

## Early and Mid-Term Outcomes of Patients Undergoing Coronary Artery Bypass Grafting in Ischemic Cardiomyopathy

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**Background**—Many observational studies and trials have shown that coronary artery bypass grafting improves the survival in patients with ischemic cardiomyopathy. However, these results are based on data generated from developed countries. Poor socioeconomic statuses, lack of uniformity in healthcare delivery, differences in risk profile, and affordability to access optimal health care are some factors that make the conclusions from these studies irrelevant to patients from India.

**Methods and Results**—One-hundred and sixty-two patients with severe left ventricular dysfunction (ejection fraction  $\leq 35\%$ ) who underwent coronary artery bypass grafting from 2009 to 2017 were enrolled for this study. Mean age of the study population was  $58.67 \pm 9.70$  years. Operative mortality was 11.62%. Thirty day/in-house composite outcome of stroke and perioperative myocardial infarction were 5.8%. The percentage of survival for 1 year was 86.6%, and 5-year survival was 79.9%. Five-year event-free survival was 49.3%. The mean ejection fraction improved from  $30.7 \pm 4.08\%$  (range 18–35) to  $39.9 \pm 8.3\%$  (range 24–60). Lack of improvement of left ventricular function was a strong predictor of late mortality (hazard ratio, 21.41; CI 4.33–105.95). Even though there was a trend towards better early outcome in off-pump CABG, the 5-year survival rates were similar in off-pump and on-pump group (73.4% and 78.9%, respectively;  $P$  value 0.356).

**Conclusions**—We showed that coronary artery bypass grafting in ischemic cardiomyopathy was associated with high early composite outcomes. However, the 5-year survival rates were good. Lack of improvement of left ventricular function was a strong predictor of late mortality. (*J Am Heart Assoc.* 2019;8:e010225. DOI: 10.1161/JAHA.118.010225.)

**Key Words:** coronary artery bypass grafting • heart failure • ischemic cardiomyopathy • myocardial ischemia • outcomes

**S**TICH (Surgical Treatment for Ischemic Heart Failure) trial<sup>1</sup> and STICHES (Surgical Treatment for Ischemic Heart Failure Extension Study)<sup>2</sup> established the role of coronary artery bypass grafting (CABG) in improving the outcome of patients with ischemic cardiomyopathy. CABG in this subgroup is associated with substantial risks and complications. Ischemic heart disease and stroke constitute 83% of cardiovascular disease mortality in India. In comparison with western population, ischemic heart disease affects the population at least a decade earlier and in the most productive mid-life years in India.<sup>3</sup> The prevalence of ischemic

heart disease in urban population increased by 7-fold and quadrupled in rural populations in recent years in India.<sup>3</sup> In contrast to high- and middle-income countries, the incidence of ST-segment-elevation myocardial infarction is more than non-ST-segment-elevation myocardial infarction or unstable angina in patients presenting with acute coronary syndrome in India.<sup>4</sup> There are also longer delays before admission to hospital and between admission and reperfusion therapy. Hence, Indian patients with acute coronary syndrome have higher morbidity and mortality than in high-income countries.<sup>5,6</sup> All these factors potentially could increase the prevalence of ischemic cardiomyopathy in Indian patients.

Many observational studies and trials have shown that CABG improves the survival and quality of life in patients with ischemic cardiomyopathy.<sup>1,2,7</sup> However, these results are based on data generated from developed countries. Poor socioeconomic status, lack of uniformity in healthcare delivery, differences in risk profile, and affordability to access optimal health care are some factors that can make the conclusions from these studies irrelevant to patients from India. In this context, it is important to understand the outcomes of Indian patients with ischemic cardiomyopathy who underwent CABG.

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## Clinical Perspective

### What Is New?

- This is the first study to examine the outcomes of coronary artery bypass grafting in ischemic cardiomyopathy in Indian patients.
- Even though early mortality was high, the late survival was excellent.
- Patients who did not show improvement of left ventricular function had poor long-term survival.

### What Are the Clinical Implications?

- Effective strategies are required to control postoperative sepsis and improve the outcomes.
- Patients with lack of improvement in the left ventricular function after coronary artery bypass grafting should be followed up more meticulously to reduce their risk of cardiovascular mortality.

## Methods

Between January 2009 and December 2016, a total of 4431 patients underwent CABG. One hundred and sixty-two consecutive (3.65%) patients with severe left ventricular dysfunction (ejection fraction [EF] <35%) who underwent either on pump or off pump CABG (147 [90.7%] men and 15 [9.3%] women) were included in this study. The primary inclusion criteria were diagnosis of coronary artery disease appropriate for CABG by preoperative angiogram and EF  $\leq$ 35% by 2-dimensional echocardiography. All patients with an associated procedure (valve replacements, mitral valve repair, or surgical ventricular restoration) were excluded. The data, analytic methods, and study materials will be/have been made available to other researchers for purposes of reproducing the results or replicating the procedure.<sup>8</sup>

## Study Design

The data were collected retrospectively. Logistic EuroSCORE II was calculated retrospectively from the patient's data.

## Follow-Up

Patients were followed up in the outpatient department. They were evaluated clinically and with ECG and echocardiography examination by an attending cardiologist. The follow-up pattern was 1 and 3 months after surgery and every 6 months thereafter. Last day of follow-up was fixed at February 1, 2018. Those patients who did not come for follow-up were contacted telephonically and interviewed by a physician assistant (V.C.) with a prepared questionnaire. The

last available echocardiography was used for left ventricular function assessment. Follow-up details are depicted in Figure 1.

## Definition of Variables

Operative mortality was defined as (1) all deaths occurring during the hospitalization in which the CABG was performed, even if after 30 days, and (2) those deaths occurring after discharge from the hospital, but within 30 days of the procedure. Renal failure was defined as an increase in serum creatinine concentration to twice preoperative levels or to >2.0 mg/dL, or new requirement for dialysis. According to the Centers For Disease Control And Prevention guidelines, mediastinitis was diagnosed if the patient presented with 1 of the following criteria: (1) an organism isolated from culture of mediastinal tissue or fluid; (2) evidence of mediastinitis seen during operation; or (3) presence of either chest pain, sternal instability, or fever (>38°C), and purulent drainage from the mediastinum, or isolation of an organism present in a blood culture or a culture of the mediastinal area. Event-free survival was defined as a composite end point of all cause deaths, myocardial infarction, stroke, target vessel revascularization, new onset of renal failure, and hospitalization for heart failure.

