	85	(20.8)	222	(36.3)	
Inotrope use:							
No	33	(16.2)	185	(45.3)	218	(35.6)	<0.001
Yes	171	(83.8)	223	(54.7)	394	(64.4)	

(*Continued*)

Table 3 (Continued).

Variable	Cases PMV n=204		Controls No PMV n=408		Total		*P* value
	n (%)		n (%)		n (%)		
Vasodilator use:							
No	109	(53.4)	224	(54.9)	333	(54.4)	0.796
Yes	95	(46.6)	184	(45.1)	279	(45.6)	
IABP use:							
No	171	(83.8)	394	(96.6)	565	(92.3)	<0.001
Yes	33	(16.2)	14	(3.4)	47	(7.7)	
Cardiogenic shock:							
No	151	(74.0)	380	(93.1)	531	(86.8)	<0.001
Yes	53	(26.0)	28	(6.9)	81	(13.2)	
Arrhythmia:							
No	125	(61.3)	350	(85.8)	475	(77.6)	<0.001
Yes	79	(38.7)	58	(14.2)	137	(22.4)	
Type of arrhythmia:							
Atrial fibrillation	65	(31.9)	46	(11.3)	111	(18.1)	<0.001
Supraventricular tachycardia	59	(4.4)	5	(1.2)	14	(2.3)	<0.001
Ventricular tachycardia	5	(2.5)	1	(0.2)	6	(1.0)	0.029
Ventricular fibrillation	2	(1.0)	1	(0.2)	3	(0.5)	0.539
Extrasystole	15	(7.4)	9	(2.2)	24	(3.9)	0.004
SvO_2:							
≥60%	152	(74.5)	367	(90.0)	519	(84.8)	<0.001
<60%	52	(25.5)	41	(10.0)	93	(15.2)	
Average ± SD*	65.2 ± 9.8		69.5 ± 7.9		68.1 ± 8.8		<0.001
Cardiorespiratory complications:							
Pulmonary edema	27	(13.2)	15	(3.7)	42	(6.9)	<0.001
AMI	3	(1.5)	2	(0.5)	5	(0.8)	0.427
ARDS	4	(2.0)	0	(0.0)	4	(0.7)	0.021
Hemothorax	9	(4.4)	3	(0.7)	12	(2.0)	0.005
Pleural effusion requiring drainage	60	(29.4)	27	(6.6)	87	(14.2)	<0.001
Tracheal reintubation	39	(19.1)	1	(0.2)	40	(6.5)	<0.001
Tracheostomy	13	(6.4)	0	(0.0)	13	(2.1)	<0.001
Pneumothorax	3	(1.5)	4	(1.0)	7	(1.1)	0.893
Postsurgical bleeding	46	(22.5)	13	(3.2)	59	(9.6)	<0.001
VAN	13	(6.4)	0	(0.0)	13	(2.1)	<0.001
Surgical reintervention	74	(36.3)	13	(3.2)	87	(14.2)	<0.001
Atelectasis	44	(21.6)	31	(7.6)	75	(12.3)	<0.001
Neurological complications:							
TIA	1	(0.5)	0	(0.0)	1	(0.2)	0.723
Ischemic CVA	9	(4.4)	5	(1.2)	14	(2.3)	0.027
Hemorrhagic CVA	1	(0.5)	0	(0.0)	1	(0.2)	0.723
Delirium	45	(22.1)	27	(6.6)	72	(11.8)	<0.001
Gastrointestinal complications							
Intestinal bleeding	12	(5.9)	0	(0.0)	12	(2.0)	<0.001

(*Continued*)

Table 3 (Continued).

Variable	Cases PMV n=204		Controls No PMV n=408		Total		*P* value
	n (%)		n (%)		n (%)		
Infectious complications:							
Sepsis	95	(46.6)	25	(6.1)	120	(19.6)	<0.001
Mediastinitis	29	(14.2)	2	(0.5)	31	(5.1)	<0.001
Surgical site infection	31	(15.2)	32	(7.8)	63	(10.3)	0.007
Kidney complications:							
Kidney failure without dialysis	26	(12.7)	15	(3.7)	41	(6.7)	<0.001
Kidney failure with dialysis	25	(12.3)	0	(0.0)	25	(4.1)	<0.001
Blood complications:							
Coagulopathy	26	(12.7)	3	(0.7)	29	(4.7)	<0.001

Notes: *Standard deviation. **Red blood cells, plasma, platelets or cryoprecipitate.
Abbreviations: PMV, Prolonged Mechanical Ventilation; IABP, Intra-aortic balloon pump; SvO_2, Venous oxygen saturation; AMI, Acute myocardial infarction; ARDS, Acute respiratory distress syndrome; VAN, Ventilation-associated pneumonia; CVA, Cerebrovascular accident; TIA, Transient ischemic attack.

