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ABOUT COVER

Editorial Board Member of *World Journal of Critical Care Medicine*, Patrick Honoré, MD, PhD, graduated from Louvain Medical School in 1988, completing advanced training as Specialist in Internal Medicine in 1993 and Intensive Care Specialist in 1994. For almost 5 years, he undertook ICU training abroad (United Kingdom and Australia). He has authored/co-authored more than 345 peer-reviewed papers. He has served as Editor-In-Chief of the *Journal of Translational Internal Medicine* and as Associate Editor-In-Chief of the *Journal of Translational Critical Care Medicine*. He holds the positions of Head of Clinics and Full Academic Professor at the Vrije Universiteit Brussel Faculty of Medicine after his PhD Thesis. Since January 2018, he has held the position of Co-Director, ICU Research Director and Professor of Medicine at CHU-Brugmann University Hospital (Belgium). (L-Editor: Filipodia)

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Retrospective Study

Intensive care outcome of left main stem disease surgery: A single center three years' experience

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Abstract

BACKGROUND

Left main coronary artery (LMCA) supplies more than 80% of the left ventricle, and significant disease of this artery carries a high mortality unless intervened surgically. However, the influence of coronary artery bypass grafting (CABG) surgery on patients with LMCA disease on morbidity intensive care unit (ICU) outcomes needs to be explored. However, the impact of CABG surgery on the

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morbidity of the ICU population with LMCA disease is worth exploring.

AIM

To determine whether LMCA disease is a definitive risk factor of prolonged ICU stay as a primary outcome and early morbidity within the ICU stay as secondary outcome.

METHODS

Retrospective descriptive study with purposive sampling analyzing 399 patients who underwent isolated urgent or elective CABG. Patients were divided into 2 groups; those with LMCA disease as group 1 (75 patients) and those without LMCA disease as group 2 (324 patients). We correlated ICU outcome parameters including ICU length of stay, post-operative atrial fibrillation, acute kidney injury, re-exploration, perioperative myocardial infarction, post-operative bleeding in both groups.

RESULTS

Patients with LMCA disease had a significantly higher prevalence of diabetes (43.3% *vs* 29%, $P = 0.001$). However, we did not find a statistically significant difference with regards to ICU stay, or other morbidity and mortality outcome measures.

CONCLUSION

Post-operative performance of Patients with LMCA disease who underwent CABG were comparable to those without LMCA involvement. Diabetes was more prevalent in patients with LMCA disease. These findings may help in guiding decision making for future practice and stratifying the patients' care.

Key Words: Cardiac surgery; Critical care; Left main disease; Coronary graft; Outcome; Cardiac output

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Core Tip: Post-operative performance of patients with left main coronary artery (LMCA) disease who underwent coronary artery bypass grafting were comparable to those without LMCA involvement.

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INTRODUCTION

Defining the intensive care unit (ICU) outcome predictors after cardiac surgery remains an optimum goal^[1]. Prolonged ICU stay is associated with increased costs and adverse patient outcome^[2]. Age, congestive cardiac failure, peripheral vascular disease, higher perioperative serum creatinine, and prior cardiac surgery had been identified by Hammermeister *et al*^[3], as potential risk factors for adverse outcome after cardiac surgery. Although the risk of mortality after cardiac surgery has been identified in several studies through various scoring systems, there is a growing need to identify morbidity predictors and factors influencing the ICU length of stay in the cardiac surgery setting^[4]. Time in blood glucose range^[5], elevated perioperative troponin^[6], and acute kidney injury (AKI) have been identified as individual risk factors for morbidity in cardiac surgery ICU^[7].

The left main coronary artery (LMCA) supplies 80% of the blood demands of the left ventricle. Obstructive lesions of the LMCA carries high mortality with medical treatment^[8], but improves markedly with surgical treatment^[9]. Some authors do not

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consider LMCA occlusion as a risk for early and late mortality^[10]. The challenges associated with LMS disease had been explored in previous work of El-Menyar *et al*^[10] to include lesion location to outcome relation, subacute thrombosis potential, left ventricular function and patient comorbidities on overall outcome; and the risk-benefit ratio of coronary artery bypass graft surgery *vs* stenting. In a cross-sectional study conducted in Qatar, isolated LMCA obstruction was 4-fold higher in women, with high prevalence of distal and proximal lesions. The authors found that renal failure was independent predictor of left main stem (LMS) disease. The mortality over one-year was higher in patients with LMS disease^[11].

