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ORIGINAL ARTICLE

Factors causing prolonged mechanical ventilation and peri-operative morbidity after robot-assisted coronary artery bypass graft surgery

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Abstract

Robot-assisted coronary artery bypass graft [robot-assisted (coronary artery bypass grafting (CABG)] surgery is the latest treatment for coronary artery disease. However, the surgery extensively affects cardiac and pulmonary function, and the risk factors associated with peri-operative morbidity, including prolong mechanical ventilation (PMV), have not been fully examined. In this retrospective cohort study, a total of 382 patients who underwent robot-assisted internal mammary artery harvesting with mini-thoracotomy direct-vision bypass grafting surgery (MIDCABG) from 2005 to 2012 at our tertiary care hospital were included. The definition of PMV was failure to wean from mechanical ventilation more than 48 h after the surgery. Risk factors for PMV, and peri-operative morbidity and mortality were analyzed with a multivariate logistic regression model. Forty-three patients (11.3%) developed PMV after the surgery, and the peri-operative morbidity and mortality rates were 38 and 2.6%, respectively. The risk factors for PMV were age, left ventricular ejection fraction (LVEF), the duration of one-lung ventilation for MIDCABG (beating time), and peak airway pressure at the end of the surgery. Furthermore, age and anesthesia time were found to be independent risk factors for peri-operative morbidity, whereas age, LVEF, and anesthesia time were the risk factors for peri-operative mortality. These findings may help physicians to properly choose patients for this procedure, and provide more attention to patients with higher risk after surgery to achieve better clinical outcomes.

Keywords Robotic · CABG · Outcome · Delayed extubation · Risk factors

Introduction

Coronary artery bypass grafting (CABG) is a well-established treatment for coronary artery disease, and recent research has confirmed its benefits in patients with complex lesions [1]. Robotic technology is a novel surgical method, and has made it possible to perform minimally invasive cardiac surgery, which can ameliorate the complications of wide sternotomy, aortic clamping, and cardiopulmonary bypass. It has been demonstrated that total endoscopic CABG (TECAB) is associated with quicker recovery and a reasonably shorter length of stay [2]. However, significant surgeon and team learning curves for the majority of single-vessel anastomoses may limit these procedures to dedicated centers and highly specialized cardiac teams [3].

Another more clinically feasible method is to harvest the internal mammary artery (IMA) using robotic technology, and the subsequent off-pump procedure can be done manually through a mini-thoracotomy, and thus the key step of the grafting anastomosis can be completed more easily [4]. However, a thoracotomy is a painful surgical wound which

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may restrict breathing postoperatively. Whether a minimally invasive approach with a thoracotomy will result in better lung function postoperatively than a median sternotomy is unknown. Rogers et al. in the sternotomy versus thoracotomy (STET) trial suggested that a thoracotomy may worsen initial pulmonary function postoperatively, but other studies have suggested it may be more painful initially with quicker recovery of pulmonary function afterward [5–7]. In addition, minimally invasive surgery requires significantly prolonged one-lung ventilation (OLV) time during harvesting the IMA and anastomosis, which may lead to serious hypoxemia events intraoperatively, and can affect the postoperative outcomes because of an increased complications related to cognitive dysfunction [8, 9]. Furthermore, prolonged OLV time (> 1 h) may generate severe oxidative stress due to lung re-expansion, and cause possible damage to the alveolar capillary membrane [10]. All of these may predispose patients to postoperative pulmonary complications.

A distinguishing feature of robot-assisted CABG is that it affects both cardiac and pulmonary function [11]. Traditional open-chest CABG, whether using an on-pump or off-pump technique, mainly affects the cardiac-vascular system [12], with relatively preserved pulmonary function. Prolonged OLV, and even lung injury, is observed with wedge resection, lobectomy, and esophagectomy [13, 14]. However, in this case cardiac function is rarely affected. Only robot-assisted CABG combines both major heart surgery and prolonged OLV time (the duration of OLV may even longer than the common chest surgery) [15], which may have a serious impact on postoperative outcomes, including pulmonary complications such as prolong mechanical ventilation (PMV).