## Myocardial Viability Assessment

One hundred and six patients (62.3%) underwent preoperative myocardial viability testing. Myocardial viability was assessed by <sup>99m</sup>Tc-sestamibi scan in 102 patients. Four patients underwent cardiac magnetic resonance imaging. Patients who showed viability in >50% of myocardium were offered CABG. In 35 patients, myocardial viability was not performed because of the need for urgent or emergent surgery. In the rest of the patients, the reason for not performing myocardial viability was not mentioned in the hospital records. Out of 106 available records, 80 patients had transmural scar in left anterior descending artery territory, 44 patients had transmural scar in right coronary artery territory, and 25 patients had transmural scar in circumflex coronary artery territory.

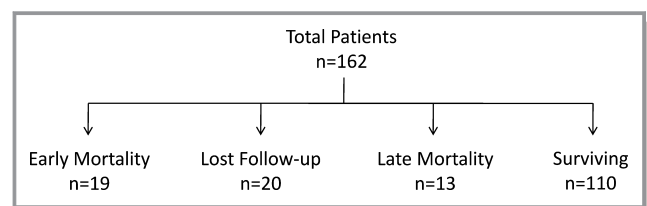


Figure 1. Follow-up.

## Ethics Committee Approval

The study was approved by the hospital ethics committee. The requirement for informed consent was waived. All personal identifying data were removed from the study database so that individuals could not be identified.

## Surgical Technique

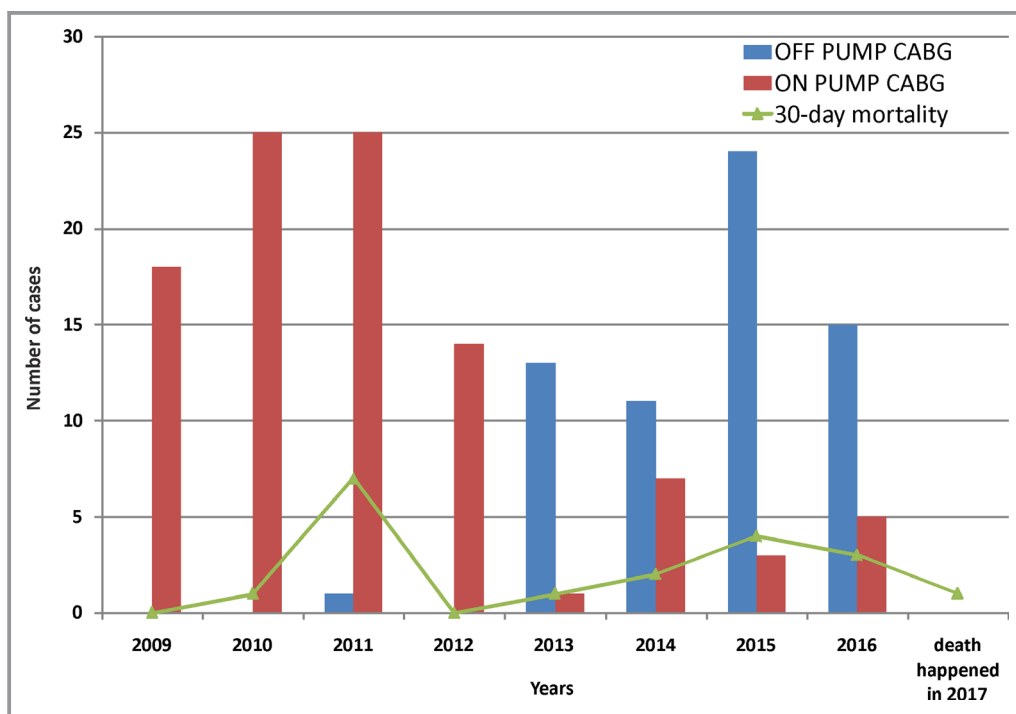
Four surgeons operated all cases. All surgeries were done through median sternotomy. Left internal mammary artery was the preferred conduit for bypassing left anterior descending artery. Saphenous vein grafts were used for bypassing the other diseased coronary arteries. In both off-pump and on-pump CABG, proximal anastomoses were constructed using partial occlusion clamp. Ninety-eight patients were operated using on-pump CABG technique and 64 patients were operated by off-pump technique. The decision to operate off-pump or on-pump was individual surgeon's preference. The number of cases performed in each year of the study period, using either technique is depicted in Figure 2. There was a trend towards more off-pump surgeries after the year 2012. The mean EuroSCORE II of patients operated with or without pump was similar (with pump  $4.83 \pm 4.98$ , without pump  $4.55 \pm 4.39$ ,  $P$  value 0.71). Twenty-two patients (13.5%) required intra-aortic balloon pump (IABP) support. IABP was inserted preoperatively in 7 patients for hemodynamic support. In 3 patients, IABP was placed intraoperatively and

in 12 patients, IABP was placed postoperatively for low cardiac output. Eighteen patients (11.1%) required endarterectomy of coronary artery. Mean number of grafts placed in on-pump patients were significantly higher than in off-pump patients ( $4.32 \pm 0.85$  versus  $3.73 \pm 0.86$ ;  $P < 0.001$ ).

## Statistical Analysis

Data were analyzed with IBM SPSS 20.0 (SPSS Inc, Chicago, USA). The results are either given in mean  $\pm$  SD for continuous variables or as percentage for categorical variables. To obtain the association of variable with 30-day mortality and mid-term mortality, Chi square statistics with continuity correction test (wherever applicable) for categorical variables and independent sample  $t$  test/Mann-Whitney  $U$  test for continuous variables were used. To determine the preoperative, intraoperative, and postoperative risk factors for mid-term mortality, multivariate backward conditional logistic regression analysis was used. Variables which showed  $P$  value up to 0.2 were included in multivariate analysis. Multivariate analysis of 30-day mortality was not done because of low event rate.