Different logistic models were developed based on the theoretical framework and according to statistical criteria in order to identify those variables whose statistical significance and theoretical importance allowed for the construction of the most parsimonious model. First, individual logistic models were built for each CABG stage and then the final model was developed. The presurgical model showed a statistically significant association and a higher PMV likelihood for subjects with history of CKD, PVD, COPD and heart failure.

The individual model for the transurgical stage showed pump time and IABP use as risk factors. The postsurgical model evidenced a significant association with the need for red blood cells transfusion, IABP use, SVO_2 <60%, pulmonary edema, surgical reintervention, delirium and sepsis.

Once the final logistic model was built, 8 variables were included (Figure 1). The presurgical variables were COPD and CKD, the transurgical variable was IABP use and the postsurgical factors associated were SVO_2<60% at ICU admission, mediastinitis, inotrope use, pleural effusion requiring drainage and delirium. The final model accounts for 23% of the variability of PMV following CABG (Pseudo R^2).

Due to variations in raw and adjusted OR (Figure 2) values and based on theoretical clinical criteria, the presence of the effect modification was assessed. However, no statistical significance was found, nor any explanation for the variability of the event.

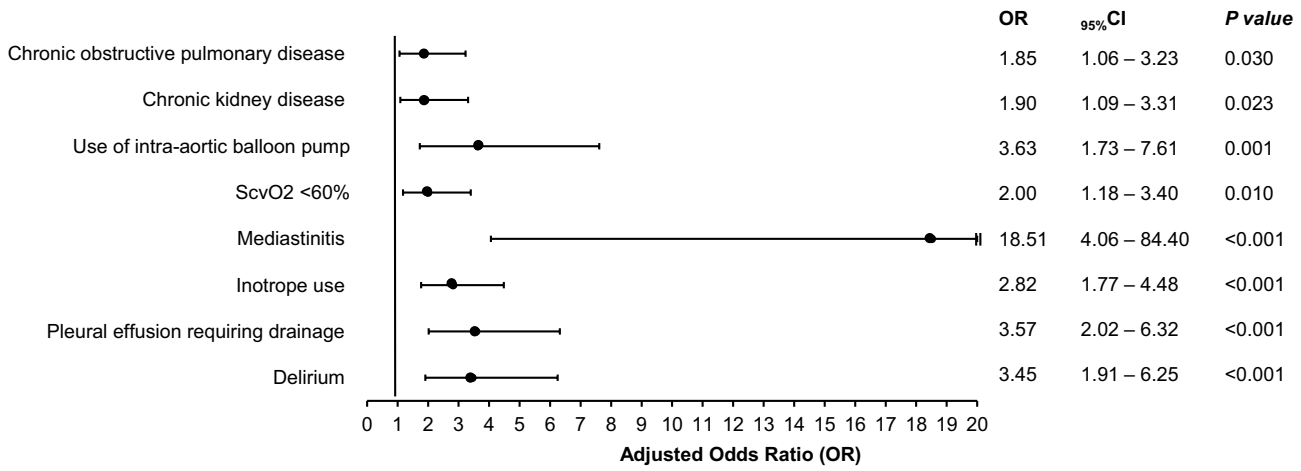

Figure 2 Forest plot final logistical model based on odds ratios (OR).

The assessment of the final adjustment of the logistic regression model showed adequate data adjustment (Hosmer-Lemeshow) with a Chi^2 of 33.82 (p=0.99). Model classification evidenced that the model had a 52.7% capacity to classify cases as cases (sensitivity) and 88.6% capacity to classify controls as controls (specificity). In other words, the model is highly capable of ruling out subjects unlikely to receive PMV. Cases predicted by the model had a 69.9% likelihood of becoming actual cases. Subjects unlikely to receive PMV according to the model had a 78.9% likelihood of becoming controls.

Discussion

Among the factors studied, the final logistic model included variables associated with the three surgical time points, such as history of COPD, CKD, IABP use during surgery, SVO_2<60%, mediastinitis, inotrope use, pleural effusion requiring drainage and delirium.

A majority of COPD subjects subject to CABG were reported as needing mechanical ventilation for more than 48 hours or prolonged intubation, since there is a significant decrease of their vital capacity, total pulmonary capacity and functional residual capacity, which results in a proportionally higher mortality rate.[18] In their study, Piotto et al[1] described COPD as a strong predictor of PMV following CABG, with an OR of 2.65 (95% CI: 1.38–5.09, p=0.004). This is consistent with our study, in which COPD had an OR of 1.85 (95% CI: 1.06–3.23, p=0.030) and a statistically significant association.