PMV is an important complication following cardiovascular surgeries. Although it occurs with an incidence of 3–9.9%, it is associated with increased morbidity and mortality [16]. Prior studies have attempted to identify risk factors for PMV after traditional CABG [17–23]. No studies, however, have examined robot-assisted IMA harvesting and mini-thoracotomy direct-vision CABG (MIDCABG). Patients undergoing this procedure have the unique characteristics of pre-existing poor heart function, prolonged OLV time with artificial lung deflation/inflation, and a painful postoperative thoracotomy wound. Thus, determining the risk factors associated with PMV and peri-operative morbidity after this procedure may help operative planning and the proper use of postoperative resource and management.

Materials and methods

Study subjects

From November 2005 to August 2012, 382 patients with coronary artery disease who underwent elective robotic-assisted CABG at our tertiary hospital were included in the study. Patient demographic data, clinical parameters, surgery details, postoperative events during hospitalization, and mortality were acquired from medical charts. Other data extracted included the length of postoperative mechanical ventilation, length of intensive care unit and hospital stay, and intraoperative data including procedure time during each surgical stage, hemodynamic and respiratory parameters, drugs and fluids administered, and emergency events that requires intervention. The study was approved by the institutional review board of Taichung Veterans General Hospital (IRB number: CE13272A).

Anesthesia and operations

The anesthesia and operative technique has been described previously [8]. In brief, during induction of anesthesia, a 32F to 37F double-lumen endotracheal tube was used for OLV. Fiber-optic bronchoscopy was used to check the positioning of double-lumen endotracheal tubes, and endobronchial secretions were suctioned every 30 min. The surgery consists of two stages, and was performed by the same experienced operator. For the first stage, the robot-assisted IMA harvesting, the patient is placed in the supine position with the left lung collapsed under OLV, followed by introducing the camera port and working ports into the left hemi-thorax with CO_2 insufflation. The IMA was then harvested under endoscopy, and prepared as the arterial graft. The second stage was the mini-thoracotomy direct-vision bypass grafting, conducted by ceasing CO_2 insufflation and creating a mini-thoracotomy at an appropriate intercostal location overlying the target coronary vessels. The IMA graft was then anastomosed directly to the target coronary artery, or to multiple coronary arteries with a radial artery graft, under direct vision through the mini-thoracotomy. After the anastomosis was completed, OLV was converted to double-lung ventilation. After the surgical wound was closed, the patient was sent to the postoperative recovery room and subsequently to the intensive care unit.

Hemodynamic indexes, such as cardiac index, stroke volume, and systemic and pulmonary vascular resistance were obtained from pulmonary artery catheterization during induction of anesthesia, at the end of surgery, and in the recovery room postoperatively. Arterial blood gas analysis was performed at the induction of anesthesia, at each surgical stage, at the end of the surgery, in the recovery room and intensive care unit, and before the endotracheal tube was removed. Ventilator settings and data, including tidal volume, respiratory rate, positive end-respiratory pressure (PEEP), and peak airway pressure were recorded at the same time points as the arterial blood gas analysis.

Definition of prolonged mechanical ventilation

PMV was defined as failure to wean from mechanical ventilation more than 48 h after surgery [23, 24]. Variables for analysis of risk factors with PMV and peri-operative morbidity include preoperative comorbidities, intraoperative length of each surgical stage, total anesthesia time, blood loss and the units of blood products transfusion, intravenous fluid administered with urine output, ventilator settings, arterial partial pressure of oxygen (PaO_2) and partial pressure of carbon dioxide ($PaCO_2$) acquired from the blood gas analyses, total fentanyl usage, and hemodynamic indexes.

A chest radiograph was obtained immediately after surgery to identify any possible pulmonary complications. A respiratory therapist assessed patients every 2 h from 07:00 to 21:00 during the first 24 h, and then once a day at 7:00 am. Respiratory parameters for weaning including rapid shallow breathing index (RSBI), maximal inspiratory pressure (PImax), maximal expiratory pressure (PEmax), and cuff leak test, and were checked before starting the pressure support trial. After starting the pressure support trial with a setting of 10 cm H_20 for 1 h, the tracheal tube was removed if the tidal volume was > 5 ml/kg, hemodynamic parameters were stable, and there was no tachypnea, anxiety, diaphoresis, decreased conscious, or paradoxical respiration.