To find the survival probability of long-term mortality, Kaplan-Meier analysis was used, and Log rank test was used for comparing the survival probability. Cox regression was used to find the most significant predictor of long-term mortality. All variables with  $P < 0.2$  were included in the multivariate analysis (Cox regression). A  $P$  value of  $< 0.05$  was considered as statistically significant "without adjustment for multiplicity".



**Figure 2.** On-pump and off-pump CABGs performed in each year with 30-day mortality. CABG indicates coronary artery bypass grafting.

## Results

Mean age of the study population was  $58.67 \pm 9.70$  years (range: 23–84 years). Operative mortality was 11.62% (19/162 patients). Low cardiac output developed in 32% of patients in the postoperative period. Thirty-day/in-house composite outcome of stroke and perioperative myocardial infarction was

5.8%. Five patients (3.08%) developed new requirement of dialysis in the postoperative period; and among them 4 patients died. A total of 7.4% patients developed mediastinitis. The average lengths of hospital stay were  $15 \pm 8.73$  days in alive patients and  $20 \pm 13.91$  days in expired patients.

Tables 1 and 2 show the Chi square and Independent sample *t* test/Mann–Whitney *U* test (parametric/non-parametric)

**Table 1.** Univariate Predictors for 30-Day Mortality

Variables	Alive n (%)	Died n (%)	Univariate Analysis	
	143 (%)	19 (%)	OR (95% of CI)	P Value
<b>Age</b>				
≤55 y	55 (38.5)	2 (10.5)	5.31 (1.18–23.89)	0.032*
>55 y	88 (61.5)	17 (89.5)		
<b>Sex</b>				
Men	131 (91.6)	16 (84.2)	0.49 (0.12–1.92)	0.413
Women	12 (8.4)	3 (15.8)		
<b>Urgency of surgery</b>				
Elective	114 (79.7)	13 (68.4)	1.00	0.006*
Urgent	21 (14.7)	1 (5.3)	0.42 (0.05–3.36)	
Emergency	8 (5.6)	5 (26.3)	5.48 (1.56–19.25)	
Diabetes mellitus, y	95 (66.4)	16 (84.2)	0.37 (0.10–1.34)	0.192
Hypertension, y	84 (58.7)	12 (63.2)	0.83 (0.31–2.24)	0.905
Myocardial infarction, y	104 (72.7)	17 (89.5)	0.31 (0.07–1.42)	0.195
Myocardial viability, y	122 (85.3)	17 (89.5)	0.68 (0.15–3.18)	0.890
Congestive heart failure, y	16 (11.2)	7 (36.8)	4.63 (1.59–13.46)	0.008*
Carotid stenosis, y	22 (15.4)	5 (26.3)	0.51 (0.17–1.56)	0.382
Renal dysfunction, y	34 (23.8)	5 (26.3)	0.87 (0.29–2.60)	1.000
COPD, y	21 (14.7)	1 (5.3)	0.32 (0.04–2.55)	0.441
PVD, y	20 (14)	5 (26.3)	0.46 (0.15–1.40)	0.289
Smoker, y	36 (25.2)	6 (31.6)	0.73 (0.26–2.06)	0.749
<b>CABG</b>				
With pump	83 (58.0)	15 (78.9)	0.37 (0.12–1.17)	0.133
Without pump	60 (41.9)	4 (21.1)		
IABP support, y	17 (11.9)	5 (26.3)	0.38 (0.12–1.18)	0.171
Perioperative MI, y	7 (4.9)	3 (15.8)	0.27 (0.07–1.17)	0.178
LIMA grafts, y	140 (97.9)	19 (100)	0.000	1.000
Postoperative stroke, y	2 (1.4)	2 (10.5)	8.29 (1.10–62.75)	0.105
Postoperative renal dysfunction, y	32 (22.4)	12 (63.2)	5.95 (2.16–16.35)	0.001*
Inotropic support, y	137 (95.8)	18 (94.7)	0.79 (0.09–6.93)	1.000
Sepsis, y	42 (29.4)	10 (52.6)	2.62 (1.01–7.05)	0.075
Mediastinitis, y	9 (6.3)	3 (15.8)	0.36 (0.09–1.46)	0.308

CABG indicates coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; IABP, intra-aortic balloon pump; LIMA, left internal mammary artery; MI, myocardial infarction; n, sample size; OR, odds ratio; PVD, peripheral vascular disease.

\*Significant  $P \leq 0.05$ .

univariate analysis of preoperative, intraoperative, and postoperative variables with operative mortality. In univariate analysis, age >55 years, urgency of surgery, congestive heart failure, postoperative renal dysfunction, EuroSCORE II, and pump time were identified as risk factors.

Median follow-up period was 1057 days. Thirteen patients expired after 30 days during follow-up. Mid-term mortality was 19.8% (19+13=32 patients). Data from 162 patients were analyzed for mid-term mortality. In Tables 3 and 4, the Chi square and Independent sample *t* test/Mann–Whitney *U* test (parametric/non-parametric) analysis of preoperative, intraoperative, and postoperative variables with mid-term mortality is listed. The risk factors such as age group >55 years, sex, emergency surgery, diabetes mellitus, myocardial infarction, congestive heart failure, pump usage, perioperative myocardial infarction, postoperative stroke, postoperative renal dysfunction, lack of improvement of EF, sepsis, mediastinitis, and EuroSCORE II were associated with mid-term mortality in univariate analysis. In multivariate backward conditional logistic regression analysis (Table 5); lack of improvement of EF, postoperative renal dysfunction, mediastinitis, and sepsis were associated with mid-term mortality.

