Acta Cardiol Sin 2017;33:195–203
Original Article
doi: 10.6515/ACS20160621A

Cardiovascular Surgery

Is Left Atrial Size a Predictor of Mortality after Coronary Artery Bypass Surgery? A Single Center Study

Khalid S. Ibrahim,[1,2] Fadia A. Mayyas,[3] Khalid Kheirallah,[4] Nizar R. AlWaqfi[1,2] and David R. Van Wagoner[5]

Background: To investigate the left atrial (LA) size as an independent predictor of mortality following coronary artery bypass surgery (CABG).

Methods: This single center study evaluated determinants of mortality in 1070 patients who underwent isolated CABG from 2005-2014. Clinical, laboratory and demographic data were obtained from medical records. Collinearity between enlarged LA size (diameter ≥ 4 cm) and covariates was identified. The adjusted effects of enlarged LA size on 30-day mortality post CABG were tested using multiple logistic regression models. Adjusted odds ratios (OR) and 95% confidence intervals (CI) were reported.

Results: The mean age was 59 ± 9.8 years, and 238 patients were female. Two multivariate logistic regression models were evaluated. In Model A, mitral regurgitation (MR), ejection fraction, intensive care unit length-of-stay and variables found to be collinear with LA size as predictors of mortality were excluded. In model B, the collinear variables were included. By multivariate analysis (Model A), the statistically significant independent predictors of 30-day mortality after CABG were: enlarged LA size (OR 4.82, 95% CI 2.16-10.79), emergency CABG (OR 3.54, 95% CI 1.75-7.18), prolonged inotropic support (OR 2.79, 95% CI 1.38-5.6), diuretic use ≥ 1 month (OR 1.29, 95% CI 1.3-8.42), and use of clopidogrel within a week before surgery (OR 3.27, 95% CI 1.28-8.36. In Model B, enlarged LA and moderate MR were identified as independent predictors of 30-day mortality.

Conclusions: Increased LA size is a strong independent predictor of mortality after isolated CABG.

Key Words: Coronary artery bypass graft surgery • Mitral regurgitation • Mortality

INTRODUCTION

Coronary artery bypass grafting (CABG) is the most common cardiac surgery performed worldwide. CABG improves quality of life in patients by improving angina and heart failure symptoms as well as increasing survival rates.[1] However, CABG has a significant risk of morbidity and mortality.[2] Previous studies reported mortality rates after isolated CABG ranging from 2.6% to 12.2%.[3-5] Predictors of post-surgical mortality have been studied thoroughly in various countries.[4,5] In Jordan, we previously found that age, female gender, heart failure, prolonged inotropic and ventilatory support, postoperative pneumonia and postoperative stroke were predictors of mortality.[6]

Left atrial enlargement is common in patients with mitral regurgitation (MR), heart failure and atrial fibrillation.[7] An enlarged left atrium (LA) is a predictor of stroke,[8] post-operative atrial fibrillation[9] and multiple morbidi-

Received: January 19, 2016 Accepted: June 21, 2016
[1]Princess Muna Heart Center, King Abdullah University Hospital; [2]Department of General Surgery, Division of Cardiac Surgery, Faculty of Medicine; [3]Department of Clinical Pharmacy, Faculty of Pharmacy; [4]Department of Public Health, Faculty of Medicine, Jordan University of Science and Technology, Irbid, Jordan; [5]Department of Molecular Cardiology, Cleveland Clinic Foundation, Cleveland, Ohio, USA.
Corresponding author: Dr. Khalid S. Ibrahim, Faculty of Medicine, Jordan University of Science and Technology, Staff Cardiac Surgeon, King Abdullah University Hospital, 8th Floor, Wing D, P.O. Box 630001, Irbid 22110, Jordan. Tel: +962 2 7200600 ext. 40625; E-mail: Ksibrahim@just.edu.jo

ties.[10,11] LA size is inversely related to left ventricular function and positively related to the severity and duration of MR, due to its impact on left atrial pressures.[7] Although MR is known to be a predictor of mortality after CABG,[12,13] little information is available about the relation of LA size to risk of mortality following isolated CABG. In a small study (n = 197), it was shown that LA size predicts mortality after CABG.[9]

In practice, LA size is commonly considered as a preoperative predictor of mortality. Systematic analysis of LA size as a predictor of mortality after CABG may enhance our ability to effectively use LA size as a risk predictor in clinical practice. However, data from the Middle East are lacking. Thus, the main goal of this study was to begin to evaluate the relation of LA size to mortality after isolated CABG in a large cohort of Jordanian patients.

