

Predictors of prolonged mechanical ventilation after coronary artery bypass grafting among Filipino adults with coronary artery disease

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ABSTRACT

Background. Identifying risk factors for prolonged mechanical ventilation (PMV) can improve postoperative outcomes of patients undergoing coronary artery bypass grafting (CABG).

Objective. To determine the occurrence rate and predictors of PMV among patients who underwent CABG.

Design. Retrospective cohort study.

Setting. Southern Philippines Medical Center Heart Institute, Davao City, Philippines.

Participants. 213 patients with coronary artery disease (CAD) who underwent CABG.

Main outcome measures. PMV occurrence rate; odds ratios (95% CI) of PMV for selected clinical characteristics.

Main results. There were 167 (78.4%) males and 46 (21.6%) females in this study. The patients had a mean age of 60.2 ± 9.68 years and a mean BMI of 25.8 ± 5.65 kg/m². Post-CABG, PMV occurred in 18.87% of the patients.

Univariate odds ratios of PMV were significantly high for renal dysfunction (OR=2.75; 95% CI 1.34-5.66), New York Heart Association functional class IV (7.53; 3.07-18.46), angina grade IV (4.52; 1.69-12.07), left ventricular ejection fraction <50% (2.80; 1.23-6.38), cardiogenic shock (12.14; 2.26-65.11), intraoperative IABP insertion (3.17; 1.46-6.88), postoperative acute kidney injury (AKI) (6.72; 2.99-15.10), postoperative hemodialysis (4.84; 2.21-10.60), postoperative neurological complications (13.04; 4.21-40.39), postoperative arrhythmia (2.59; 1.19-5.63), pulmonary complications (3.50; 1.67-7.34), and other complications (3.44; 1.22-9.68). On multiple regression analysis, AKI after CABG significantly increased the odds ratio of PMV (11.82; 1.03-135.35).

Conclusion. PMV after CABG occurred in 18.87% of the patients in our study and was associated with poor preoperative cardiac and renal conditions, intraoperative IABP insertion, and postoperative complications. The development of AKI after CABG independently increased the odds ratio of PMV.

Keywords. early extubation, acute kidney injury, EuroSCORE II, Society of Thoracic Surgeons Adult Cardiac Surgery Risk

INTRODUCTION

Prolonged mechanical ventilation (PMV) after coronary artery bypass grafting (CABG) increases postoperative morbidity, mortality, and the cost of hospitalization.¹ Post-cardiac surgery patients who are reintubated following extubation are likewise prone to more complications and have a higher mortality rate.²⁻³ In recent years, early extubation (EE)—or extubation within 8 hours of arrival at the postoperative care unit—has gained popularity because the practice has been shown to improve cardiac performance, reduce respiratory complications, allow early mobilization and feeding, increase patient autonomy and comfort,⁴ and reduce the workload of medical and nursing staff.⁵ EE, however, may not apply to all patients such as those who are at high risk for postoperative complications.^{4,5}

Identifying patients who are at high risk for PMV can help physicians optimize health care to improve the outcomes of patients

undergoing CABG. However, the key factors associated with early PMV and EE are poorly understood.⁶ To start with, PMV has been defined differently from study to study, with some setting the cutoff at 12 hours or less after surgery,^{2,6,7} and then others at 24 hours.⁸⁻¹¹

IN ESSENCE

It is important to identify patients at risk of prolonged mechanical ventilation (PMV) after coronary artery bypass grafting (CABG).

In this study, clinical factors associated with PMV include poor preoperative cardiac, renal and pulmonary status, long operative procedure and development of postoperative complications. Postoperative acute kidney injury independently increased the odds ratio of having PMV.

Coming up with local prediction models for PMV and regularly reassessing these models can help improve the outcomes of patients who undergo CABG.

48 hours,^{3 12 13} or even 72 hours^{14 15} post-operatively. Studies with PMV cutoffs lower than 24 hours usually report only a few predictors for PMV while in studies that report PMV as more than 72 hours, only patients with serious, non-transient issues remained ventilated.^{6 7}

In a study that defined PMV as mechanical ventilation for more than 12 hours after CABG, redo surgery, cardiopulmonary bypass (CPB) time of more than 91 minutes, intraoperative transfusion of more than 4 units of red blood cells, and left ventricular ejection fraction (LVEF) of $\leq 30\%$ all increased the odds of having PMV.² Another study, which set the PMV cutoff at 72 hours post-CABG, reported that advanced age, renal dialysis, peripheral vascular disease, hypertension, advanced stage of heart failure, elevated body mass index (BMI), reduced forced expiratory volume at 1 second, and prolonged CPB are all associated with PMV.¹⁵ Age >70 years, diabetes, and the use of an intra-aortic balloon pump (IABP) have been identified as significant predictors of failure of EE among patients on off-pump CABG.¹⁶ Another study suggested that reducing the CPB time and keeping blood glucose levels low during CPB can help avoid delayed extubation.¹⁰

The predictors of PMV identified in previously reported studies were varied, and sometimes conflicting.²⁻¹⁶ One study was able to show that the predictors of PMV may even change within the same institution, owing to the changes within patient demographics, and surgical and anesthetic techniques over time.³ This suggests that predictors are context-specific and that the application of previous findings on predictors of PMV cannot be fully extended to any other patient groups. We thought of doing this study since, as far as we know, there were no previous attempts to explore the risk factors for PMV among Filipino patients undergoing CABG. In this study, we aimed to determine the rate of occurrence of PMV after CABG among patients with CAD and to identify the preoperative, intraoperative and postoperative factors that are associated with PMV.

METHODOLOGY

Study design and setting

We employed a retrospective cohort study design in reviewing and analyzing the

medical records of patients who underwent CABG at the Southern Philippines Medical Center Heart Institute (SPMC-HI) in Davao City, Philippines. Cardiac interventions and open heart surgical procedures have been offered by SPMC-HI since its opening in 2007. The institute caters to an average of 428 surgical procedures per year, around 15% of which are CABG.