During follow-up, 10 patients died of cardiac cause, 1 from stroke, and 2 patients died of non-cardiac causes. The follow-up data were listed in Table 6. Nineteen patients (14.6%) were in NYHA (New-York Heart Association) class 3/4 heart failure. Four patients received implantable cardioverter-defibrillator for documented ventricular tachycardia. Survival curve was plotted in Figure 3 using Kaplan–Meier estimator. Mean survival time was 2501.63 days. The percentage of survival for 1 year was 88.1% with 127 patients at risk, 3-year survival was 84.5% with 79 patients at risk, and 5-year survival was 81.5% with 51 patients at risk. In event-free survival analysis, mean survival time was 1662.85±91.47, and 5-year event free survival was 43.8% (Figure 4).

The mean EF improved from 30.7±4.08% (range 18%–35%) to 39.9±8.3% (range 24%–60%) at the last follow-up echocardiogram (Figure 5). In 25 patients left ventricular (LV) function

improved to >50% and all these patients are alive during follow-up. In 13 patients LV function did not improve and 10 of these patients died because of cardiac cause during follow-up. Lack of improvement of left ventricular function was a strong predictor of late mortality (odds ratio 25.20; CI 5.40–117.55). Even though there was a trend towards better early outcome in off-pump CABG, the 5-year survival rates were similar in the off-pump and on-pump group (Figure 6).

Time to event analysis of long-term mortality was analyzed using Kaplan–Meier and Log rank test. In this analysis, 162 cases were included and preoperative, intraoperative, and postoperative variables were analyzed for their impact on overall survival (Table 7). A *P* value ≤0.19 was included in the multivariate analysis (Cox regression). The variables included in the Cox regression (Table 8) were age, sex, urgency of surgery, EuroSCORE II, diabetes mellitus, congestive heart failure, IABP usage, perioperative myocardial infarction, postoperative stroke and renal dysfunction, sepsis, mediastinitis, and improved EF. The results of multivariate analysis (Cox regression) showed lack of improvement in postoperative EF was the most significant predictor of long-term mortality with *P*<0.001 (hazard ratio 7.08; CI 3.24–15.49). Postoperative renal dysfunction had a significant negative impact on survival days with *P* value 0.002 (hazard ratio 3.18; CI 1.52–6.64). Postoperative stroke and sepsis significantly reduced the overall survival.

## Discussion

We present a single-center retrospective study of CABG in patients with ischemic cardiomyopathy, which represent 3.6% of all CABGs performed at our hospital during this period. Our study showed that mid-term outcome of CABG was excellent with 5-year survival approaching 80%, but offset by high perioperative mortality and morbidity. The composite outcome of operative mortality and morbidity was 17.4%. This finding is similar to other studies in ischemic cardiomyopathy.<sup>9,10</sup>

The early mortality was higher than reported in many studies and trials.<sup>1,11,12</sup> There are several reasons for this. Ours is a tertiary referral hospital where the sickest of patients are referred for management. By policy, we do not reject any patients based on frailty or poor coronary anatomy or comorbidity. Five patients out of 19 expired were taken up as salvage or emergency surgery. The mean EuroSCORE II for the expired patients was 7.48±5.76, meaning that majority of patients who died after surgery were in the high-risk group.

Best strategy for revascularization in ischemic cardiomyopathy is debatable. Both ROOBY (Randomized On/Off Bypass)<sup>13</sup> and CORONARY trials (CABG Off or On Pump Revascularization Study)<sup>14</sup> did not show any substantial benefit to off-pump technique for composite 30-day outcome.

**Table 2.** Univariate Predictors (Continuous Variables) for 30-Day Mortality

Variables	Alive n (%)	Died n (%)	<i>P</i> Value
	143 (%)	19 (%)	
EuroSCORE II	4.36±4.49	7.48±5.76	0.033*
Number of grafts	4.09±0.903	4.05±0.85	0.862
Pump time	104.48±27.22	129.87±44.82	0.05*
Cross-clamp time	50.36±16.81	49.50±11.49	0.813

n indicates sample size.

\*Significant *P*≤0.05.



**Table 3.** Univariate Predictors for Mid-Term Mortality

Variables	Alive n (%)	Died n (%)	Univariate Analysis	
	130 (%)	32 (%)	OR (95% of CI)	P Value
<b>Age</b>				
<55 y	51 (39.2)	6 (18.8)	2.80 (1.08–7.27)	0.03*
>55 y	79 (60.8)	26 (81.3)		
<b>Sex</b>				
Men	120 (92.3)	27 (84.4)	0.22 (0.70–7.03)	0.17
Women	10 (7.7)	5 (15.6)		
<b>Urgency of surgery</b>				
Elective	102 (78.5)	25 (78.1)	1.00	0.11
Urgent	20 (15.4)	2 (6.3)	0.41 (0.09–1.86)	
Emergency	8 (6.2)	5 (15.6)	2.55 (0.77–8.47)	
Diabetes mellitus, y	85 (65.4)	26 (81.3)	2.29 (0.88–5.98)	0.08
Hypertension, y	78 (60)	18 (56.3)	0.86 (0.39–1.87)	0.70
MI, y	94 (72.3)	27 (84.4)	2.07 (0.74–5.78)	0.16
Myocardial viability, y	112 (86.2)	27 (84.4)	0.87 (0.30–2.55)	0.80
Congestive heart failure, y	13 (10)	10 (31.3)	4.09 (1.60–10.49)	0.002*
Carotid stenosis, y	21 (16.2)	6 (18.8)	1.20 (0.44–3.27)	0.72
Renal dysfunction, y	30 (23.1)	9 (28.1)	1.30 (0.55–3.12)	0.55
COPD, y	18 (13.8)	4 (12.5)	0.89 (0.248–2.84)	1.00
PVD, y	19 (14.6)	6 (18.8)	1.35 (0.49–3.71)	0.56
Smoker, y	35 (26.9)	7 (21.9)	0.76 (0.30–1.91)	0.56
<b>CABG</b>				
With pump	73 (56.2)	25 (78.1)	2.79 (1.13–6.91)	0.02*
Without pump	57 (43.8)	7 (21.9)		
IABP support, y	14 (10.8)	8 (25)	2.76 (1.04–7.31)	0.04*
Perioperative MI, y	6 (4.6)	4 (12.5)	2.95 (0.78–11.16)	0.21
LIMA grafts, y	127 (97.7)	32 (100)	0.000	0.89
Postoperative stroke, y	2 (1.5)	2 (6.3)	4.27 (0.58–31.52)	0.37
Postoperative renal dysfunction, y	26 (20)	18 (56.3)	5.14 (2.27–11.68)	<0.001*
Inotropic support, y	124 (95.4)	31 (96.9)	1.5 (0.17–12.92)	1.00
Sepsis, y	35 (26.9)	17 (53.1)	3.08 (1.39–6.81)	0.004*
Mediastinitis, y	6 (4.6)	6 (18.8)	4.77 (1.43–15.96)	0.006*
<b>Postoperative EF</b>				
Improved EF	127 (97.7)	22 (68.8)	19.24 (4.90–75.52)	<0.001*
No improvement of EF	3 (2.3)	10 (31.3)		