PATIENTS AND METHODS

This retrospective cohort study included all patients who underwent isolated CABG at Princess Mona Heart Institute / King Abdullah University Hospital in the north of Jordan from January 2005 through June 2014. This study was approved by the Institutional Review Board of King Abdullah University Hospital. Exclusion criteria included redo surgery, valve surgery and combined CABG and valve surgery. A total of 1070 consecutive patients were included.

Clinical, laboratory and demographic data were obtained retrospectively from patient's medical records. Plasma glucose and lipid levels (low density lipoprotein), high density lipoprotein, triglycerides and total cholesterol were obtained from the King Abdullah University Hospital information registry. Pre-operative medication use was collected from all patients and assessed in relation to mortality at 30 days post-CABG. Recent myocardial infarction was defined as elevation of cardiac enzymes or as evidenced by electrocardiogram within 4 weeks before surgery. Heart failure was considered if patients were symptomatic or on anti-failure treatment. Diabetes status (taking either oral hypoglycemic agents or insulin), hypertension status (on treatment), renal dysfunction (creatinine serum level $\geq$ 2.0 mg/dl or on chronic dialysis), post operative renal impairment was considered if serum creatinine doubled after surgery, chronic obstructive pulmonary disease (if diagnosed at any time before surgery), peripheral vascular disease (a positive history of intermittent claudication or had a documented clinical evidence of ischemia) were all recorded. Left ventricular ejection fraction was obtained from transthoracic echocardiography measurements. Left ventricular ejection fraction (LVEF) was classified into three groups according to the degree of dysfunction; normal (LVEF $\geq$ 50%), mild to moderate impairment (LVEF between 36 and 49%) or severe impairment (LVEF $\leq$ 35%). The number of diseased coronary arteries was obtained from the coronary angiography report. Patients with significant coronary artery disease underwent CABG according to American College of Cardiology (ACC)/American Heart Association(AHA) guidelines.[14] Surgery was considered emergency or urgent if the patient was sent to the operating room within 24 hours from the time of cardiac catheterization, due to unstable angina, hemodynamic instability, or an untoward event in the catheterization suite.

Pre-operative trans-thoracic echocardiography studies were performed using two-dimensional imaging with an ALT (HD1) 6000 ht, (2-4 MHz probe, Philips Medical Systems Inc., Bothell, WA, USA) to evaluate LVEF, the degree of mitral/aortic/tricuspid valve regurgitation, and LA size (diameter). MR was graded (0-4) with 0 = Competent, 0-1 = trace MR, 1-2 = mild MR, 2-3 = Moderate MR and 3-4 = Severe MR. Left atrial diameter was calculated using the long axis view, measuring the anteroposterior dimension in M-mode, with normal diameters ranging from 2.5-4 cm.

Pre-, peri- and postoperative measurements were evaluated as possible independent risk factors for mortality.

Operative procedure

CABG was performed under general anesthesia, and all patients were operated on using a median sternotomy approach and cardiopulmonary bypass with full heparinization (3 mg/kg). The left internal mammary artery was harvested with a pedicle. Cardiopulmonary bypass was performed by cannulation of the ascending aorta and the right atrium. After aortic cross-clamping, a cold crystalloid cardioplegia solution was infused into the aortic root, and cardiopulmonary bypass was per-

formed with systemic cooling to 28-34 °C. Perfusion pressure was maintained at a mean of 60-80 mmHg.

Distal anastomoses were performed using a 7-0 polypropylene suture on an 8 mm needle by continuous method. The right coronary artery was typically the first target, followed by the circumflex, obtuse marginal, diagonals and lastly the left internal mammary artery (LIMA) to the left anterior descending artery. After release of the aortic cross clamp, the proximal anastomoses were sutured with 5-0 or 6-0 polypropylene with partial cross clamp. Ventricular fibrillation was terminated by use of 10-30 J direct current shocks. The patient was then weaned from cardiopulmonary bypass, given protamine to restore hemostasis, and the chest was closed. Norepinephrine was used as inotrope to maintain systolic blood pressure at around 120 mmHg when needed.