Participants

All adult patients aged 19 to 75 years old with coronary artery disease (CAD) who underwent CABG at the SPMC-HI from 2007 to 2015 were eligible for inclusion in this study. We excluded patients who had previous percutaneous cardiac intervention or cardiac surgery.

Data collection

We collected sociodemographic data, which included age, sex, weight, and height. We also gathered clinical data such as smoking history, history of myocardial infarction within 3 months pre-CABG, comorbidities (hypertension, diabetes and chronic obstructive pulmonary disease [COPD]), Canadian Cardiovascular Society Angina Grading Scale (CCS AGS), New York Heart Association functional classification (NYHA FC) of heart failure, number of diseased coronary vessels, and LVEF from the last 2D echocardiography prior to the CABG procedure.

We calculated BMI from the weight and height of each patient. The glomerular filtration rate (GFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula¹⁷ available online. We also determined the chronic kidney disease (CKD) stage of each patient, albeit based on the calculated GFR alone and without considering urine findings or structural abnormalities. For each patient, we either noted the EuroSCORE (European System of Cardiac Operative Risk Evaluation) II¹⁸ and the online Society of Thoracic Surgeons Adult Cardiac Surgery Risk (STS ACSR) v2.81¹⁹ score as recorded in the patient's chart, or calculated one or both scores using their respective calculators available online. Both EuroSCORE II and STS ACSR were based on models developed from pooled patients in Europe and America, respectively, and have been repeatedly validated in several studies.²⁰⁻²³ Both scores are commonly used to calculate the risks of morbidity and mortality from cardiac pro-

cedures and are presently used to screen patients for CABG under the Z-package program of the Philippine Health Insurance Corporation.²⁴

We also collected data on preoperative, intraoperative and postoperative clinical characteristics of patients in relation to the CABG procedure. The preoperative variables we noted included demographic characteristics, comorbidities, severity of CAD, preoperative intubation status, presence of cardiogenic shock (with inotropic or intra-aortic balloon pump support), and the urgency of the surgery (elective or emergency). The intraoperative variables we collected were cardiopulmonary bypass (CPB) time, aortic cross-clamp (ACC) time, whether CABG was done off-bypass, number of units of blood products transfused, the use of Cell Saver[®] (autologous blood transfusion), the use of IABP, and the use of more than two kinds of inotropic agents. We also gathered postoperative variables such as hematocrit level, PaO₂/FiO₂ ratio, and the occurrence of postoperative complications, namely, acute kidney injury (AKI; as defined by the Kidney Disease: Improving Global Outcomes (KDIGO)²⁵—increase in creatinine by more than 0.3 mg/dL (26.5 μmol/L) from baseline within 48 hours or increase to 1.5 times from baseline within seven days), neurological sequelae, new onset arrhythmia, myocardial infarction, acute respiratory distress syndrome, pulmonary complications (i.e., nosocomial pneumonia, pleural effusion, atelectasis, pulmonary congestion, pulmonary edema), and other non-pulmonary complications (i.e., upper gastrointestinal bleed, decubitus ulcer, device related infection, surgical site infection, ischemic hepatitis, postoperative myasthenia gravis).

The main outcome measures for this study were the rate of occurrence and predictors of PMV. Since it has been the prevailing practice among cardiologists and pulmonologists in our institution to extubate patients the day (i.e., within 24 hours) after performing CABG, we operationally defined PMV as mechanical ventilation beyond 24 hours after the end of the CABG procedure. Patients who were immediately extubated (within 24 hours postoperatively) but who required reintubation within 72 hours of weaning from the mechanical ventilator were also classified as belonging to the PMV group. Patients who were successfully

Table 1 Demographic and preoperative clinical characteristics of patients

Characteristics	n*	Values
Mean age ± SD, years	213	60.20 ± 9.68
Sex, frequency (%)	213	
Male		167 (78.40)
Female		46 (21.60)
Mean BMI ± SD, kg/m ²	212	25.80 ± 5.65
Smoker, frequency (%)	213	108 (50.70)
Hypertension, frequency (%)	213	154 (72.30)
Diabetes mellitus, frequency (%)	213	123 (57.75)
COPD, frequency (%)	213	17 (7.98)
Mean GFR ± SD, mL/min/1.73 m ²	206	71.48 ± 26.31
CKD stage†, frequency (%)	206	
1		58 (28.16)
2		82 (39.81)
3A		29 (14.08)
3B		25 (12.14)
4		6 (2.91)
5		6 (2.91)
Renal dysfunction‡, frequency (%)	206	69 (33.50)
On hemodialysis, frequency (%)	213	6 (2.82)
CAD severity		
CCS AGS classification, frequency (%)	123	
I		34 (27.64)
II		41 (33.33)
III		12 (9.76)
IV		36 (29.27)
NYHA FC, frequency (%)	199	
I		59 (29.65)
II		80 (40.20)
III		35 (17.59)
IV		25 (12.56)
Recent myocardial infarction§, frequency (%)	211	73 (34.60)
LVEF	140	
Mean ± SD, %	140	50.33 ± 13.54
<50%, frequency (%)	140	59 (42.14)
Number of diseased coronary vessel, frequency (%)	212	
1		12 (6.13)
2		27 (12.74)
3		172 (81.13)
Preoperative condition		
Cardiogenic shock , frequency (%)	213	8 (3.76)
Intubated preoperatively, frequency (%)	213	4 (1.88)
Urgency of procedure, frequency (%)	213	
Elective		211 (99.06)
Emergency		2 (0.94)

*Value of n varies because of missing data.

†CKD stage solely based on calculated GFR.

‡Patients with GFR <60 mL/min/1.73 m².

§Within 3 months.

|| Use of inotropic agents or IABP.