To the best of our knowledge no previous studies have addressed the short-term morbidity based on the ICU outcome; hence LMS morbidity measures need to be explored further.

MATERIALS AND METHODS

Methods

This was a retrospective study conducted in Cardiothoracic Surgery Department, Heart Hospital, Hamad Medical Corporation, Qatar. The Heart Hospital is a tertiary cardiac care center and is currently performing over 350 cardiac surgeries annually. The study was conducted after approval of the local research committee of the institution review board (MRC-01-17-058). The review board waived the informed consent as this was a retrospective study. The patient data in the period from January 2015 to January 2018 were analyzed. We included all patients with isolated coronary artery bypass grafting (CABG). Patients with combined surgeries, were excluded. We screened 421 patients, and a total of 22 patients were excluded. Remaining 399 Patients were divided into 2 groups - those with LMCA disease as group 1 (75 patients) and those without LMCA disease, as group 2 (324 patients). They were then correlated with ICU outcome parameters.

The following set of data were analyzed and reported for all patients: Age, gender, past history of diabetes or hypertension, total anesthesia duration, time of cardiopulmonary bypass (CPB), time of aortic cross clamp (ACC), utilization of intra-aortic balloon pump (IABP), inotropes score, and Euro SCORE.

We had chosen the primary outcome variable to be the length of stay in the ICU (LOS_{ICU}), other variables collected included length of mechanical ventilation (LOV), and the length of stay in the hospital (LOS_{Hosp}), complications, including infections, AKI, post-operative atrial fibrillation (POAF), perioperative myocardial infarction (PMI), stroke, the need for veno-arterial extra corporeal membrane oxygenation (VA-ECMO) and early mortality within the hospital stay were reported for each patient. Dendrite Clinical Systems (London, United Kingdom) and (Cerner, United States) were used to retrieve data. In our institution we have a fast track approach in transferring patients to the step down, we transfer patients when they are off inotropes/vasopressors, no need for invasive or noninvasive ventilatory support, not requiring early kind of renal replacement therapy, awake started pain medications, chest drain is our or minimal chest drain, and started oral medication.

Outcome definitions

The primary outcome was the LOS_{ICU} , the secondary outcomes were LOV, LOS_{Hosp} , complications, as POAF, AKI, PMI, infection, mortality within the hospital.

AKI was defined as an acute post-operative (within 48 h) reduction in kidney function, with absolute increase in the serum creatinine concentration of 0.3 mg/dL or greater (26.4 μ mol/L), or an increase in serum creatinine of 1.5-fold from baseline) or dropping of urine volume to < 0.5 mL/kg/h for 6 h^[12]. POAF is defined as a new onset of atrial fibrillation (AF) after cardiac surgery in patients who were in sinus rhythm before surgery and had no prior history of AF. Significant LMS disease was defined as a more than 50% narrowing of the lumen diameter as determined by angiography^[13]. The vasoactive active inotrope score was calculated according to Gaies *et al*^[14]. The LOV was defined according to our institute rule as the time from ICU admission to tracheal extubation. We define early mortality as mortality within the first 28 d within the hospital as per our organization rules. Bleeding events that mandate surgical re-exploration were also recorded. We defined PMI as post-operative rise of highly sensitive troponin T to level of 3466 ng/L associated with electrocardiographic, echocardiographic or angiographic evidence^[6].

Statistical analysis

Normally distributed continuous variables were expressed as the mean \pm SD. Skewed variables were presented as the median (interquartile range). The patients were divided into two groups according to the association of LMS disease. Continuous variables were compared using the Student's *t*-test and the Mann Whitney *U* test, as found appropriate. Chi-square or Fisher's exact tests were used to compare categorical variables between the two groups. A significant association was defined by a *P* value \leq 0.05 (two-tailed). Patients undergoing isolated CABG were included in the study and they were divided in two groups according to significant LMS disease. Group I: Patients without significant LMS disease (control group) and Group II: Patients with significant LMS disease (study group). Statistical analysis was performed using the SPSS software (version 22, Chicago, IL, United States).