Statistical analysis

The primary outcome variable in this study was 30-day mortality. Data were analyzed for descriptive and inferential statistics using the Statistical Package for Social Sciences software (SPSS, version 20). Descriptive characteristics are reported using counts, percentages, means and standard deviations (SD) as appropriate. Bivariate analyses were conducted to assess differences in 30-day mortality by patient characteristics using univariate logistic regression models. The unadjusted odds ratios (OR) and 95% confidence interval (CI) were reported for each variable. To select the most parsimonious binary logistic model and avoid including unnecessary covariates, collinearity between covariates was first detected using chi-square or t-tests, as appropriate. Then, selected variables with $p < 0.2$ at the bivariate level were considered for inclusion in the models, in addition to age and gender. Finally, other variables that showed collinearity were excluded. Adjusted ORs, 95% confidence intervals (OR, 95% CI) are reported. Statistical significance was set at alpha level (P) = 0.05.

RESULTS

The mean age of our study participants was 59 years, with males comprising about three quarters of the cohort (77.8%). Approximately two-thirds of the subjects had hypertension, and half had diabetes mellitus, whereas only 12.1% had heart failure. Table 1 shows the main pre-, intra- and post-operative demographic and clinical characteristics of the study participants (N = 1070). As expected for a CABG population, 80% had stable angina, while ~20% had experienced a recent (≤ 28 days) myocardial infarction. Most patients had a normal LA diameter, with about one-third of subjects having an enlarged LA diameter (≥ 4 cm). No patients had severe (4+) MR.

Preoperatively, most patients received aspirin, statins, beta blockers, clopidogrel and angiotensin-converting enzyme inhibitors, with 27.3% receiving diuretics. About 16% of patients reported stopping clopidogrel within a week before surgery. Most participants had 4-6 bypass grafts, with the left internal mammary artery to the left anterior descending artery used in the majority of patients. Extended pump time (≥ 120 minutes) and aortic clamp time (≥ 90 minutes) were documented in 15.5% and 7.2 % of patients, respectively. Sternal wound infections and pneumonia were diagnosed in 3.3% and 5.1% of patients, respectively, while 6.0% of patients had an intensive care unit stay of a week or more. The prevalence of post-operative renal failure was 8.1%. Incident of postoperative atrial fibrillation was documented in 25.5% of the patients. Overall, 60 patients (5.6%) died within thirty days.

The unadjusted risks of clinical variables on 30-day mortality are reported in the first column of Table 2. Unadjusted variables with a p-value less than 0.2 for association with 30-day mortality were considered for inclusion in the adjusted regression models. As post-operative atrial fibrillation was documented in a limited number of patients, it was not included in the analysis. Collinearity was detected between LA size and MR, LVEF, and intensive care unit length-of-stay ($p < 0.01$ for all three comparisons). Other collinear variables (chronic obstructive pulmonary disease, peripheral vascular disease hyperlipidemia, pre-operative intra-aortic balloon pump, angiotensin-converting enzyme inhibitors, stroke, and post-operative renal failure) were excluded from the models based on collinearity or lack of clinical significance.

In multivariate model A (where variables collinear with LA size were excluded), subjects with enlarged LA size were about 5 times as likely to die 30-day following CABG, after controlling for other variables in the model. In model B where variables collinear with LA size (LVEF,

Table 1. Patient characteristics (N = 1070)