BMI — body mass index; CAD — coronary artery disease; CCS AGS — Canadian Cardiovascular Society Angina Grading Scale; CKD — chronic kidney disease; COPD — chronic obstructive pulmonary disease; GFR — glomerular filtration rate; IABP — intra-aortic balloon pump; LVEF — left ventricular ejection fraction; NYHA FC — New York Heart Association Functional Class.

Table 2 Comparison of outcomes between patients who had early extubation (EE) and patients with prolonged mechanical ventilation (PMV)

Outcomes	n*	EE	n*	PMV	p-value
Mortality after 24 hours, frequency (%)	171	3 (1.75)	39	10 (25.64)	<0.0001†
Mean length of ICU stay ± SD, hours					
Overall	170	113.24 ± 69.58	39	222.48 ± 292.02	<0.0001†
Survivors‡	167	113.24 ± 69.88	29	165.16 ± 119.37	0.0013†
Mean length of hospital stay ± SD, days					
Overall	170	17.95 ± 9.35	37	30.08 ± 411.24	<0.0001†
Survivors‡	167	17.89 ± 9.33	27	31.30 ± 376.52	<0.0001†

*Value of n varies because of missing data.

†Significant at p<0.05.

‡Among those who survived.

ICU — intensive care unit.

extubated within 24 hours from end of the CABG procedure comprised the EE group. We also looked at other outcomes including mortality, length of hospital stay, and length of intensive care unit (ICU) stay.

The varying value of the sample size n in the Results section of this report reflects some missing data from patient records. Of the 213 patients included in this study, one patient died within 24 hours postoperatively, so only 212 could be assessed for the outcome of either EE or PMV. Two additional patients were transferred to another institution within 24 hours postoperatively, but after extubation, so only 210 could be assessed for mortality after 24 hours. Data on duration of stay were either missing from or inaccurate in some patient records, so only 209 could be assessed for length of ICU stay, and only 207 could be assessed for length of hospital stay.

Statistical analysis

We summarized continuous variables as means and standard deviations, and categorical variables as frequencies and percentages. We then used student t-test to compare continuous variables and chi-square test or Fisher's exact test (for variables with frequencies of <5 to compare categorical variables. To calculate the odds ratios (95% confidence intervals) of having PMV for each predetermined preoperative, intraoperative or postoperative variable, we performed univariate logistic regression. We dichotomized non-binary variables prior to performing logistic regression. For continuous variables, we determined the following cutoff points based either on the mean or on a clinically significant value: age >60 years; abnormal BMI (either less than 18.5 or more than 25);

GFR <60 mL/min/1.73m² (renal dysfunction); LVEF <50%; EuroSCORE II mortality >5.0%; STS ACSR mortality >5.0%; CBP duration >180 min; ACC time >150 min; transfusion of packed red blood cells (PRBC) and/or whole blood (WB) >4 units; transfusion of total blood products >10 units; use of >2 kinds of inotropic agents; hematocrit level <0.38 for males or <0.34 for females; and PaO₂/FiO₂ ratio <200. We also dichotomized categorical variables with more than two categories as follows: NYHA FC IV (yes/no); CCS AGS IV (yes/no); and 3-vessel CAD (yes/no). For factors that significantly increased or decreased the odds ratios of having PMV by univariate logistic regression, we performed multivariable logistic regression to determine independent predictors of the outcome. For all statistical tests, the level of significance was set at <5%. All statistical tests were performed using Epi Info 7.1.4.0.

RESULTS

A total of 213 patient charts were included in the analysis for this study. The summary of the sociodemographic and clinical profiles of patients are shown in Table 1. The mean age of the patients was 60.20 ± 9.68 years old, and the mean BMI was 25.80 ± 5.65 kg/m². Among the patients 167/213 (78.40%) were males and 46/213 (21.60%) were females. Half of the patients (108/213, 50.70%) were smokers. Hypertension was the most common comorbidity, with 154/213 (72.30%) of the patients having it. More than half of the patients (123/213; 57.75%) had diabetes mellitus, while 17/213 (7.98%) had COPD.

The mean GFR was 71.48 ± 26.31 mL/min/1.73 m²; 69/206 (33.50%) patients had renal dysfunction (GFR <60 ml/min/1.73 m²), and 6/213 (2.82%) were on hemodialysis prior to the CABG procedure. The most frequent CKD stage among the patients was stage 2 (82/206; 39.81%).

In terms of cardiovascular status, the most frequent CCS AGS category among the patients was class II (41/123; 33.33%), while the most frequent NYHA FC was II (80/199; 40.20%). There were 73/211 (34.60%) patients who had a history of myocardial infarction within 3 months prior to CABG. The mean LVEF was 50.33 ± 13.54%, and 59/140 (42.14%) of the patients had LVEF less than 50%. Most of the patients (172/212; 81.13%) had 3-vessel

Table 3 Comparison of preoperative characteristics between patients who had early extubation (EE) and patients with prolonged mechanical ventilation (PMV)