Statistical analysis

Continue variables are expressed as mean ± standard deviation and range. Normally distributed continuous data were compared using the unpaired Student's *t* test to examine patients with and without PMV, while the Mann–Whitney *U* test was used for nonparametric continuous data. Categorical variables were described as percentage, and compared by χ^2 analysis or Fisher's exact correction. If a *p* value in the univariate was < 0.05, the variable was included in the multivariate logistic regression model to identify independent factors of PMV and peri-operative morbidity. In all analysis, a value of $p < 0.05$ was considered statistically significant. The relative risk estimation was acquired from the logistic regression analyses based on the odds ratio (OR) and 95% confidence interval (CI). All analyses were performed using SPSS software version 22 (SPSS, Chicago, IL).

Results

Demographic data

The demographic characteristics and comorbid illnesses of the patients are shown in Table 1. The mean age of the 382 patients was 64 ± 11 years, and 80.6% were male. The average LVEF was 51 ± 12%. Thirty-three (8.6%) patients had chronic obstructive pulmonary disease, 63 (16.5%) had a history of stroke, and 15 (3.9%) patients were receiving regular hemodialysis for uremia.

Intraoperative parameters

Intraoperative parameters, length of each surgical stage, and the number of coronary grafts are shown in Table 2. The mean duration of the first surgical stage of IMA take down with OLV was 113 ± 42 min, and the mean duration of one-lung ventilation (OLV) for MIDCABG (beating time) was 187 ± 50 min. There were 288 (75.4%) patients with triple-vessel disease, and the majority of patients (292, 76.4%) received anastomosis of more than three vessels.

Outcomes and complications

Intra- and postoperative complications are summarized in Table 3. The mean length of postoperative mechanical ventilation was 22 ± 27 h, and the mean length of hospital stay was 8 ± 9 days. A total of 145 patients (38%) had one or more peri-operative morbidities during their hospital course. Among them, 43 patients meet the criteria for PMV. New-onset atrial fibrillation was the most frequent adverse event following surgery, with an incidence of 15.4% (59 patients). Pulmonary complications, including pulmonary edema and pneumonia, occurred in 36 (9.4%) patients and 9 (2.4%) patients, respectively. Renal function impairment, defined as a postoperative serum creatinine level > 2.0 mg/dl, was found in 41 patients (10.7%).

The overall hospital mortality rate was 2.6% (10 patients). Three of the 10 patients experienced serious intraoperative hypoxemia that required ECMO support; however, the three

Table 1 Demographic characteristics and comorbid illnesses of patients undergoing robot-assisted CABG

Characteristics	*N* = 382
Age, years (range)	64 ± 11 (27–87)
Sex, male/female (male %)	308/74 (80.6)
Height, cm/weight, kg (range)	163 ± 8 (140–185)/68 ± 12 (38–111)
Body mass index (range)	25.5 ± 3.6 (16.8–35.6)
LVEF, % (range)	51 ± 12 (10–79)
Hypertension (%)	293 (76.7)
Diabetes mellitus (%)	173 (45.3)
Smoking (%)	175 (45.8)
COPD (%)	33 (8.6)
Old cerebral stroke (%)	63 (16.5)
Uremia under hemodialysis (%)	15 (3.9)

LVEF left ventricle ejection fraction, *COPD* chronic obstructive pulmonary disease

Table 2 Intraoperative parameters

Duration of anesthesia, min (range)	634 ± 80 (405–960)
Duration of OLV for IMA takedown, min (range)	113 ± 42 (20–300)[a]
Duration of OLV for MIDCABG (beating time), min (range)	187 ± 50 (40–470)
CAD: LM/SVD/DVD/TVD	121/20/74/288
Number of coronary grafts: 1/2/3/4/5	15/75/193/91/8
Cardiac index, L/min/m^2 (range)	2.3 ± 0.7 (1.1–6.9)
PVR index, dyne. s. cm ± 5.m ± 2 (range)	242 ± 367 (14–6730)
SVR index, dyne. s. cm ± 5.m ± 2 (range)	2690 ± 893 (615–5476)
IABP usage	169 (44.2)