A. Pre-operative characteristics	
Clinical characteristics	
Age, years (SD)	59.07 (9.8)
Male sex, n (%)	832 (77.8)
BMI	28.6 ± 14.96
Hypertension, n (%)	655 (61.6)
Heart failure, n (%)	129 (12.1)
Diabetes mellitus, n (%)	567 (54.2)
COPD, n (%)	35 (3.3)
History of recent MI (≤ 28 days), n (%)	198 (18.5)
Hyperlipidemia, n (%)	351 (34.0)
Stable angina, n (%)	856 (80.0)
Lower limbs edema, n (%)	98 (9.2)
PVD, n (%)	50 (4.7)
History of atrial fibrillation, n (%)	3 (0.3)
Orthopnea, n (%)	108 (10.1)
PND, n (%)	88 (8.3)
Current smoking (≥ 20 cigarette), n (%)	144 (13.5)
Lab tests (mean ± SD)	
Low density lipoprotein (LDL, mmole/L)	2.58 ± 1.10
High density lipoprotein (HDL, mmole/L)	1.00 ± 0.34
Triglyceride (mmole/L)	2.50 ± 1.72
Total cholesterol (Tch, mmole/L)	4.68 ± 1.38
Tch/HDL	5.00 ± 1.80
Fasting plasma glucose (mmole/L)	9.81 ± 5.14
Packed cell volume (%)	39.49 ± 5.61
Serum K (mmole, L)	4.31 ± 0.56
Serum Mg (mmole/L)	0.82 ± 0.17
Preoperative creatinine level (mmole/L)	94.61 ± 49.80
Postoperative creatinine level (mmole/L)	100.22 (64.70)
Echocardiographic measurements	
≥ 4 cm, n (%)	304 (32.4)
LA diameter (mean ± SD), cm	3.83 ± 0.36
Left ventricular ejection fraction, %	
≥ 50%, n (%)	486 (55.0)
49-35%, n (%)	322 (36.5)
< 35%, n (%)	75 (8.5)
Mitral valve regurgitation, n (%)	
Grade 0-1	568 (58.3)
Grade 1-2	345 (35.4)
Grade 2-3	54 (5.5)
Grade 3-4	8 (0.8)
Use of medications, n (%)	
ACE inhibitors/never users	457 (43.1)
Less than one month	191 (18.0)
More than one month	413 (38.9)
Diuretics/never users	770 (72.7)
Less than one month	101 (9.5)
More than one month	188 (17.8)
Beta blockers/never users	296 (27.9)
Less than one month	261 (24.6)
More than one month	504 (47.5)
Statins/never users	248 (23.4)
Less than one month	255 (24.0)
More than one month	558 (52.6)
Aspirin use/never use	101 (9.5)
Continued until the day of CABG	706 (66.4)
Stop for < a week prior to CABG	256 (24.1)
Clopidogrel/Never use	383 (36.0)
Stop for > week prior to CABG	511 (48.0)
Stop for < week prior to CABG	170 (16.0)
B. Intra-Operative characteristics	
CABG	
1-3 graft, n (%)	464 (44.1)
4-6 graft, n (%)	587 (55.9)
LIMA-LAD, n (%)	1017 (95)
Pump time > 120 min, n (%)	160 (15.5)
Aortic clamp > 90 min, n(%)	75 (7.2)
C. Post-Operative	
Sternal wound infection, n(%)	35 (3.3)
Pneumonia, n(%)	54 (5.1)
ICU stay (≥ one week), n (%)	63 (6.0)
Prolonged support (≥ 36 hours), n (%)	205 (19.8)
Blood transfusion, n (%)	771 (73.6)
Renal failure, n (%)	82 (8.1)
Stroke TIA, n (%)	11 (1.0)
Mortality (30-days)	60 (5.6)

Data is presented as mean ± SD for continuous variables and counts (%) for categorical variables.
ACE, angiotensin converting enzyme; BMI, body mass index; CABG, coronary artery bypass graft; COPD, chronic obstuctive pulmonary disease; HDL, high-density lipoprotein; ICU, intensive care unit; K, Potassium; LA, left atrium; LAD, left anterior descending; LIMA, left internal mammary artery; Mg, magnesium; MI, myocardial infarction; PND, paroxysmal nocturnal dyspnea; PVD, peripheral vascular disease; SD, standard deviation; Tch/HDL, total cholesterol high density lipoprotein; TIA, transient ischemic attack.

MR, and intensive care unit length of stay) were not excluded from the model, enlarged LA size still significantly predicted 30-day mortality following CABG (OR 3.15, 95% CI 1.29-7.67).