Characteristics	n*	EE	n*	PMV	p-value
Mean age \pm SD, years	172	60.04 \pm 9.63	40	60.51 \pm 10.01	0.7506
Sex, frequency (%)	172		40		0.8913
Male		135 (78.49)		31 (77.50)	
Female		37 (21.51)		9 (22.50)	
BMI	172		40		
Mean \pm SD, kg/m ²		26.08 \pm 6.00		24.58 \pm 3.58	0.1307
Obese†, frequency (%)		104 (60.47)		21 (52.50)	0.3563
Malnourished patients‡, frequency (%)		7 (4.07)		3 (7.50)	0.3567
Hypertension, frequency (%)	172	124 (72.09)	40	29 (72.50)	0.9587
Diabetes, frequency (%)	172	102 (59.30)	40	20 (50.00)	0.2836
COPD, frequency (%)	172	12 (6.98)	40	4 (10.00)	0.5144
Mean GFR \pm SD, mL/min/1.73 m ²	167	74.77 \pm 24.83	38	57.68 \pm 28.46	0.0003§
CKD stage , frequency (%)	167		38		0.0213§
1		53 (31.74)		5 (13.51)	
2		67 (40.12)		15 (39.47)	
3A		23 (13.77)		5 (13.16)	
3B		18 (10.78)		7 (18.24)	
4		3 (1.80)		3 (7.89)	
5		3 (1.80)		3 (7.89)	
Renal dysfunction¶, frequency (%)	167	48 (28.74)	38	20 (52.63)	0.0047§
On hemodialysis, frequency (%)	172	3 (1.74)	40	3 (7.50)	0.0480§
Smoker, frequency (%)	172	86 (50.00)	40	21 (52.50)	0.8592
CCS AGS classification, frequency (%)	101		21		0.0158§
I		31 (30.69)		3 (14.29)	
II		37 (36.63)		4 (20.05)	
III		10 (9.90)		2 (9.52)	
IV		23 (22.77)		12 (57.14)	
NYHA FC, frequency (%)	159		39		<0.0001§
I		51 (32.08)		8 (20.51)	
II		67 (42.14)		12 (30.77)	
III		30 (18.87)		5 (12.82)	
IV		11 (6.92)		14 (35.90)	
Recent myocardial infarction**, frequency (%)	170	54 (31.76)	40	18 (45.00)	0.1452
Mean LVEF \pm SD, %	109	51.72 \pm 12.80	31	46.16 \pm 15.04	0.0516
LVEF <50%, frequency (%)	109	40 (36.70)	31	19 (61.29)	0.0144§
Number of diseased vessels, frequency (%)	171		40		0.7940
1		10 (5.85)		3 (7.50)	
2		23 (13.45)		4 (10.00)	
3		138 (80.70)		33 (82.50)	
Preoperative condition, frequency (%)					
Cardiogenic shock††	172	2 (1.16)	40	5 (12.50)	0.0003§‡‡
Intubated preoperatively	172	0 (0.00)	40	4 (10.00)	<0.0001§‡‡
Urgency of procedure, frequency (%)	172		40		0.0032§‡‡
Emergency		0 (0.00)		2 (5.00)	
Elective		172 (100.00)		38 (95.00)	
Mean % risk of mortality by EuroSCORE II \pm SD	92	2.16 \pm 2.17	26	5.09 \pm 4.97	<0.0001§
Mean % risk of mortality by STS ACSR \pm SD	102	1.74 \pm 3.04	26	3.85 \pm 4.54	0.0055§

*Value of n varies because of missing data.

†BMI >25 kg/m².‡BMI <18.5 kg/m².

§Significant at p<0.05.

||CKD stage solely based on calculated GFR

¶GFR <60 mL/min/1.73 m².

**Within 3 months prior to CABG.

††Use of inotropic agents or IABP.

‡‡Fisher's exact test.

BMI — body mass index; CCS AGS — Canadian Cardiovascular Society Angina Grading Scale; CKD — chronic kidney disease; COPD — chronic obstructive pulmonary disease; EuroSCORE II — European System for Cardiac Operative Risk Evaluation II; GFR — glomerular filtration rate; IABP — intra-aortic balloon pump; LVEF — left ventricular ejection fraction; NYHA FC — New York Heart Association Functional Class; STS ACSR — Society of Thoracic Surgeons Adult Cardiac Surgery Risk.

CAD. Prior to CABG, 8/213 (3.76%) patients had cardiogenic shock, 4/213 (1.88%) were intubated for an indication that occurred preoperatively, and 2/213 (0.94%) had to undergo emergency CABG.

Of 212 patients, 172 (81.13%) had EE (within 24 hours postoperatively), while 40 (18.87%) had PMV (after 24 hours postoperatively). Table 2 shows the comparison of outcomes between patients who had EE and those with PMV. The PMV group had significantly higher mortality rate after 24 hours (10/39; 25.64% versus 3/171; 1.75%); <0.001), longer mean length of ICU stay (222.48 \pm 292.02 hours versus 113.24 \pm 69.58 hours; p<0.001), and longer mean length of hospital stay (30.08 \pm 411.24 days versus 17.95 \pm 9.35 days; p<0.001) compared to patients in the EE group.

Table 3 shows the comparison of demographic and preoperative clinical characteristics between patients who had EE and patients with PMV. The preoperative GFR of patients with PMV (57.68 \pm 28.46 mL/min/1.73 m²) was significantly lower compared to that of patients who had EE (74.77 \pm 24.83 mL/min/1.73 m²; p=0.0003). There were more patients with early-stage CKD in the EE group (53/167; 31.74% with CKD stage 1 and 67/167; 40.12% with CKD stage 2) than in the PMV group (5/38; 13.51% with CKD stage 1 and 15/38; 39.47% CKD stage 2). The PMV group had significantly higher proportions of patients with renal dysfunction (20/38; 52.63% versus 48/167; 28.74%; p=0.0047) and patients on hemodialysis (3/40; 7.50% versus 3/172; 1.74%; p=0.0480) compared to the EE group.