N = 382

OLV one-lung ventilation, *IMA* internal mammary artery, *MIDCABG* mini-thoracotomy direct-vision coronary artery bypass graft surgery, *CAD* coronary artery disease, *LM* left main artery, *SVD/DVD/TVD* single/double/triple vessels disease, *PVR* pulmonary vascular resistance, *SVR* systemic vascular resistance, *IABP* intra-aortic balloon pump

[a]Duration of OLV for IMA takedown include port placement and IMA take down

Table 3 Intra- and postoperative outcomes

Outcomes	
Length of hospital stays, day (range)	8 ± 9 (1–92)
Length of post-OP mechanical ventilation, hour (range)	22 ± 27 (2–243)
Length of ICU stays, hour (range)	56 ± 67 (13–915)
Intraoperative events (%)	11 (2.9)
Pulmonary hemorrhage (%)	2 (0.5)
Intraoperative VT/VF (%)	7 (1.8)
ECMO usage (%)	2 (0.5)
Cardiac massage (%)	2 (0.5)
Postoperative complications (%)	139 (36.4)
Pulmonary edema (%)	36 (9.4)
Pneumonia (%)	9 (2.4)
Post-OP MV longer than 48 h (%)	43 (11.3)
Reintubation (%)	12 (3.1)
Postoperative Cr > 2.0 (%)	41 (10.7)
Delirium (%)	19 (5)
Stroke (%)	2 (0.5)
Newly onset atrial fibrillation (%)	59 (15.4)
Postoperative VT/VF (%)	6 (1.6)
Reoperation due to bleeding (%)	9 (2.4)
ECMO (%)	9 (2.4)
Any of above (%)	145 (38)[a]
Mortality (%)	10 (2.6)

ICU intensive care unit, *VT/VF* ventricular tachycardia/fibrillation, *ECMO* extracorporeal membrane oxygenation, *MV* mechanical ventilation, *Cr* serum creatinine

[a]Some patient have multiple (≥ 2) complications during hospitalization

patients died in the first 1 and 2 days after surgery. Of the other 7 patients, one had gastrointestinal bleeding, three had pulmonary edema or pneumonia that eventually progressed to ARDS, and three had persistent atrial fibrillation or ventricular fibrillation with hemodynamic changes and died during hospitalization.

Risk factors for PMV, and peri-operative morbidity and mortality

Multivariate logistic regression indicated that age, LVEF, duration of OLV for MIDCABG, and peak airway pressure at the end of the surgery were independent risk factors for PMV after surgery; age and anesthesia time were independent risk factors for peri-operative morbidity, and age, LVEF, and anesthesia time were risk factors for peri-operative mortality (Table 4).

Discussion

Robotic technology is the latest innovation in minimally invasive cardiac surgery, and is becoming more widely used as a revascularization procedure for patients with coronary artery disease [25]. Currently, in our center and possibly in most others, robot-assisted CABG is being considered feasible for almost all patients except those in cardiogenic shock, with unstable hemodynamics, or with poor lung function intolerant of OLV [26]. However, this is the only surgery that extensively affects both heart and lung function, and patients undergoing this surgery are inherently at a relatively high risk of complications due to pre-existing coronary artery disease, depressed heart function, and potential myocardial ischemia during the procedure. In addition, prolonged OLV during the surgery may impose transient trauma to the lung and result in peri-operative morbidity. These unfavorable patient and procedural characteristics may contribute to the considerable incidence of PMV (11.3%), morbidity (38%), and mortality (2.6%) in our study, as well as in other studies (morbidity rate of 16–37%, mortality rate of 0–3.8% for

Table 4 Multivariate logistic regression analysis for risk factors for prolong mechanical ventilation, and peri-operative morbidity and mortality

Variables	Odds ratio	95% CI	p^a	p^b
Risk factors for prolong mechanical ventilation				
Age	1.052	1.015–1.091	< 0.001	0.006
LVEF	0.956	0.93–0.984	0.001	0.002
Duration of OLV for MID-CABG, beating time	1.017	1.01–1.025	< 0.001	< 0.001
Peak airway pressure at the end of the surgery	1.096	1.021–1.177	0.001	0.011
Risk factors for peri-operative morbidity				
Age	1.061	1.019–1.105	< 0.001	0.004
Anesthesia time	1.009	1.002–1.015	< 0.001	0.008
Risk factors for mortality				
Age	1.128	1.015–1.254	0.004	0.025
LVEF	0.897	0.842–0.956	0.000	0.001
Anesthesia time	1.014	1.001–1.027	0.004	0.031

CI confidence interval

[a]From univariate regression analysis

[b]From multivariate regression analysis

off-pump multi-vessel, minimally invasive CABG) [27–29]. As such, identification of periprocedural complication-correlating factors is needed to improve the surgical outcomes.