CABG indicates coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; EF, ejection fraction; IABP, intra-aortic balloon pump; MI, myocardial infarction; LIMA, left internal mammary artery; n, sample size; OR, odds ratio; PVD, peripheral vascular disease.

\*Significant  $P \leq 0.05$ .

However, large retrospective studies have shown significant reductions in 30-day mortality and operative mortality, and with a significantly lower incidence of reoperation for bleeding, mediastinitis, perioperative transfusion, prolonged

mechanical ventilation, and duration of intensive care unit stay<sup>15,16,17</sup> in off-pump CABG. The risk profile of both off-pump group and on-pump group was similar in our study. Even though statistically insignificant, we found a tendency to

**Table 4.** Univariate Predictors (Continuous Variables) for Mid-Term Mortality

Variables	Alive n (%)	Died n (%)	P Value
	130 (%)	32 (%)	
EuroSCORE II	4.38±4.69	6.12±4.79	0.63
Number of grafts	4.10±0.92	4.03±0.78	0.70
Pump time	105.86±27.97	115.68±40.29	0.27
Cross-clamp time	50.82±17.35	48.21±10.85	0.54

n indicates sample size.

better outcome of early mortality in patients who underwent off-pump CABG compared with on-pump CABG. Reduced transfusion requirement, better renal and myocardial protection, decreased neurological dysfunction are some of the factors thought to be associated with improved early outcomes with off-pump CABG in patients with depressed LV function.<sup>18–20</sup> However, this advantage was not seen in the long-term; both groups showed similar survival at 5 years (Figure 4).

In this study group, 68.5% patients had diabetes mellitus compared with 39.9% reported in STICH trial.<sup>1</sup> Diabetes mellitus is usually associated with diffuse and severe coronary artery disease, with a tendency for early calcification.<sup>21</sup> Poor quality of target vessels is considered by some to be a contraindication to CABG even if the patient has angina.<sup>22,23</sup> Moreover diabetes mellitus leads to general frailty, chronic kidney disease, and worsens the left ventricular function; all these factors can potentially increase the perioperative morbidity and mortality.<sup>24,25</sup> Combination of low cardiac output and poor glycemic control also increases the chance of developing mediastinitis.<sup>26</sup> Mediastinitis was seen in 7.4% of patients which was significantly >0.9% patients developing mediastinitis in routine CABG cases in our center.

In India, we do not have a system of public reporting of results of cardiac surgery nor a central registry or database. Hence, we relied on EuroSCORE II for assessing the risk profile of patients.<sup>27</sup> Even though it is still not well validated in

**Table 5.** Multivariate Predictors for Mid-Term Mortality

Variables	Multivariate Analysis	
	OR (95% of CI)	P Value
Postoperative EF	25.20 (5.40–117.55)	<0.001*
Postoperative renal dysfunction	5.64 (2.15–14.80)	<0.001*
Mediastinitis	4.79 (1.17–19.57)	0.03*
Sepsis	3.16 (1.21–8.26)	0.02*

EF indicates ejection fraction; OR, odds ratio.

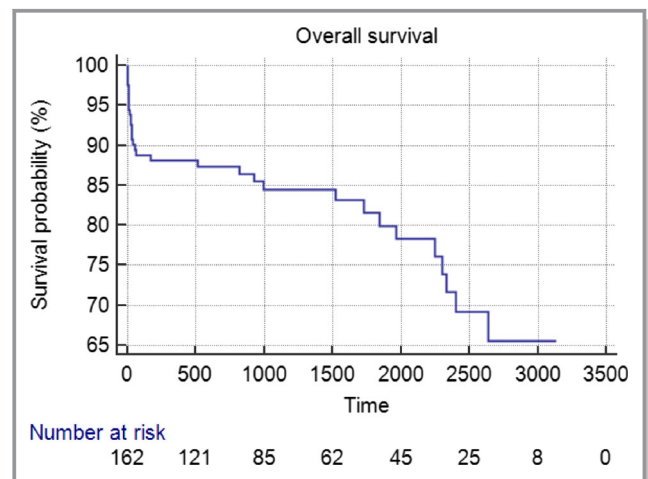
\*Significant  $P \leq 0.05$ .

**Table 6.** Follow Up

Variables	Alive (n=130) n (%)
	110 (%)
Heart failure	19 (14.6)
Angina	1 (0.8)
Myocardial infarction	1 (0.8)
Renal dysfunction	6 (4.6)
Dialysis	2 (1.5)
Stroke	3 (2.3)
Revascularizations	1 (0.8)
New onset disease	7 (5.4)

n indicates sample size.

Indian patients,<sup>28</sup> it is important to measure risk adjusted mortality to ensure the quality of healthcare delivery.<sup>29</sup> The mean EuroSCORE II of the entire cohort was  $4.7 \pm 4.7$ ; however, the observed mortality was 11.7%. There could be many reasons for this increased observed mortality compared with the expected result. Risk scoring systems are most reliable when the patient characteristics and quality of healthcare delivery are comparable with those on which the system originated.<sup>29</sup> Also; EuroSCORE II does not take into account the poor quality of target coronary arteries, often seen in diabetic mellitus patients.<sup>30</sup> Probably a combination of EuroSCORE II with SYNTAX score would have better predicted the operative risk.<sup>30</sup>



**Figure 3.** In overall survival analysis of patients after coronary artery bypass grafting with severe left ventricular dysfunction with mean survival time  $2501.63 \pm 96.85$  was plotted in the graph using Kaplan–Meier estimator. One-year survival: 88.1% and numbers at risk: 127; 3-year survival: 84.5% and numbers at risk: 79; 5-year survival: 81.5% and numbers at risk: 51; 9-year survival 65.5%.