The most frequent angina CCS AGS classifications were class II among patients who had EE (37/101; 36.63%) and class IV among patients with with PMV (12; 57.14%; p=0.0158). Likewise, the most frequent NYHA FC were class II among patients who had EE (67/159; 42.14%) and class IV among patients with with PMV (14/39; 35.90%; p<0.0001). The PMV group had significantly higher proportions of patients with LVEF less than 50% (19/31; 61.29%), in cardiogenic shock (5/40; 12.50%), patients intubated preoperatively (4/39; 10.00%) and patients requiring emergency CABG (2/39; 5.00%) compared to the EE group. Patients with PMV group had significantly higher mean risk of mortality by EuroSCORE II (5.09 \pm 4.97%) and mean mean risk of

Table 4 Comparison of intraoperative characteristics between patients who had early extubation (EE) and patients with prolonged mechanical ventilation (PMV)

Characteristics	n*	EE	n*	PMV	p-value
CPB duration	163		38		
Mean \pm SD, minutes		180.96 \pm 41.87		200.23 \pm 51.93	0.0147†
Proportion of CPB >180mins, frequency (%)		78 (47.56)		25 (64.10)	0.0633
Mean ACC time \pm SD, minutes	161	149.54 \pm 34.81	39	162.79 \pm 46.16	0.0476†
OPCAB, frequency (%)	171	8 (4.65)	39	0 (0.00)	0.3571‡
Mean number of units of blood products transfused \pm SD					
PRBC	172	2.13 \pm 1.88	40	2.55 \pm 1.97	0.2193
WB	172	0.70 \pm 1.23	40	0.63 \pm 1.21	0.7164
PC	172	2.48 \pm 2.45	40	2.28 \pm 2.63	0.6440
FFP	172	1.75 \pm 1.73	40	1.73 \pm 2.15	0.9376
Total blood products	172	9.97 \pm 6.89	40	10.55 \pm 7.80	0.6413
Use of Cell Saver®, frequency (%)	172	58 (33.72)	40	13 (32.50)	0.8828
Intraoperative insertion of IABPs, frequency (%)	172	25 (14.53)	40	14 (35.00)	0.0026†
Use of >2 kinds of inotropic agents, frequency (%)	172	10 (5.85)	40	6 (15.00)	0.0476†
Other surgical procedures, frequency (%)	172	6 (3.49)	40	1 (2.50)	0.6072‡

*Value of n varies because of missing data.

†Significant at $p < 0.05$.

‡Fisher's exact test.

§Excluding those with IABP preoperatively.

ACC — aortic cross-clamp; CPB — cardiopulmonary bypass; FFP — fresh frozen plasma; IABP — intra-aortic balloon pump; OPCAB — off-pump coronary artery bypass; PC — platelet concentrate; PRBC — packed red blood cells; WB — whole blood.

Table 5 Comparison of postoperative characteristics between patients who had early extubation (EE) and patients with prolonged mechanical ventilation (PMV)

Characteristics	n*	EE	n*	PMV	p-value
Mean hematocrit level \pm SD	170	0.35 \pm 0.05	38	0.33 \pm 0.04	0.4555
PaO ₂ /FiO ₂					
Mean \pm SD	169	272.01 \pm 119.50	39	277.23 \pm 215.33	0.8363
PaO ₂ /FiO ₂ <200, frequency (%)	169	45 (26.04)	39	13 (35.90)	0.2157
Acute kidney injury†, frequency (%)	166	45 (27.11)	35	25 (71.43)	<0.0001‡
New indication for hemodialysis†, frequency (%)	169	23 (13.61)	37	16 (43.24)	<0.0001‡
Neurologic complications§, frequency (%)	172	5 (2.91)	40	12 (30.00)	<0.0001‡
Arrhythmia, frequency (%)	172	27 (15.70)	40	13 (32.50)	0.0144‡
New myocardial infarction , frequency (%)	172	2 (1.16)	40	2 (5.00)	0.1621¶
Acute respiratory distress syndrome, frequency (%)	172	10 (5.81)	40	5 (12.50)	0.1374
Other pulmonary complications**, frequency (%)	172	30 (17.44)	40	17 (42.50)	0.0006‡
Other non-pulmonary complications††, frequency (%)	171	10 (5.81)	39	7 (17.50)	0.0142‡

*Value of n varies because of missing data.

†Excluding those on hemodialysis preoperatively.

‡Significant at $p < 0.05$.

§Including seizures, cerebrovascular infarct, cerebrovascular bleed, transient ischemic attack.

||Excluding pre-existent myocardial infarction.

¶Fisher's exact test.

**Including nosocomial pneumonia, pleural effusion, atelectasis, pulmonary congestion, pulmonary edema.

††Including upper gastrointestinal bleed, decubitus ulcer, device related infection, surgical site infection, ischemic hepatitis, postoperative myasthenia gravis.

FiO₂ — fraction of inspired oxygen; PaO₂ — partial pressure of oxygen in arterial blood.

mortality by STS ACSR (3.85 \pm 4.54%) than those who had EE. The rest of the demographic and preoperative clinical characteristics were comparable in between the two groups.

Comparison of the intraoperative characteristics between patients who had EE and those with PMV are presented in Table 4. The mean CPB time of patients with PMV (200.23 \pm 51.93 minutes) was significantly

higher compared to that of patients who had EE (180.96 \pm 41.87 minutes; $p=0.0147$). Likewise, the mean ACC time of patients with PMV (162.79 \pm 46.16 minutes) was significantly higher than that of patients who had EE (149.54 \pm 34.81 minutes; $p=0.0476$). The PMV group (14/40; 35.00%) had a significantly higher proportion of patients who had intraoperative insertion of IABP, than those in EE group (25/172; 14.53%;

Table 6 Univariate odds ratios (95% CI) of having prolonged mechanical ventilation (PMV) for selected preoperative, intraoperative, and postoperative characteristics of patients who underwent coronary artery bypass grafting (CABG)