DISCUSSION

Several studies have discussed the risk factors associated with mortality following CABG.[2] We recently re-

Table 2. Effect of patients' characteristics on 30-day mortality

Variable	Unadjusted effect		Adjusted effect			
			Model A*		Model B#	
	OR	p-value	AOR†	CI 95%	AOR†	CI 95%
Age (in years)	1.01	.70	1.01	0.98-1.04	1.01	0.97-1.05
Male gender	1.35	.35	1.36	0.58-3.21	1.64	0.64-4.21
Hypertension‡	1.21	.45	--	--		
BMI	0.99	.89	--	--		
Tch/HDL	1.01	.91	--	--		
Heart failure‡	0.88	.76	--	--		
Diabetes mellitus‡	0.86	.53	--	--		
COPD‡	2.36	.09	--	--	--	--
History of recent MI (≤ 28 days)‡	2.48	< .001	1.68	0.77-3.70	1.74	0.74-4.09
Hyperlipidemia‡	0.66	.13	--	--		
Stable angina‡	0.44	< .001	0.63	0.29-1.37	0.64	0.27-1.52
Lower limbs edema‡	1.24	.59	--	--		
PVD‡	1.94	.15	--	--		
Current smoking (≥ 20 cigarette)‡	1.37	.37	--	--		
Emergency‡	4.15	< .001	3.54	1.75-7.18§	4.20	1.93-9.14§
Pre op IABP‡	5.55	.002	--	--		
LA size (≥ 4 cm)‡	3.06	< .001	4.82	2.15-10.79§	3.15	1.29-7.67§
Left ventricular ejection fraction (less than 50%)‡	2.30	.003	--	--	1.11	0.52-2.34
MR (normal)	Ref	--			Ref	--
Grade 1	3.31	< .001	--	--	2.22	0.97-5.01§
Grade 2	6.48	< .001			7.85	2.45-24.84§
Grade 3	4.63	.16			2.40	0.19-30.05
ACE inhibitors (never use)	Ref	--				
Less than one month	2.16	.01	--	--		
More than one month	1.07	.82				
Diuretics (never use)	Ref	--	Ref	--	Ref	--
Less than one month	2.17	.02	0.74	0.26-2.12	0.62	0.20-1.94
More than one month	1.50	.18	3.30	1.30-8.42§	2.85	1.08-7.56§
Statins (never use)	Ref	--	Ref	--	Ref	--
Less than one month	1.54	.18	2.23	0.94-5.69	2.63	0.99-7.03
More than one month	0.77	.41	0.55	0.21-1.45	0.68	0.25-1.94
Beta blockers (never users)	Ref	--				
Less than one month	1.26	.45				
More than one month	0.80	.45				
Aspirin use/never use	Ref	--				
Continued until the day of CABG	1.73	.33				
Stop for < a week prior to CABG	2.28	.14				
Clopidogrel/never use	Ref	--	Ref	--	Ref	--
Stop for > week prior to CABG	2.84	.002	1.3	0.58-3.12	0.79	0.30-2.08
Stop for < week prior to CABG	5.03	< .001	3.27	1.28-8.36§	2.00	0.73-5.45
CABG (4 or more grafts)‡	0.689	.13	0.67	0.35-1.28	0.79	0.391-1.60
LIMA-LAD‡	0.99	.91		--		
Pump time > 120 min‡	0.95	.89		--		
Aortic clamp > 90 min‡	2.05	.06	2.34	0.87-6.29	2.18	0.76-6.29
Sternal wound infection‡	0.88	.86				
Pneumonia‡	4.25	< .001	2.48	0.85-7.27	2.61	0.56-12.16

Table 2. Continued

Variable	Unadjusted effect		Adjusted effect			
			Model A*		Model B#	
	OR	p-value	AOR†	CI 95%	AOR†	CI 95%
ICU stay (≥ one week)‡	6.02	< .001			1.95	0.50-7.64
Prolonged support‡	3.44	< .001	2.79	1.38-5.62§	3.23	1.53-6.80§
Blood transfusion‡	1.41	.21				
Post operative stroke	8.77	< .001				
Post-operative renal failure	8.72	< .001				

* Model A includes variables with unadjusted effect p-value of < 0.2 and excluding collinear variables (MR, LVEF, and ICU stay).
# Model B includes variables with unadjusted effect p-value of < 0.2 including colinear variables. † Adjusted OR. ‡ Coded as 0 (no), and 1 (yes). § Variables with p-value < 0.05.
ACE, angiotensin converting enzyme; AOR, adjusted odds ratios; BMI, body mass index; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; IABP, intraaortic ballon pump; ICU, intensive care unit; LA, left atrim; LAD, left anterior descending; LIMA, left internal mammary artery; LVEF, left ventricular ejection fraction; MI, myocardial Infarction; MR, mitral regurgitation; NE, not entered into the regression model; PVD, peripheral vascular disease; TCh/HDL, total cholesterol high density lipoprotein.

ported the predictors of mortality in northern Jordan.[6] Considering the ethnic differences and the relatively young age of CABG patients in our study, it was unclear if LA size would predict post-CABG mortality among Jordanian patients. Here, we have focused on the role of enlarged LA size on 30-day mortality following CABG.