CKD subjects are prone to present adverse results, and this variable was observed to be associated with critical conditions such as pulmonary edema, sepsis and metabolic dysfunction, which may result in prolonged intubations.[19] This condition is also considered a PMV predictor following cardiac surgery. This study yielded relevant findings, with a significant association between CKD and PMV (OR 1.90, 95% CI: 1.09–3.31, p=0.023) regardless other risk factors. In addition, a higher frequency was observed (19.1%) for subjects needing prolonged respiratory support. Likewise, subjects with kidney injury following cardiac surgery have a high death probability. In the study performed by Fernández et al,[2] a relatively small fraction (10–15%) of subjects admitted to the ICU following CABG required PMV, 72.8% of which reported CKD, resulting in a positive association (OR 2.14; 95% CI: 1.1–4.07, p= 0.027).

Similarly, Gumus et al[11] found that this type of subjects had high mortality rates and a PMV frequency of 58.7%, and concluded that kidney injury is one of the most significant risk factors in this critical condition (OR 7.7, 95% CI: 1.3–47.6, p=0.00). On the other hand, Shirzad et al,[20] reported a lower incidence (6.6%) of subjects with CKD requiring PMV following CABG (OR 5.65; 95% CI: 1.42–22.48, p=0.01).

Regarding IABP use, this was the only transurgical variable identified as a predictor of PMV in this study (OR 3.63, 95% CI: 1.73–7.61, p=0.001). In their study, Helena et al[8] suggested that IABP use time is associated with prolonged ventilatory support following CABG, with an OR of 1.12 (95% CI: 0.96–1.31, p=0.001). It should be mentioned that the exact moment to remove MV following a CABG that required IABP use is still under debate. However, it is known that complications associated with MV —such as atelectasis, pneumothorax and pneumonia— are directly correlated with the duration of endotracheal intubation.[21] The reporting frequency of these conditions was higher (p<0.05) in this study population.

IABP use is associated with PMV in subjects subject to CABG and other cardiovascular surgeries. Graziela et al[22] assessed the efficacy of IABP in subjects undergoing high risk cardiac surgery, in which 47.8% of the IABP group required PMV, and no decrease in associated mortality and morbidity rates was observed. Moreover, Ranucci et al[23] conducted a study with 110 subjects and observed a higher PMV frequency in subjects needing IABP cardiovascular support as opposed to those who did not need it (31% vs 27%). They also found incidence of other complications, such as acute kidney failure, surgical reintervention and cerebrovascular accident.

In the postsurgical stage, we found that SVO_2 <60% was a predictive variable for PMV with an OR of 2.0 (95% CI: 1.18–3.40, p=0.010). We also found that average and standard deviation values were lower for cases than for controls (65.2 ± 9.8). There are several studies which evidence that low SvO_2 levels are not associated with PMV. Greg et al[24] concluded that SvO_2 <70% at ICU admission following cardiac surgery was not associated with morbidity increase or the duration of mechanical ventilation. Conversely, Hitendra et al[25] evidenced that hemodynamic, oximetric and laboratory alterations, including SvO_2, were associated with a significantly prolonged need of mechanical ventilation and ICU stay.

As for mediastinitis, it has been described as a condition related to prolonged ventilatory support, which can also increase mortality rates among these subjects.[26] Charbonneau et al[27] assessed and described the characteristics of a large cohort of subjects with postsurgical mediastinitis, particularly analyzing gram-negative bacteria. Mediastinitis occurred in 309 of these subjects (mean age 65 years), and a significant association with PMV was described (p=0.004). Gustavo et al[28] conducted an analytical retrospective case-control study regarding the presence of mediastinitis, and built a predictive model for this condition using risk factors, which revealed a strong association with PMV (OR 2.66; 95% CI: 1.02–6.93, p=0.045). Our study is highly consistent with the studies above, since mediastinitis was considered a postsurgical predictor associated with PMV following CABG (OR 18.51; 95% CI: 4.06–84.40, p=<0.001).

The use of inotropic agents in subjects subject to CABG and staying in the ICU with invasive MV may improve myocardial contractility through diverse mechanisms and result in a quicker MV removal. However, it should be considered that each agent affects systemic and pulmonary vasculature in a different way, which may cause characteristic hemodynamic effects that are strongly associated with PMV following CABG or any cardiac surgery. In this study, inotrope use as a postsurgical variable was evidenced as a strong predictor for PMV following CABG (OR 2.82; 95% CI: 1.77–4.48, p=<0.001). Moreover, Umar et al[29] conducted a retrospective analysis on 690 subjects subject to isolated emergency CABG surgery in a tertiary center in West Australia, in which IABP was used in 78 subjects (11.3%), and prolonged inotrope use was widely considered a postoperative secondary outcome (OR 6.11; 95% CI: 2.77–13.48, p= <0.001). An association with PMV was also found (OR 20.2; 95% CI: 8.24–49.74, p= <0.001).