Characteristics	Odds ratio (95% CI)	p-value
Preoperative variables		
Demographic/clinical profile		
Age >60 (mean)	1.12 (0.56 to 2.24)	0.7403
Male	0.94 (0.41 to 2.16)	0.8899
Abnormal BMI*	0.81 (0.40 to 1.64)	0.5606
Hypertension	1.02 (0.47 to 2.20)	0.9587
Diabetes	0.69 (0.34 to 1.37)	0.2851
Smoking	1.11 (0.56 to 2.20)	0.7758
COPD	1.48 (0.45 to 4.86)	0.5162
Renal dysfunction	2.75 (1.34 to 5.66)	0.0058†
ESRD on hemodialysis	4.57 (0.89 to 23.53)	0.0694
CAD severity		
NYHA FC IV	7.53 (3.07 to 18.46)	<0.0001†
CSS AGS IV	4.52 (1.69 to 12.07)	0.0026†
Recent MI	1.76 (0.87 to 3.55)	0.1150
LVEF <50%	2.80 (1.23 to 6.38)	0.0141†
3 vessel disease	1.13 (0.46 to 2.77)	0.7940
Preoperative condition		
Cardiogenic shock	12.14 (2.26 to 65.11)	0.0036†
EuroScore II mortality >5.0%	5.56 (1.88 to 16.46)	0.0020†
STS mortality >5.0%	7.34 (1.90 to 28.42)	0.0039†
Intraoperative variables		
CPB duration >180 mins	1.97 (0.96 to 4.05)	0.0662
ACC time >150 mins	1.75 (0.85 to 3.57)	0.1271
PRBC+WB >4	1.05 (0.44 to 2.50)	0.9053
Total blood >10	0.77 (0.39 to 1.55)	0.4704
Use of Cell Saver®	0.95 (0.45 to 1.97)	0.8831
Intraoperative insertion of IABP	3.17 (1.46 to 6.88)	0.0036†
Use of >2 kinds of inotropic agents	2.86 (0.97 to 8.40)	0.0561
Other procedure	0.71 (0.08 to 6.06)	0.7540
Postoperative variables		
Low hematocrit	1.01 (0.43 to 2.39)	0.9865
Low PaO ₂ :FiO ₂ ratio	1.59 (0.76 to 3.33)	0.2179
Acute kidney injury	6.72 (2.99 to 15.10)	<0.0001†
New indication for hemodialysis	4.84 (2.21 to 10.60)	<0.0001†
Neurological complications	13.04 (4.21 to 40.39)	0.0001†
Arrhythmia	2.59 (1.19 to 5.63)	0.0168†
New myocardial infarction	4.47 (0.61 to 32.77)	0.1403
Other pulmonary complications‡	3.50 (1.67 to 7.34)	0.0009†
Other non-pulmonary complications§	3.44 (1.22 to 9.68)	0.0195†

*BMI <18.5 and >25.

†Significant at p<0.05.

‡Including nosocomial pneumonia, pleural effusion, atelectasis, pulmonary congestion, pulmonary edema.

§Including upper gastrointestinal bleed, decubitus ulcer, device related infection, surgical site infection, ischemic hepatitis, postoperative myasthenia gravis.
ACC — aortic cross-clamp; BMI — body mass index; CAD — coronary artery disease; CCS AGS — Canadian Cardiovascular Society Angina Grading Scale; COPD — Chronic Obstructive Pulmonary Disease; CPB — cardiopulmonary bypass; ESRD — end stage renal disease; EuroSCORE II — European System for Cardiac Operative Risk Evaluation II; IABP — intra-aortic balloon pump; LVEF — left ventricular ejection fraction; NYHA FC — New York Heart Association Functional Class; PRBC — packed red blood cells; STS ACSR — Society of Thoracic Surgeons Adult Cardiac Surgery Risk; WB — whole blood.

p=0.0026). Similarly, the proportion of patients who were given more than two kinds of inotropic agents intraoperatively in the PMV group (6/40; 15.00%) was significantly higher than that in the EE group (10/172; 5.85%; p=0.0476). The two groups

were comparable in terms of the rest of the intraoperative characteristics.

Table 5 shows the comparison of the postoperative characteristics of patients who had EE and patients with PMV. Patients with PMV had significantly higher frequencies of the following postoperative complications: AKI (25/35; 71.43% versus 45/166; 27.11%; p<0.0001), new indication for hemodialysis (16/37; 43.24% versus 23/169; 13.61%; p<0.0001), neurologic sequelae (12/40; 30.00% versus 5/172; 2.91%; p<0.0001), arrhythmia (13/40; 32.50% versus 27/172; 15.70%; p=0.0144), other pulmonary complications (17/40; 42.50% versus 30/172; 17.44%; p=0.0006), and other non-pulmonary complications (7/39; 17.50% versus 10/171; 5.81%; p=0.0142) compared to patients who had EE. Other postoperative characteristics between the two groups were comparable.

Presented in table 6 are the univariate odds ratios of PMV for preoperative, intraoperative and postoperative characteristics. Among the preoperative variables, renal dysfunction (OR=2.75; 95% CI 1.34 to 5.66; p=0.0058), NYHA FC IV (OR=7.53; 95% CI 3.07 to 18.46; p<0.0001), CCS AGS IV (OR=4.52; 95% CI 1.69 to 12.07; p=0.0026), LVEF <50% (OR=2.80; 95% CI 1.23 to 6.38; p=0.0141), cardiogenic shock (OR=12.14; 95% CI 2.26 to 65.11; p=0.0036), EuroSCORE II mortality >5.0% (OR=5.56; 95% CI 1.88 to 16.46; p=0.0020), and STS ACSR mortality >5.0% (OR=7.34; 95% CI 1.90 to 28.42; p=0.0039) all significantly increased the odds ratio of having PMV. Only intraoperative insertion of IABP (OR=3.17; 95% CI 1.46 to 6.88; p=0.0036) among the intraoperative variables increased the odds ratio of PMV. Postoperative variables that significantly increased the odds of PMV include postoperative AKI (OR =6.72; 95% CI 2.99 to 15.10; p<0.0001), a new postoperative indication for hemodialysis (OR =4.84; 95% CI 2.21 to 10.60; p<0.001), postoperative neurological complications (OR =13.04; 95% CI 4.21 to 40.39; p=0.0001), postoperative arrhythmia (OR =2.59; 95% CI 1.19 to 5.63; p=0.0168), other pulmonary complications (i.e., nosocomial pneumonia, pleural effusion, atelectasis, pulmonary congestion, or pulmonary edema) (OR=3.50; 95% CI 1.67 to 7.34; p=0.0009), and other non-pulmonary complications (i.e., surgical site infection, upper gastrointestinal bleed,