LA size has been reported to predict morbidity and mortality in many clinical settings.[10,15] Ferreira et al.,[10] showed that increased LA volume was the only echocardiographic determinant associated with a need for mechanical ventricular assist device, heart transplant and death in dilated cardiomyopathy patients. LA enlargement has also been reported to predict incident heart failure,[16] atrial fibrillation,[17] stroke,[18] and death.[18,19] Further, LA enlargement has also been reported to be an independent predictor of cardiovascular morbidity and mortality in type II diabetes mellitus patients.[11]

There is little data regarding the impact of LA enlargement on postoperative mortality following isolated CABG. In a small study of 197 CABG patients, Wang, et al. found that left atrial expansion index predicts postoperative atrial fibrillation and mortality after CABG.[9] In a larger population, we found that the odds of mortality increase 4.81 times for patients with LA size ≥ 4 cm. Although LA contraction at the end of diastole contributes only ~20% to LV filling, this contribution is very important for patients with LV dysfunction.[20,21]

LA enlargement has adverse myocardial hemodynamic consequences due to impaired left ventricular filling during diastole in these patients. Increased left ventricular stiffness with progressive left ventricular dysfunction may lead to progressive MR and thus increased LA size.[22] In a vicious circle, enlarged LA size can then further impair the filling of the left ventricle due to increased filling pressures. Mitral regurgitation also causes atrial enlargement and systolic dysfunction,[7] so left atrial size can also reflect the "history" (severity and duration) of MR. Thus, the association of LA size with mortality can sometimes be related to the presence of mitral regurgitation, and MR can result from ischemic ventricular remodeling after a myocardial infarction. Ischemia and dilatation both promote endothelin-1 (ET-1) synthesis. We previously demonstrated that atrial ET-1 levels are strongly and independently correlated with both LA enlargement and MR severity in atrial fibrillation patients.[21]

As LA size is collinear with MR and LVEF, we excluded these variables from our first analysis and found that LA size is strongly associated with mortality. To evaluate whether this association was independent of MR and reduced LVEF, we included all collinear variables in a secondary analysis and found that both MR and enlarged LA were independently associated with mortality; however, the estimate (effect size) was decreased. Together, these data suggest that LA size is primarily (but

not entirely) associated with mortality by mechanisms independent of MR.

Thus, LA enlargement can be used in practice as a clinical indicator for mortality risk.

Left atrial enlargement is associated – among other factors,[23] with an increased risk of postoperative atrial fibrillation,[19] suggesting one mechanism whereby LA enlargement can contribute to post-surgical morbidity and mortality. In some studies, postoperative atrial fibrillation has been reported to be a predictor of morbidities and mortality after CABG,[23,24] while other studies could not find such a relation.[9] It seems quite likely that the impact of post-operative atrial fibrillation is dependent on the degree of ventricular dysfunction. In a subgroup analysis of our study (data not shown), post-operative atrial fibrillation AF was not associated with mortality, which supports our conclusion that LA enlargement is an independent predictor of mortality. However, a lack of complete data on post-operative atrial fibrillation in our study (with data available only for one quarter of the cohort) may have underestimated its relation to mortality.

Most of our patients presented with mild to moderate ischemic MR (grade 1-2), with only a few presenting with grade 3 MR (n = 8). For six of the eight patients, undergoing intraoperative transesophageal echocardiography before starting cardiopulmonary bypass showed that MR was 2-3, and it further indicated resolution of MR upon weaning from the bypass machine and restoration of cardiac perfusion and pump function; in the remaining two patients, no explanation was found. Presence of severe MR (grade 3-4) indicates a need for surgical intervention during CABG.[24] Interestingly, our analysis suggested that grade 2 MR is also associated with mortality, with an odds ratio of 7.8. The degree of MR degree may be underestimated by surface echocardiography; more careful assessment by intraoperative transesophageal echocardiography and exercise testing may help to more precisely evaluate the degree of regurgitation and posterior LV wall motion abnormality.[25] On the other hand, grade 2 MR by itself and regardless of posterior wall motion might have an impact on LVEF and mortality, indicating a need for surgical intervention during CABG.[26] It is now routinely practiced at our institution to use intraoperative transesophageal echocardiography in CABG patients to evaluate for the presence of LA thrombus, the extent of MR, and left ventricular function.