**Table 7.** Impact of Variables on Overall Survival-Time to Event Analysis (n=162)

Variables	Mean±SE	P Value
<b>Age</b>		
≤55 y	2811.50±121.92	0.02*
>55 y	2275.12±126.79	
<b>Sex</b>		
Men	2547.88±99.24	0.104
Women	2078.54±297.52	
<b>Urgency of surgery</b>		
Elective	2550.18±101.66	0.004*
Urgent	2766.40±221.52	
Emergency	460.23±97.13	
<b>EuroSCORE II</b>		
<6	2574.27±102.28	0.10
≥6	2090.05±226.69	
<b>Diabetes mellitus</b>		
Yes	2397.86±117.84	0.14
No	2721.73±156.48	
<b>Hypertension</b>		
Yes	2523.42±125.54	0.53
No	2459.97±147.17	
<b>MI</b>		
Yes	2430.42±116.04	0.76
No	2684.10±165.01	
<b>Myocardial viability</b>		
Yes	2512.18±104.91	0.78
No	24.37.92±226.92	
<b>Congestive heart failure</b>		
Yes	1867.43±296.33	0.01*
No	2603.06±99.43	
<b>Carotid stenosis</b>		
Yes	2301.88±237.25	0.65
No	2520.48±104.58	
<b>Renal dysfunction</b>		
Yes	2270.44±211.94	0.39
No	2549.40±107.02	
<b>COPD</b>		
Yes	2604.98±206.22	0.67
No	2488.81±106.229	
<b>PVD</b>		
Yes	2230.49±260.10	0.71
No	2516.39±104.16	

Continued

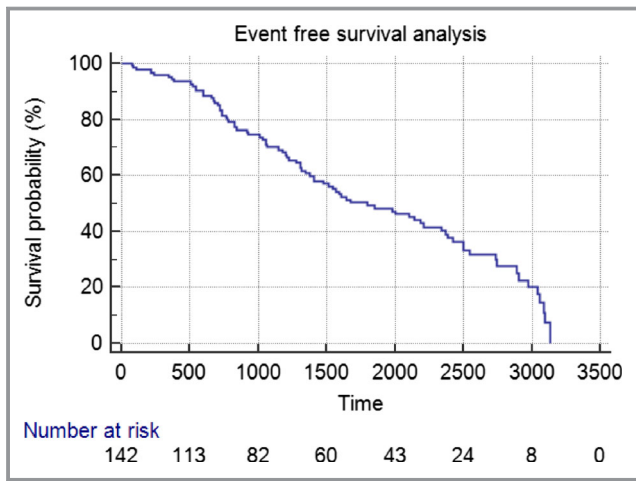
**Table 7.** Continued

Variables	Mean±SE	P Value
<b>Smoker</b>		
Yes	2583.78±175.33	0.52
No	2452.58±115.51	
<b>CABG</b>		
With pump	2424.14±123.88	0.36
Without pump	1936.48±148.81	
<b>IABP</b>		
Yes	2021.70±290.76	0.03*
No	2578.08±100.01	
<b>Perioperative MI</b>		
Yes	1042.57±233.32	0.01*
No	2552.74±96.14	
<b>Postoperative stroke</b>		
Yes	426.00±173.44	0.01*
No	2529.16±96.04	
<b>Postoperative renal dysfunction</b>		
Yes	1916.35±201.00	<0.001*
No	2737.17±96.96	
<b>Inotropic support</b>		
Yes	2502.406±98.21	0.90
No	1831.00±282.38	
<b>Sepsis</b>		
Yes	2103.45±198.04	0.004*
No	2671.14±100.99	
<b>Mediastinitis</b>		
Yes	1889.94±280.04	0.05*
No	2565.18±99.13	
<b>Postoperative EF</b>		
Improved EF	2648.13±92.957	<0.001*
No improvement of EF	1101.123±350.85	

CABG indicates coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; EF, ejection fraction; IABP, intra-aortic balloon pump; MI, myocardial infarction; n, sample size; OR, odds ratio; PVD, peripheral vascular disease. \*Significant  $P \leq 0.05$ .

In spite of the high early composite outcome, the late results were excellent with 80% survival in 5 years. There could be many reasons for this. Left internal mammary artery was used to bypass left anterior descending artery in 98.12% (159/162) patients. Use of left internal mammary artery has shown survival advantage even in patients with severe LV dysfunction.<sup>31</sup> Another reason could be the younger age at the time of CABG in this study group compared with western patients; 35% of patients were aged <55 years.