RESULTS

Of the 421 patients screened, 399 patients were enrolled in this study; the remaining 22 patients met the exclusion criteria. The mean age was 51.9 ± 11.3 years. The rest of the baseline descriptive data are highlighted (Table 1). The predominant gender in this study were males, accounting for 245 patients (82.2%). The high prevalence of diabetes was noted in our study where 141 patients (47.3%) were diabetics. Patients were divided based on the association of LMS disease into 2 groups. Both groups were matched regarding the age, gender, association of hypertension, Euro score, baseline ejection fraction (EF), baseline creatinine and need for elective surgery (Table 2). We noted that diabetes was significantly more prevalent in LMS group (53% *vs* 44.4%, *P* = 0.05). The usage of IABP was significantly higher percentage among LMS group (*P* = 0.05).

There was no significant difference between both groups regarding inotropic and vasopressors demands. We did not encounter significant differences between the groups in terms of anesthesia, CPB and ACC times as well as number of grafts. The postoperative lengths of mechanical ventilation, ICU stay, and hospital stay did not show any significant differences between both groups (Table 3). Post-operative complications, including POAF, AKI, hospital-mortality, ventilator associated pneumonia, need for VA-ECMO, vasoactive inotrope score (VIS), re-admission to ICU, surgical re-exploration, major bleeding and PMI did not make significant differences between groups.

DISCUSSION

The salient findings of this work were: (1) The primary outcome which was the LOS_{ICU} was not different between the studied groups; (2) The secondary outcome measures did not show any significant differences; (3) Need for IABP support for LMS group was significantly higher than the group without LMS; and (4) Diabetes was more prevalent in patients with LMS.

To the best of our knowledge, this is the first study to address the ICU outcome of LMS disease after CABG. Chaitman *et al*^[15] have highlighted the high morbidity and mortality of LMS disease and its frequent association with multi-vessel disease.

LMS disease patients comprised 18.7% of the patients in our study, compared with 30% in the Keogh *et al*^[16] database. According to the guidelines of the American College of Cardiology/American Heart Association (ACC/AHA), CABG is a class I one recommendation for LMS stenosis in asymptomatic patients^[17]. The most important coronary lesion in prognosis prediction is LMS, the latter is diagnosed in 5%-7% of patients who underwent coronary angiography^[18]. The mortality in our LMS group was 2.7%. Conley and colleagues pointed to the contributing factors in LMS mortality to include age, diabetes, left ventricular function and dyslipidemia^[19]. Su *et al*^[20] in their review observed a mortality of 3.4% with conventional CABG in patients having LMS disease. Lower mortality in our series may be related to younger age.

In our study, patients with LMS disease were older and having higher prevalence of diabetes compared to those without LMS disease, but this did not attain statistical significance. Older patients may have more advanced form of CAD^[21]. Usage of IABP was significantly higher in patients with LMS. In a meta-analysis of randomized controlled trials Rampersad *et al*^[22] concluded that preoperative utilization of IABP

Table 1 Description of the studied group

| Variable | n | Minimum | Maximum | mean \pm SD |
|---------------------------|-----|---------|---------|------------------|
| Age | 399 | 18 | 79 | 51.9 \pm 11.3 |
| BMI (kg/m ²) | 399 | 18.8 | 43.7 | 25.1 \pm 7.1 |
| Creatinine (μ mol/L) | 397 | 54.9 | 378.1 | 99.8 \pm 55.8 |
| EF% | 388 | 18 | 65 | 45.8 \pm 8.9 |
| Additive Euro score | 398 | 0 | 19 | 4.6 \pm 3.1 |
| CPB time (min) | 393 | 0 | 377 | 118.1 \pm 46.9 |
| ACC time (min) | 392 | 0 | 188 | 86.1 \pm 38.7 |
| Anesthesia time (min) | 398 | 220 | 630 | 295.7 \pm 71.2 |
| VIS | 398 | 0 | 29 | 6 \pm 2.1 |
| LOS _{ICU} (h) | 397 | 26 | 320 | 65.9 \pm 46.1 |
| LOV (min) | 397 | 190 | 17300 | 432 \pm 65 |
| LOS _{hosp} (d) | 394 | 6 | 245 | 28.1 \pm 12.9 |