Ischemic mitral regurgitation in patients undergoing CABG usually results from impaired LV function due to ischemic injury. Long-term survival following CABG in patients with severe LV dysfunction is affected by MR.[27] In a step-wise analysis, LVEF was a strong predictor of mortality, but this effect was masked in the presence of MR as both factors are collinear, where poor left ventricular function promotes MR and vice versa.

Previous studies have reported that clopidogrel use within 3-5 days before surgery increases the risk of bleeding and reopening, and increases the length of hospital stay after CABG.[28] However, few studies have evaluated the impact of clopidogrel use on mortality. Here we show that the timing of clopidogrel discontinuation before CABG has an impact on 30-day mortality; and those patients who discontinued clopidogrel within the week before surgery were at significantly greater mortality risk.

Bandeali et al. reported that use of diuretics before cardiac surgery is associated with increased risk of postoperative major adverse events, mainly due to renal dysfunction.[29] Similarly, we found that use of diuretics for more than a month before surgery was associated with increased mortality, relative to non-users or those who used diuretics for less than a month before CABG.

Study limitations

This was a retrospective study, and LA diameter was used as a measure of LA size. While LA volume may be a more precise estimate of atrial size, it could not be assessed in our study. The echocardiographic data for these patients were not stored as well. Measurement of end-diastolic pressures was also lacking. Data on postoperative AF was documented in only a minority of our patients.

CONCLUSIONS

Increased left atrial size is a strong predictor of mortality after isolated CABG independent of MR. In addition, our observation that moderate mitral valve regurgitation was associated with increased risk of mortality after CABG independent of LA size warrants a prospec-

tive and more detailed evaluation. In future studies, we plan to prospectively study the impact of left atrial size and MR on outcomes in CABG patients, and to integrate LA size into a scoring system for calculating the risks of morbidity and mortality.

ACKNOWLEDGMENT

We would like to thank Dr. Anas Gharaebeh MD, (Intern) for the distinguished effort in the data collection.

DISCLOSURE

None.

FUNDING

None.