Pleural effusion requiring drainage is a postsurgical variable of CABG and is a common complication, widely associated with PMV. Few studies reporting an association between pleural effusion and PMV following CABG or any other cardiac surgery have been found. Williams et al[30] conducted a retrospective cohort study that assessed risk factors for pleural effusion requiring drainage following CABG, including 409 subjects, of which, 53 (12.9%) underwent this procedure. In these subjects, PMV following CABG was reported to be associated with pleural effusion requiring drainage (p=0.049). In our study, results of the final logistic model showed that pleural effusion requiring drainage is associated with PMV (OR 3.57; 95% CI: 2.02–6.32, p= ≪0.001).

Delirium is considered a neuropsychiatric complication after major surgery in elderly adults, which is frequently reported and which is prevalent among subjects subject to cardiac surgery.[31] This condition occurs acutely after surgery and is characterized by fluctuant changes in consciousness, mental state, attention, feelings, cognition, memory, perception and diurnal cycle. It is considered as a strong postsurgical predictor associated with postsurgical PMV. Tania et al[32] identified predictive factors of delirium in 501 subjects admitted to acute cardiac care units following transcatheter aortic valve replacement, resulting in an association between delirium and PMV (OR 18.86; 95% CI: 1.85–192.58, p=0.013). On the other hand, in a retrospective observational study including 2447 subjects subject to cardiac surgery, delirium was independently and strongly associated with a higher risk of PMV (OR 113.7; 95% CI: 99.7–127.7, p=0.00).[33]

Matthew et al[34] conducted a retrospective cohort study which included 250 subjects undergoing cardiac surgery, in which PMV was identified as a triggering factor for delirium, as well as surgery duration, transfusion of blood products, conscious sedation and duration of ICU stay. Based on the above, these studies are highly consistent with our research, in which the multiple logistic model yielded a correlation between delirium and PMV (OR 3.45; 95% CI: 1.91–6.25, p=0.00). So far, few studies performed with subjects subject to CABG have identified this risk factor, such as the one conducted by Stransky et al,[35] in which hypoactive delirium was evidenced as an independent predictor of PMV (OR 1.56; 95% CI: 1.25–1.92, p<0.01). Another example is the study conducted by Norkiene et al,[36] who found an association between postsurgical delirium and PMV over time (9.2±3.1 vs 2.0±2.7 days, p=0.001).

Finally, regarding hospital mortality observed in subjects requiring PMV following surgery, 46 of 204 subjects died, representing 22.5%. The main causes of death included sepsis, cardiogenic shock and postsurgical bleeding. This is consistent with the study performed by Ibañez et al,[37] in which 69% of subjects died due to cardiogenic and septic shock. Moreover, Fernández et al[2] studied whether PMV is a predictor of mortality in subjects subject to cardiac surgery, in which the main causes of death were multiorgan failure and sepsis (50.3%).

This study has some limitations. The research was conducted on a specific population group with similar healthcare affiliation characteristics, so the "type of subject" factor could not be evaluated. The ethnic variable was reported in a low proportion of clinical records, so it had to be removed from the analysis. The final logistic regression model included

presurgical, transurgical and postsurgical variables consistent with what has been reported in scientific literature. However, strongly associated factors such as age, sex and pump time were excluded from the model, possibly due to the sample size of this study. Based on the findings of this study, multicentric studies should be conducted throughout the country in order to reinforce the purposes of the research by using a sample size that allows for the assessment of a wider range of variables of interest.

Conclusion

The final logistic model included the presurgical variables chronic obstructive pulmonary disease and chronic kidney disease, the transurgical variable IABP use and the postsurgical variables oxygen venous saturation, mediastinitis, inotrope use, pleural effusion requiring drainage and delirium.

Delirium and pleural effusion requiring drainage were novel risk factors. Therefore, the research invites the intensive care team to carry out an early and adequate intervention of delirium in search of achieving timely ventilatory weaning.

Take Home

PWV variables associated with cardiovascular surgery (CABG) were identified, such as COPD, CKD, intraoperative IABP use, SVO2 <60%, mediastinitis, inotrope use, pleural effusion, and delirium, the latter being a new risk factor.

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Disclosure

The authors report no conflicts of interest in this work.

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