BMI: Body mass index; EF: Ejection fraction; CPB: Cardiopulmonary bypass; ACC: Aortic cross clamp; WBCs: White blood cells; LOS_{ICU}: Length of stay in intensive care unit; LOV: Length of mechanical ventilation; LOS_{hosp}: Hospital length of stay; VIS: Vasoactive inotrope score.

Table 2 Demographic differences between both groups

| Variable | Group I (LMS), 75 (%) | Group II (no LMS), 324 (%) | P value |
|---------------------------------|-----------------------|----------------------------|---------|
| Age | 58.3 \pm 11.8 | 55.19 \pm 9.7 | 0.06 |
| Gender (male) | 62 (82.6) | 264 (81.4) | 0.34 |
| Diabetes | 39 (52) | 144 (44.4) | 0.05 |
| Hypertension | 32 (42.6) | 144 (44.4) | 0.13 |
| Euro score | 5.8 \pm 3.9 | 5.0 \pm 3.6 | 0.6 |
| BMI | 30.1 \pm 6.3 | 27.9 \pm 5.8 | 0.6 |
| EF < 40 | 24 (32) | 86 (26.5) | 0.07 |
| IABP | 28 (37.3) | 80 (24.6) | 0.05 |
| Elective surgery | 45 (60) | 224 (66.6) | 0.5 |
| Basal creatinine (μ mol/L) | 98.7 \pm 46.5 | 94.7 \pm 43.1 | 0.6 |

BMI: Body mass index; EF: Ejection fraction; IABP: Intra-aortic balloon pump; LMS: Left main stem.

reduced the early mortality in high-risk patients undergoing elective CABG. The IABP has been the most widely used mechanical circulatory support device. In cardiac surgery, the placement of the IABP was indicated when post-cardiotomy cardiogenic shock or mechanical complications appeared. Although preoperative IABP is frequently used by some clinicians in high-risk patients undergoing cardiac surgery, its effectiveness has not been confirmed^[23].

In our study, patients with LMS had significantly more IABP utilization than the other group. IABP is the most commonly used mechanical circulatory device, and it is used in some centers as preoperative prophylaxis for high-risk CABG surgeries, although this practice is debatable^[24]. In our study we followed an earlier study that supported the use of IABP preoperatively when 2 of the following factors were associated with LMS ejection fraction EF below 35%, re-do CABG, LMS stenosis more than 70%, unstable angina in the preoperative period^[25]. Pilarczyk *et al*^[26] mentioned that utilization of IABP in high risk patients could help the intra-operative hemodynamic management with trend towards clinical stability and better prognosis. The authors found that usage of IABP in the preoperative period could reduce ICU