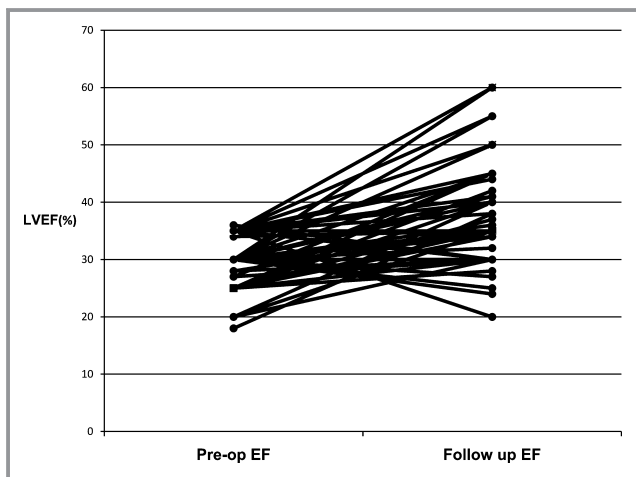




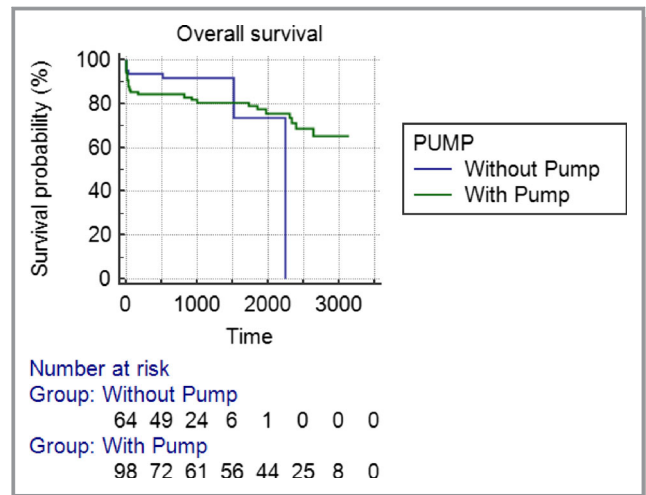
**Figure 4.** In event-free survival analysis, mean survival time was  $1662.85 \pm 91.47$  and 1-year survival was 89%, 3-year survival was 62.2%, 5-year survival was 43.8%. The graph was plotted using Kaplan–Meier estimator.

Lack of improvement of left ventricular function was a strong predictor of late mortality in this study group. However, this is in contrast to other studies<sup>32</sup> that showed no difference in survival after CABG between patients with left ventricular ejection fraction improvement and patients without. Low EF is associated with poor outcomes in medically managed patients. Hence, it is not surprising that the patients who did not show improvement of EF fared poorly compared with patients who showed significant improvement in left ventricular function. However, since the number of patients were small, this is only a hypothesis generating finding.

India is ranked 121 among 191 World Health Organization member countries in overall healthcare performance. Availability, accessibility affordability are the main challenges



**Figure 5.** The change in ejection fraction after CABG. CABG indicates coronary artery bypass grafting; EF, ejection fraction; LVEF, left ventricular ejection fraction.



**Figure 6.** In overall survival analysis, comparison of with pump and without pump cases of patients after coronary artery bypass grafting with severe left ventricular dysfunction with mid-term mortality showed mean mortality time of with-pump cases was  $2424.14 \pm 123.88$ , 5-year survival 78.9% and without-pump cases was  $1936.48 \pm 148.81$ , 5-year survival 73.4% plotted in the graph using Kaplan–Meier estimator with *P* value 0.356.

facing the healthcare system in India.<sup>5,33</sup> Only 3% to 4% of population is covered by insurance and only 20% patients receive treatment from public health facilities. Up to 80% of patients bear their cost of treatment. Hence, economic factors rather than evidence-based medicine, play a major role in the decision-making algorithm. This is attested by the fact that only 13.2% received IABP and only 4 patients received automated implantable cardioverter-defibrillator (AICD); all as secondary prophylaxis. None of the patients received AICD for primary prevention.

Coronary revascularization and CABG are thought to be particularly difficult in Indian patients because of a smaller caliber of vessels, diffuse nature of disease, and tendency to early calcification.<sup>3,4,21</sup> This is attested by the fact that 11.2% of patients required coronary endarterectomy in this study group. In India, currently off-pump CABG surgery is performed

**Table 8.** Multivariate Analysis-Cox Regression

Variables	Wald	<i>P</i> Value	HR (95.0% CI for HR)
Postoperative stroke	7.468	0.006*	9.37 (1.88–46.63)
Postoperative EF	24.050	<0.001*	7.08 (3.24–15.49)
Postoperative renal dysfunction	9.448	0.002*	3.18 (1.52–6.64)
Sepsis	8.518	0.004*	3.01 (1.44–6.32)
Congestive heart failure	3.499	0.061	2.18 (0.964–4.91)

EF indicates ejection fraction; HR, hazard ratio.  
\*Significant  $P \leq 0.05$ .

in >60% of patients undergoing surgery; mainly because of shorter operative time and reduced procedure cost. This trend was the main reason for increasing numbers of off-pump CABG in our center. Like in many centers in India, off-pump CABG is the standard of care in our institute and currently our both elective and emergency conversion rate to on-pump is only 3.2%.<sup>34</sup> Economic reasons could explain a relatively low number of cases who underwent surgery for ischemic cardiomyopathy. Many patients may not be willing to undergo surgery or are not referred for surgery because of economic reasons or may prefer to undergo surgery at any public health facility where the cost of treatment is free for the patient.

The burden of sepsis and, typically, Gram-negative sepsis is unique to low- and middle-income countries. Healthcare systems in low- and middle-income countries face unique challenges in this domain ranging from preventive steps, appropriate and early institution of anti-microbial (including a need to ration use for propagating multi-drug resistant organisms) and the scourge of multi-drug resistant and extremely drug resistant microbes. A study on the exact impact of infections on cardiovascular outcomes done at this center showed that unadjusted 30-day mortality rates in patients who suffered an infection in the immediate postoperative period was 26.8% as against 3.7% in those who did not (Sreelakshmi P Leeladharan, personal communication, March, 2018). Although this study was performed in serial patients presenting for cardiac surgery in our center, and not specifically this cohort, the staggering difference in outcomes speaks for itself. Sepsis and its attendant consequences are therefore one of the key factors that modify operative outcomes in this setting.

Our study has significant limitations. There were 12.5% patients lost to follow-up. We were not able to calculate the SYNTAX score because of non-availability of coronary angiograms of many patients. Also; there are many potential biases to a retrospective study design; the results might have been affected by unmeasured confounding variables, procedure bias, and detection bias. The results of outcome between off-pump and on-pump group should be interpreted with caution as the numbers in each group are small and could be affected by selection bias. Coronary angiography was performed only in symptomatic patients, and there was no information about patency of coronary grafts in most patients. We did not check angiograms on those patients who did not show improvement of left ventricular function, so the reason for non-improvement of left ventricular function is not clear. However, our study has many advantages. To our knowledge, it is the first study to examine the early and long-term outcomes of CABG in ischemic cardiomyopathy in Indian patients. The study also showed interesting differences in the demographic profile of Indian patients compared with western patients who dominate the current literature on CABG in ischemic cardiomyopathy.