Table 7 Multivariable odds ratio (95% CI) of having prolonged mechanical ventilation (PMV)

Characteristics	Adjusted odds ratio (95% CI)	p-value
Renal dysfunction	1.16 (0.13 to 10.15)	0.8913
NYHA FC IV	1.64 (0.10 to 28.15)	0.7342
CCS AGS IV	7.74 (0.49 to 121.28)	0.1449
LVEF <50	0.52 (0.07 to 3.96)	0.5256
Preoperative cardiogenic shock	10.79 (0.13 to 913.76)	0.2937
Intraoperative insertion of IABP	8.43 (0.97 to 72.96)	0.0530
Acute kidney injury	11.82 (1.03 to 135.35)	0.0470*
New indication for hemodialysis	2.75 (0.27 to 27.68)	0.3909
Neurological complications	2.98 (0.17 to 52.24)	0.4549
Arrhythmia	2.32 (0.32 to 17.16)	0.4069
Other pulmonary complications	5.27 (0.59 to 46.97)	0.1361
Other non-pulmonary complications	1.94 (0.12 to 30.45)	0.6382

*Significant at p<0.05

CCS AGS — Canadian Cardiovascular Society Angina Grading Scale; IABP — intra-aortic balloon pump; LVEF — left ventricular ejection fraction; NYHA FC — New York Heart Association Functional Class.

decubitus ulcer, device related infection, surgical site infection, ischemic hepatitis, or postoperative myasthenia gravis) (OR =3.44; 95% CI 1.22 to 9.68; p=0.0195).

All significant variables in the univariate logistic regression analyses were entered into a multiple regression model. The multivariable odds ratio (95% CI) of PMV are presented in Table 7. In this regression model, only AKI independently increased the odds ratio of having PMV (adjusted OR=11.82; 95% CI (1.03 to 135.35; p=0.0470).

DISCUSSION

Key results

The frequency of PMV after CABG among patients with CAD in this study was 18.87%. Preoperative patient characteristics that increased the odds ratios of having PMV include renal dysfunction, cardiogenic shock, NYHA FC IV, CCS AGS class IV, LVEF <50%, greater than 5% mortality risk by EuroSCORE II, and greater than 5% mortality risk by STS ACSR. The intraoperative use of IABP and the postoperative development of AKI, neurological complications, arrhythmia, other pulmonary and non-pulmonary complications, as well as a new postoperative indication for hemodialysis, all significantly increased the odds ratios of having PMV. Multiple regression analysis showed that postoperative AKI was an independent predictor of PMV.

Strengths and limitations

This is the first systematic and comprehensive description of the demographic and clinical profiles of patients with CAD who

underwent CABG that has been reported from our heart institute since its opening in 2007. To the best of our knowledge, this is also the first time that predictors of PMV have been explored among Filipino patients belonging to this subpopulation.

We identified some limitations that are inherent to the retrospective design of this study. Some important data on potential predictors and outcomes, which could possibly influence our results, were not reflected in the patient records that we reviewed. Moreover, we were not able to accurately account for potential variations in medical and surgical technology, surgical technique and experience, as well as prevailing health care approach to patients, throughout the 8-year span covered by this study. It is possible that these variations have significant impact on the outcomes that we measured in this study.

Interpretation

The demographic and clinical profiles of patients in our study were similar to those in previous studies done among similar patients in other older heart institutions in the Philippines (Table 8). The previous studies reported that the average ages of Filipino patients with CAD who underwent CABG were within the range of 59-62 years,²⁶⁻²⁸ and that the mean BMI was 24.8 kg/m².²⁷ As in our study, majority of the patients in previous studies (75-85%) were males²⁶⁻²⁸ and had hypertension (69-72%).^{26, 27} The mean LVEF of patients in our study was comparable to that of patients in another study.²⁷ Our study however recorded higher rates of smoking, diabetes and COPD among patients. There were also more patients who presented with 3-vessel disease and who were admitted for elective surgery in our study. The observed differences in the rates of comorbidities probably reflect the increasing trends of these medical conditions over the years.^{29, 30} This could also mean that more and more patients with comorbidities undergo CABG as a therapeutic procedure. Another possibility is that this is a form of selection bias. Further studies are needed to explore these differences.

Compared to the PMV rates reported in other studies, which range from 2.4 to 10.4,^{3, 5, 8, 9, 12, 14} the rate in our study (18.87%) appears to be the highest. The definition of PMV varied among the previous reports, with time cutoffs ranging from 12 hours to 72 hours

Table 8 Comparison of demographic and clinical profiles of patients with coronary artery disease (CAD) who underwent coronary artery bypass grafting (CABG) in different heart institutions in the Philippines

Outcomes	This study 2015 n=213	Enriquez 2008 ²⁶ n=225	Bastan 2007 ²⁷ n=296	Vilela 2005 ²⁸ n=298
Number of years covered by the study	8	1	7	1
Mean age \pm SD, years	60.20 \pm 9.68	59.76 \pm 9.18	59.7 \pm 9.69	61.6 \pm 9.15
BMI \pm SD, kg/m ²	25.80 \pm 5.65	---	24.8 \pm 3.58	---
Male sex, %	78.40	85.3	79	75.48
Hypertension, %	72.30	71.6	69.6	---
Diabetics, %	57.75	41.3	38.8	---
Smokers, %	50.70	33.3	38.2	---
COPD, %	7.98	---	---	4.7
Previous history of MI, %	34.60	---	40.5	40.93
LVEF				
Mean \pm SD	50.33 \pm 13.54	---	53.4 \pm 21.73	---
<40%, %	---	---	---	10.4
<50%, %	30.71	---	---	---
3-vessel disease, %	81.13	---	59.5	---
Elective CABG, %	99.06	---	68.5	64.76