Table 3 Main differences in both studied groups

| Variable | Group I (LMS), 75 (%) | Group II (no LMS), 324 (%) | P value |
|---|--------------------------|-----------------------------|------------|
| Inotrops | | | |
| Dopamine, mean dose ($\mu\text{g/kg/min}$), mean \pm SD | 9 (12), 6.50 \pm 3.10 | 31 (9.6), 7.23 \pm 15.2 | 0.5, 0.34 |
| Adrenaline, mean dose ($\mu\text{g/kg/min}$), mean \pm SD | 6 (8), 0.06 \pm 0.01 | 27 (8.3), 0.05 \pm 0.009 | 0.6, 0.8 |
| Noradrenline, mean dose ($\mu\text{g/kg/min}$), mean \pm SD | 12 (16), 0.08 \pm 0.01 | 43 (13.2), 0.07 \pm 0.008 | 0.4, 0.7 |
| Dobutamine, mean dose ($\mu\text{g/kg/min}$), mean \pm SD | 4 (5.3), 4.5 \pm 1.4 | 11 (3.3), 3.9 \pm 1.1 | 0.06, 0.09 |
| Milrinone, mean dose ($\mu\text{g/kg/min}$), mean \pm SD | 3 (4), 0.56 \pm 0.05 | 7 (2.1), 0.6 \pm 0.04 | 0.9, 0.4 |
| Intraoperative parameters | | | |
| CPB time (min) | 139 \pm 43 | 125 \pm 69.6 | 0.6 |
| ACC time (min) | 87.1 \pm 34 | 79.3 \pm 30.1 | 0.9 |
| Anesthesia time (min) | 6.6 \pm 1.4 | 6.5 \pm 1.8 | 0.9 |
| Grafts | 3.1 \pm 0.8 | 3.4 \pm 1.01 | 0.7 |
| Postoperative parameters | | | |
| LOV (min) | 384.1 \pm 123 | 375.1 \pm 119 | 0.8 |
| LOS _{ICU} (h) | 65.9 \pm 46.1 | 63.4 \pm 43.9 | 0.6 |
| LOS _{hosp} (d) | 16.1 \pm 4.2 | 14.7 \pm 3.7 | 0.6 |
| VIS | 6.4 \pm 2.6 | 6.1 \pm 2.2 | 0.4 |
| Post-operative outcome | | | |
| POAF | 12 (16) | 39 (12) | 0.06 |
| AKI | 20 (26.7) | 75 (23.1) | 0.09 |
| In-hospital-mortality | 2 (2.7) | 7 (2.1) | 0.8 |
| VAP | 1 (1.3) | 5 (1.5) | 0.7 |
| VA-ECMO | 2 (2.7) | 4 (1.2) | 0.08 |
| Re-admission ICU | 2 (2.7) | 8 (2.5) | 0.8 |
| Re-exploration | 6 (8) | 26 (8.6) | 0.5 |
| PMI | 3 (4) | 11 (3.3) | 0.4 |

AKI: Acute kidney injury; CPB: Cardiopulmonary bypass; ACC: Aortic cross clamp; ECMO: Extracorporeal membrane oxygenation; LOV: Length of mechanical ventilation; LOS_{ICU}: Length of stay in intensive care unit; LOS_{hosp}: Hospital length of stay; POAF: Post-operative atrial fibrillation; VIS: Vasoactive inotrope score; VAP: Ventilator associated pneumonia.

and hospital lengths of stay as well as death within the hospital. Similarly, Christenson *et al*^[25] found reduction in mortality, postoperative ICU and hospital stay with use of IABP. Our study is a retrospective data review. Our institutional preference is to insert IABP prophylactically after induction in patients with high risk LMCA disease. Takaro *et al*^[27] mentioned that stenosis greater than 75% especially in the presence of left ventricular dysfunction is considered a high risk.

The assumption that LMS disease portends higher risk is due to the fact that 75% to 100% of myocardial territory is at risk when dominance of the left system is associated. Revascularization is recommended when more than 50% LMS disease is present, regardless of the symptoms or other ischemic association. CABG is recommended according to the American guidelines - when surgical bypass is feasible and SYNTAX score is more than 33, which define complexity of the multi-vessel disease^[13]. The primary outcome in our study was the ICU length of stay, which was not significantly different in both groups (65.9 \pm 46.1 *vs* 63.4 \pm 43.9, *P* = 0.6). Many studies have showed LMS disease as a risk factor for surgery. In a systemic review over 172000 patients after cardiac surgery, the authors found LMS to be predictive of short-term adverse outcome^[28].

In our study urgent procedures in the LMS group was 40%, which was not significantly different from patients without LMS 36.4% (Table 2). Sher-I-Murtaza *et al*^[29] conducted a single center study and found the ICU length of stay to be higher in patients with LMS disease. The LMS population in this study was older and had more cases done on urgent basis. This was not the case in our study where both groups were matched regarding the age, Euro score and urgency. In our institution, LMS involvement alone does not warrant urgent surgical intervention. This probably has accounted for the difference in the ICU length of stay compared to Sher-I-Murtaza *et al*'s^[29] study.