Surgical procedures

The relatively high rate of IABP use in our study (44%) might partially be related to the high rate of prior stroke (16.5%) and uremia receiving hemodialysis (3.9%) in our population. But it may also be more related to the therapeutic strategy of our heart team. Since most of our patients received multi-vessel off-pump CABG [292 patients (76.4%) for ≥ 3 vessels] under mini-thoracotomy with prolonged one-lung ventilation, our heart team tended to establish IABP in advance to avoid intraoperative conversion to full median sternotomy because of severe hypotension and hypoxemia during beating procedure. This strategy has been proven beneficial in previous studies demonstrating that for off-pump sternotomy CABG, severe hypotension may occur during displacement of the heart for target vessels exposure, yet could be prevented by placement of an IABP before surgery [30]. The benefit of prophylaxis IABP placement has also been shown to lower peri-operative morbidity and mortality in hemodynamically stable, but high-risk patients [30–32].

The duration for IMA takedown in our study was defined as from the very beginning of starting OLV through completion of IMA isolation. The duration has often been divided into two separate portions in other studies, i.e., port placement (average 15 min) and then IMA harvesting (average 65 min) [33]. The slightly longer time needed in our study for IMA takedown (113 min) is the same as in our prior report (114 min) [8]. Differences in duration between studies may due to the definitions of time periods, or less likely level of surgeon's experience or caution. In addition, the total length of anesthesia time in our study consists of anesthesia induction, radial artery harvesting, OLV for LIMA takedown and MIDCABG, achieving hemostasis, and exchange of the double-lumen endotracheal tube to a standard tube. It was nearly identical to the total operating room time and was comparable to the length of 695 min reported in other studies [27].

Risk factors for PMV

PMV after on-pump or off-pump CABG is an important issue, but has not been examined with robot-assisted, multi-vessel, minimally invasive CABG. The definition of PMV has been reported to range from 12 to 72 h, and the incidence of PMV varies with the definition, from 43.4 to 1.96% [19, 20, 23, 24]. Prapas et al. found that old age, history of neurological events, and preoperative IABP were associated with PMV using a cutoff value of 48 h [24]. They did not analyze the operative parameters, such as beating time and peak airway pressure. In addition, the duration of OLV was longer in our study, which may account for the differences in factors associated with PMV.

Our study demonstrated that the independent risk factors for PMV after the surgery were age, LVEF, duration of OLV for MIDCABG, and the peak airway pressure at the end of the surgery. Advanced age and lower LVEF have been reported as risk factors for PMV after cardiac surgery [17–23]. Patients with advanced age have a decreased ventilation response to hypoxia and hypercapnia, and this can be exaggerated when respiratory depressants are administered (opioids and inhalational agents). Furthermore, the closing capacity increases with age, and will equal the functional residual capacity in the supine position at the age of 45, and in the upright position at the age of 65 [35]. This will exaggerate the ventilation–perfusion mismatch (V/Q mismatch) with the result of decreasing arterial PaO_2. All of these make an aging patient more susceptible to postoperative hypoxemia. As for cardiac dysfunction, a lower LVEF could cause a higher filling pressure and low cardiac output, which can lead to greater hemodynamic instability and complications postoperatively [18, 19, 23].