BMI — body mass index; COPD — chronic obstructive pulmonary disease; EF — ejection fraction; LVEF — left ventricular ejection fraction; MI — myocardial infarction.

postoperatively.²⁻¹⁶ Studies with cutoffs of >24 hours cutoffs for PMV will tend to exclude more patients from being classified as having PMV and report lower PMV rates. On the other hand, a cutoff of 12 hours would further increase the PMV rate in our study because of our practice of extubating patients the day after the CABG procedure. The relatively high rate of PMV in our study could be due to the inclusion of more patients with worse preoperative cardiac, renal, and pulmonary conditions, higher operative mortality risks, worse intraoperative hemodynamic conditions, longer operative durations, and postoperative complications—clinical factors that proved to be associated with PMV.

In this study, PMV is associated with poor preoperative cardiac and renal status, and postoperative complications. Low cardiac output syndrome (LCOS), which is a consequence of myocardial dysfunction, is a common complication of CABG that requires intraoperative placement of IABP and the use of more than two kinds of inotropic agents.³¹⁻³² LCOS is associated with poorer outcomes and increased incidence of pulmonary complications, myocardial infarction and renal failure.³³ The risk factors for LCOS are similar to the ones that we identified as associated with PMV, including low LVEF,³²⁻³³ renal failure,³² and emergency

nature of the CABG procedure,³³ probably suggesting a common pathophysiology for the two conditions. Higher operative risks scores (EuroSCORE II and STS ACSR) are associated with PMV because these scores are calculated based on preoperative variables that influence PMV, including cardiopulmonary and renal parameters.

The incidence of AKI after CABG may range from 3.6% to 30%, depending on the definition used,³⁴⁻³⁶ and around 1% of the patients undergoing the procedure develop new indications for hemodialysis.³⁷ Following the KDIGO definition of AKI—increase in creatinine by 0.3 mg/dL (26.5 μ mol/L) from baseline within 48 hours or increase 1.5 times from baseline within seven days—²⁶ we found that 34.83% of the patients in our study developed AKI post-CABG, and that 18.93% of patients who underwent CABG had new indications for hemodialysis post-operatively.

AKI can develop from several conditions, including intraoperative hypotension, postoperative cardiac complications that compromise kidney perfusion, hemolysis, atheroemboli, and contrast media exposure.³⁷ AKI after surgery was the only independent risk factor for PMV among patients in our study. This is the first time that postoperative AKI is reported to be associated with PMV. AKI will ultimately manifest as low urine output and volume overload in the lungs and heart, exacerbating cardiac dysfunction and pulmonary congestion, which will require extended mechanical ventilation support.

In prolonged CABG procedures, both CPB and ACC durations are increased. Unlike other open heart surgeries, those that require CPB have been known to decrease pulmonary function and increase the risk for postoperative pulmonary complications.³⁸ This dysfunction, otherwise known as the pump lung or the post pump syndrome, is due to an acute pulmonary inflammatory response that can arise from ischemia-reperfusion injury, endotoxemia, operative trauma, pre-existing left ventricular dysfunction, non-pulsatile blood flow, or contact of blood components with the artificial surface of the bypass circuit.³⁷ Many studies have looked into CPB time as a risk factor for PMV.²⁻³⁻⁸⁻⁹⁻¹³ Two studies were able to establish CPB time as an independent predictor of PMV.²⁻⁹ In one study, a CPB duration of more than 91 minutes significantly increased the odds ratio of

having PMV of more than 12 hours to 1.39.² The other reported that a CPB duration of more than 120 mins significantly increased the odds ratio of having PMV of more than 24 hours to 9.6.⁹ ACC time, on the other hand, refers to the duration that the aorta is clamped during bypass. Aorta clamping increases brain circulation but compromises the blood supply to the lower extremities and, more importantly, to the kidneys. Prolonged ACC, because of its strong association with postoperative AKI,¹² may indirectly result in PMV.

Generalizability

CABG is an important surgical procedure in the treatment of CAD. Postoperative complications related to a patient's preoperative medical condition and to the complexity of the CABG procedure—especially AKI—can predispose the patient to PMV. PMV, in turn, has been associated with prolonged hospital stay and mortality. Reducing the risk for AKI can reduce the incidence of PMV and subsequently reduce duration of hospital stay and mortality post-CABG. Every attempt should be made in order to avoid events or interventions that predispose patients to postoperative AKI such as exposure to contrast media, intraoperative hypotension, and cardiac complications that result in hypoperfusion of the kidneys.

We hope to be able to develop pre-emptive strategies for reducing the occurrence of PMV based on the findings of this study. To account for differences or changes in patients' demographic and clinical characteristics, the growing experience of health care providers, as well as improvements in surgical and anesthetic techniques over time,³ other institutions can come up with their own prediction models for PMV after CABG and regularly reassess or update their findings.

CONCLUSION

PMV occurred in 18.87% of the patients with CAD who had CABG in this study. Preoperative renal dysfunction, cardiogenic shock, NYHA FC IV, CCS AGS class IV, LVEF <50%, EuroSCORE II of >5% mortality risk, and STS ACSR score of >5% mortality risk increased the odds ratio of having PMV. The intraoperative insertion of IABP, as well as the occurrence of postoperative complications, namely—AKI, neuro-

logical complications, arrhythmia, other pulmonary and non-pulmonary complications, and a new postoperative indication for hemodialysis, all significantly increased the odds ratios of having PMV. On multiple regression analysis, postoperative AKI proved to be an independent predictor of PMV.

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Ethics approval

This study was reviewed and approved by the Department of Health XI Cluster Ethics Review Committee (DOHXI CERC reference P15101201).

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