According to the SYNTAX trial, the postoperative outcome is related to the burden of atherosclerosis of the native coronary vessels where percutaneous coronary revascularization strategy is adopted but not if CABG is applied^[30]. In our study, the postoperative lengths of mechanical ventilation, ICU stay, and hospital stay did not show any significant differences between both groups (Table 3). Post-operative complications, including POAF, AKI, hospital-mortality, ventilator-associated pneumonia, need for VA-ECMO, re-admission to ICU, surgical re-exploration and PMI did not make significant differences between groups. The in-hospital mortality after CABG range from 1%-3% and its related to age, female gender, re-do surgery, low EF, degree of LMS stenosis and other coronary vessel involvement^[31]. Mortality was equal in our studied groups, the low mortality in our patient population did not allow us to analyze the predictive factors beyond mortality. Both our groups were matched regarding the ACC, CPB, VIS, anesthesia time. Some authors refer the outcome to the type of cardioplegia used and the length of ACC^[32]. All our patients underwent on-pump CABG, we used the same cardioplegia. Sher-I-Murtaza *et al*^[29] reported worse outcome with LMS when compared to non LMS groups with regard to length of ventilation, mortality and need for inotropic support. This can be explained by the older age and the association of other lesions in their population while we operated on younger population. Blood consumption rate was not different among the two groups. This may be due to timely stoppage of antiplatelet therapy with appropriate bridging and use of antifibrinolytics in high risk patients.

Finally, we noted that diabetes was significantly more prevalent in LMS group (53% vs 44.4%, $P = 0.05$). Diabetes is known to increase the cardiovascular disease risk^[33].

Study limitations: This study had the following limitations: (1) Being retrospective and conducted in a single center; (2) The revascularization strategy was based on the physician discretion; (3) Difficulty in doing long term follow up. Our study conclusions should be confirmed with larger randomized trials to better define mortality and morbidity variation in LMS patients in relation to the others; and (4) Low sample size.

CONCLUSION

Patients with LMS disease showed similar outcome as those without LMS in this study. Diabetes was more prevalent in patients with LMS. We observed that patients with LMS had significantly more IABP utilization. These findings may help in guiding decision making for future practice and stratifying the patients' care.

ARTICLE HIGHLIGHTS

Research background

Left main coronary artery (LMCA) supplies more than 80% of the left ventricle, and significant disease of this artery carries a high mortality unless intervened surgically. However, the influence of coronary artery bypass grafting (CABG) surgery on patients with LMCA disease on morbidity intensive care unit (ICU) outcomes needs to be explored.

Research motivation

However, the impact of CABG surgery on the morbidity of the ICU population with LMCA disease is worth exploring.

Research objectives

We aim at determining whether LMCA disease is a definitive risk factor of prolonged ICU stay as a primary outcome and early morbidity within the ICU stay as secondary

outcome.

Research methods

Retrospective descriptive study with purposive sampling analyzing 399 patients who underwent isolated urgent or elective CABG. Patients were divided into 2 groups; those with LMCA disease as group 1 (75 patients) and those without LMCA disease as group 2 (324 patients). We correlated ICU outcome parameters including ICU length of stay, post-operative atrial fibrillation, acute kidney injury, re-exploration, perioperative myocardial infarction, post-operative bleeding in both groups.

Research results

In this study, patients with LMCA disease had a significantly higher prevalence of diabetes (43.3% *vs* 29%, $P = 0.001$). However, we did not find a statistically significant difference with regards to ICU stay, or other morbidity and mortality outcome measures.

Research conclusions

Patients with left main stem (LMS) disease showed similar outcome as those without LMS in this study. Diabetes was more prevalent in patients with LMS. We observed that patients with LMS had significantly more intra-aortic balloon pump (IABP) utilization. These findings may help in guiding decision making for future practice and stratifying the patients' care.

Research perspectives

(1) The hospital length of stay did not differ between the studied groups with and without LMS disease; (2) The secondary outcome measures did not show any significant differences among the studied population; (3) Need for IABP support for LMS group was significantly higher than the group without LMS; and (4) Diabetes was more prevalent in patients with LMS.

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