The OLV duration during MIDCABG was an independent risk factor for PMV in this study. Regional ischemia combined with global hypoxemia during this specific stage of the surgery is important. In traditional on-pump CABG, a duration of global cold ischemia with a cardiopulmonary bypass time > 91 min has been recognized as a risk factor for PMV [19]. In off-pump CABG or MIDCABG, global cold ischemia can be avoided, but the risk of regional warm myocardial ischemia during the beating procedure still exists. Higher levels of creatine kinase-MB (CK-MB) and cardiac troponin-I (cTnI) have been found after off-pump CABG, and are associated with longer mechanical ventilation and ICU stay [36, 37]. Moreover, global hypoxemia is likely to occur during this stage of surgery. During open-chest surgery, the patient is placed in a more ventilation–perfusion matched lateral decubitus position (ventilation and perfusion both predominantly occur on the same non-surgical side). Hypoxemia and postoperative pulmonary complications such as acute lung injury (ALI) can still occur, especially if the OLV time is longer than 100 min [38]. For the MIDCABG procedure on the beating heart, the patient placed in a supine position in which the intrapulmonary shunt is increased with V/Q mismatch (the surgical side now still has perfusion, but without ventilation), thus the possibility of hypoxemia is higher during this stage of the procedure [8]. The combination of regional myocardial ischemia and global hypoxemia during the beating procedure made it one of the independent risk factors for PMV.

The peak airway pressure at the end of the surgery was also a risk factor for PMV. The peak airway pressure is recognized as part of the dynamic compliance of the lung (tidal volume/peak airway pressure). Worsening of lung compliance, either caused by the baseline condition of the lung or exogenous force such as mechanical ventilation setting, may lead to serious pulmonary complications afterward. A study revealed that in patients undergoing high-risk elective surgery, only intraoperative peak airway pressure, not the tidal volume, was the ventilator setting that caused postoperative acute lung injury (ALI) [39]. For patients receiving mechanical ventilation, Gagic et al. suggested that increased peak airway pressures (> 30 cm H_2O) are a risk factor associated with development of acute respiratory distress syndrome (ARDS) [40]. Several factors may have caused worsening of lung compliance in our study, including sputum impaction, fluid overload, blood transfusion, prolong OLV time (average 300 min) with injurious ventilator settings, or oxidative stress/ischemia–reperfusion injury [14]. Nevertheless, increased peak airway pressures at the end of the surgery should be regarded as the precursor of potential postoperative pulmonary complications, and any management that can help avoid lung injury should be used, such as fluid restriction and protective ventilator settings.

Risk factors for peri-operative morbidity and mortality

Our study found that age and anesthesia time were risk factors for peri-operative morbidity, whereas age, LVEF, and anesthesia time were risk factors for mortality. Aged people often have more comorbidities, and these can make them more susceptible to peri-operative morbidities and mortality. Lower LVEF also contributed to the mortality risk, with more hemodynamic instability encountered peri-operatively. Another risk factor correlated with peri-operative morbidity and mortality was the anesthesia time. The average anesthesia time for each one-vessel robotic-assisted CABG, two-vessel TECAB, three- or four-vessel TECAB, and conventional CABG are 336, 466, 695, and 396 min, respectively [27, 41]. Although multi-vessel robot-assisted surgery is associated with a longer surgical time compared with traditional CABG, literature linking operation time to peri-operative morbidity is scarce. For the TECAB procedure, longer operation time, especially longer than 478 min (8 h), could lead to greater postoperative morbidity, longer hospital stay, and lower long-term survival. Morbidity correlates positively with the complexity of the surgical procedure (multi-vessel anastomosis), and technical problems encountered during surgery as IMA injury, epimyocardial lesions, and anastomotic problems [27, 34]. Efforts have been made to shorten the operation time, including fixed teams of surgeons and some technical improvements [42].

Limitations

There are limitations to this study. Patients in our study predominately underwent more than three- or four-vessel anastomosis, which may be different from other robotic-assisted CABG studies. Some variables were not included in our study, such as ethnic group or Euroscore. In addition, our institution did not provide a fast-track protocol for these patients, which may cause a longer duration of mechanical ventilation since the respiratory therapist assessed the patients as often as the other cardiac surgery patients.

Conclusions

In conclusion, our study found that age, LVEF, the duration of OLV for MIDCABG (beating time), and peak airway pressure at the end of the surgery are risk factors for PMV in robotic-assisted CABG. Furthermore, age and anesthesia time were risk factors for peri-operative morbidity, and age, LVEF, and anesthesia time were risk factors for mortality. These findings may help physicians with proper patient selection, pay more attention to higher risk patients afterward, and use lung protective strategies to achieve better clinical outcomes.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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