REFERENCES

1. Velazquez EJ, Lee KL, Jones RH, et al. Coronary-artery bypass surgery in patients with ischemic cardiomyopathy. *N Engl J Med* 2016;374:1511-20.
2. Okrainec K, Banerjee DK, Eisenberg MJ. Coronary artery disease in the developing world. *Am Heart J* 2004;148:7-15.
3. Sa MP, Soares EF, Santos CA, et al. EuroSCORE and mortality in coronary artery bypass graft surgery at Pernambuco Cardiologic Emergency Medical Services [Pronto Socorro Cardiologico de Pernambuco]. *Rev Bras Cir Cardiovasc* 2010;25:474-82.
4. Seccareccia F, Perucci CA, D'Errigo P, et al. The Italian CABG Outcome Study: short-term outcomes in patients with coronary artery bypass graft surgery. *Eur J Cardiothorac Surg* 2006;29:56-62; discussion 62-4.
5. Shroyer AL, Coombs LP, Peterson ED, et al. The Society of Thoracic Surgeons: 30-day operative mortality and morbidity risk models. *Ann Thorac Surg* 2003;75:1856-64; discussion 64-5.
6. AlWaqfi N, Khader Y, Ibrahim K. Coronary artery bypass: predictors of 30-day operative mortality in Jordanians. *Asian Cardiovasc Thorac Ann* 2012;20:245-51.
7. Rusinaru D, Tribouilloy C, Grigioni F, et al. Left atrial size is a potent predictor of mortality in mitral regurgitation due to flail leaflets: results from a large international multicenter study. *Circ Cardiovasc Imaging* 2011;4:473-81.
8. Shin HY, Jeong IH, Kang CK, et al. Relation between left atrial enlargement and stroke subtypes in acute ischemic stroke patients. *J Cerebrovasc Endovasc Neurosurg* 2013;15:131-6.
9. Wang WH, Hsiao SH, Lin KL, et al. Left atrial expansion index for predicting atrial fibrillation and in-hospital mortality after coronary artery bypass graft surgery. *Ann Thorac Surg* 2012;93:796-803.
10. Ferreira F, Galrinho A, Soares R, et al. Prognostic value of left atrial volume in patients with dilated cardiomyopathy. *Rev Port Cardiol* 2013;32:865-72.
11. Poulsen MK, Dahl JS, Henriksen JE, et al. Left atrial volume index: relation to long-term clinical outcome in type 2 diabetes. *J Am Coll Cardiol* 2013;24;62:2416-21.
12. Sirivella S, Gielchinsky I. Results of coronary bypass and valve operations for mitral valve regurgitation. *Asian Cardiovasc Thorac Ann* 2007;15:396-404.
13. Wong DR, Agnihotri AK, Hung JW, et al. Long-term survival after surgical revascularization for moderate ischemic mitral regurgitation. *Ann Thorac Surg* 2005;80:570-7.
14. Hillis LD, Smith PK, Anderson JL, et al. 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* 2011;124:2610-42.
15. Paoletti E, Zoccali C. A look at the upper heart chamber: the left atrium in chronic kidney disease. *Nephrol Dial Transplant* 2014; 29:1847-53.
16. Takemoto Y, Barnes ME, Seward JB, et al. Usefulness of left atrial volume in predicting first congestive heart failure in patients > or = 65 years of age with well-preserved left ventricular systolic function. *Am J Cardiol* 2005;96:832-6.
17. Vaziri SM, Larson MG, Benjamin EJ, Levy D. Echocardiographic predictors of nonrheumatic atrial fibrillation. The Framingham Heart Study. *Circulation* 1994;89:724-30.
18. Laukkanen JA, Kurl S, Eranen J, et al. Left atrium size and the risk of cardiovascular death in middle-aged men. *Arch Intern Med* 2005;165:1788-93.
19. Benjamin EJ, D'Agostino RB, Belanger AJ, et al. Left atrial size and the risk of stroke and death. The Framingham Heart Study. *Circulation* 1995;92:835-41.
20. Patel DA, Lavie CJ, Milani RV, et al. Clinical implications of left atrial enlargement: a review. *Ochsner J* 2009;9:191-6.
21. Grigioni F, Avierinos JF, Ling LH, et al. Atrial fibrillation complicating the course of degenerative mitral regurgitation: determinants and long-term outcome. *J Am Coll Cardiol* 2002;40:84-92.
22. Mayyas F, Niebauer M, Zurick A, et al. Association of left atrial endothelin-1 with atrial rhythm, size, and fibrosis in patients with structural heart disease. *Circ Arrhythm Electrophysiol* 2010; 3:369-79.
23. Tsai YT, Lai CH, Loh SH, et al. Assessment of the risk factors and outcomes for postoperative atrial fibrillation patients undergoing isolated coronary artery bypass grafting. *Acta Cardiol Sin* 2015;31:436-443.
24. Sabena A, Dinah DT, Smith JA, et al. Usefulness of postoperative

atrial fibrillation as an independent predictor for worse early and late outcomes after isolated coronary artery bypass grafting (multicenter Australian study of 19,497 patients). *Am J Cardiol* 2012;109:219-25.
25. Elmistekawy E, Mesana T, Chan V. Ischemic mitral regurgitation: current trends and treatment. *Curr Opin Cardiol* 2013;28:661-5.
26. Fattouch K, Sampognaro R, Speziale G, et al. Impact of moderate ischemic mitral regurgitation after isolated coronary artery bypass grafting. *Ann Thorac Surg* 2010;90:1187-94.
27. Yoo JS, Kim JB, Jung SH, et al. Coronary artery bypass grafting in patients with left ventricular dysfunction: predictors of long-term survival and impact of surgical strategies. *Int J Cardiol* 2013; 168:5316-22.
28. Berger JS, Frye CB, Harshaw Q, et al. Impact of clopidogrel in patients with acute coronary syndromes requiring coronary artery bypass surgery: a multicenter analysis. *J Am Coll Cardiol* 2008; 52:1693-701.
29. Bandeali SJ, Kayani WT, Lee VV, et al. Association between preoperative diuretic use and in-hospital outcomes after cardiac surgery. *Cardiovasc Ther* 2013;31:291-7.

中華民國心臟學會 TAIWAN SOCIETY OF CARDIOLOGY