## Conclusions

We showed that CABG in severe LV dysfunction was associated with high early composite outcomes. There was a trend towards better early outcomes in patients if the surgery was done by the off-pump technique. However, the late survivals were similar in both on-pump and off-pump groups. In late survivors; 17% of patients continued to have heart failure symptoms. We also showed that lack of improvement in LV function was a strong predictor of late deaths. Only a large multicenter trial will give dependable evaluation of the outcomes of CABG in ischemic cardiomyopathy in Indian patients.

## Disclosures

None.

## References

1. Velazquez EJ, Lee KL, Deja M, Jain A, Sopko G, Marchenko A, Ali IS, Pohost G, Gradina S, Abraham WT, Yui M, Prabhakaran D, Szwed H, Ferrazzi P, Petrie MC, O'Connor CM, Panchavinnin P, She L, Bonow RO, Rankin GR, Jones RH, Rouleau JL. Coronary-artery bypass surgery in patients with left ventricular dysfunction. *N Engl J Med*. 2011;364:1607–1616.
2. Velazquez EJ, Lee KL, Jones RH, Al-Khalidi HR, Hill JA, Panza JA, Michler RE, Bonow RO, Doenst T, Petrie MC, Oh JK, She L, Moore VL, Desvigne-Nickens P, Sopko G, Rouleau JL; STICHES Investigators. Coronary-artery bypass surgery in patients with ischemic cardiomyopathy. *N Engl J Med*. 2016;374:1511–1520.
3. Gupta R, Joshi P, Mohan V, Reddy KS, Yusuf S. Epidemiology and causation of coronary heart disease and stroke in India. *Heart*. 2008;94:16–26.
4. Ajay VS, Prabhakaran D. Coronary heart disease in Indians: implications of the INTERHEART study. *Indian J Med Res*. 2010;132:561–566.
5. Xavier D, Pais P, Devereaux PJ, Xie C, Prabhakaran D, Reddy KS, Gupta R, Joshi P, Kerkar P, Thanikachalam S, Haridas KK, Jaison TM, Naik S, Maity AK, Yusuf S; CREATE Registry Investigators. Treatment and outcomes of acute coronary syndromes in India (CREATE): a prospective analysis of registry data. *Lancet*. 2008;371:1435–1442.
6. Kumar N, Sharma S, Mohan B, Beri A, Aslam N, Sood N, Wander GS. Clinical and angiographic profile of patients presenting with first acute myocardial infarction in a tertiary care center in northern India. *Indian Heart J*. 2008;60:210–214.
7. O'Connor CM, Velazquez EJ, Gardner LH, Smith PK, Newman MF, Landolfo KP, Lee KL, Califf RM, Jones RH. Comparison of coronary artery bypass grafting versus medical therapy on long-term outcome in patients with ischemic cardiomyopathy (a 25-year experience from the Duke Cardiovascular Disease Databank). *Am J Cardiol*. 2002;90:101–107.
8. Varma P. "CABG for ischemic cardiomyopathy", Mendeley Data, v1. 2019.
9. Passamani E, Davis KB, Gillespie MJ, Killip T. A randomized trial of coronary artery bypass surgery. Survival of patients with a low ejection fraction. *N Engl J Med*. 1985;312:1665–1671.
10. Mitropoulos FA, Elefteriades JA. Myocardial revascularization as a therapeutic strategy in the patient with advanced ventricular dysfunction. *Heart Fail Rev*. 2001;6:163–175.
11. Dietl CA, Berkheimer MD, Woods EL, Gilbert CL, Pharr W, Benoit CH. Efficacy and cost-effectiveness of preoperative IABP in patients with ejection fraction of 0.25 or less. *Ann Thorac Surg*. 1996;62:401–408.
12. Elefteriades JA, Morales DL, Gradel C, Tollis G, Levi E, Zaret BL. Results of coronary artery bypass grafting by a single surgeon in patients with left ventricular ejection fractions  $\leq$  30%. *Am J Cardiol*. 1997;79:1573–1578.
13. Shroyer AL, Hattler B, Wagner TH, Collins JF, Baltz JH, Quin JA, Almassi GH, Kozora E, Bakaeen F, Cleveland JC Jr, Bishawi M, Grover FL; Veterans Affairs ROOBY-FS Group. Five-year outcomes after on-pump and off-pump coronary-artery bypass. *N Engl J Med*. 2017;377:623–632.
14. Lamy A, Devereaux PJ, Prabhakaran D, Taggart DP, Hu S, Straka Z, Piegas LS, Avezum A, Akar AR, Lanus Zanetti F, Jain AR, Noiseux N, Padmanabhan C,

- Bahamondes JC, Novick RJ, Tao L, Olavegogeoascoechea A, Airan B, Sulling TA, Whitlock RP, Ou Y, Gao P, Pettit S, Yusuf S; CORONARY Investigators. Five-year outcomes after off-pump or on-pump coronary-artery bypass grafting. *N Engl J Med*. 2016;375:2359–2368.
15. Rastan AJ, Eckenstein JI, Hentschel B, Funkat AK, Gummert JF, Doll N, Walther T, Falk V, Mohr FW. Emergency coronary artery bypass graft surgery for acute coronary syndrome: beating heart versus conventional cardioplegic cardiac arrest strategies. *Circulation*. 2006;114(suppl 1):I-477–I-485.
  16. Livesay JL. The benefits of off-pump coronary bypass. A reality or an illusion?. *Tex Heart Inst J*. 2003;30:258–260.
  17. Al-Ruzzeh S, George S, Yacoub M, Amrani M. The clinical outcome of off-pump coronary artery bypass surgery in the elderly patients. *Eur J Cardiothorac Surg*. 2001;20:1152–1156.
  18. Filardo G, Hamman BL, da Graca B, Sass DM, Machala NJ, Ismail S, Pollock BD, Collinsworth AW, Grayburn PA. Efficacy and effectiveness of on- versus off-pump coronary artery bypass grafting: a meta-analysis of mortality and survival. *J Thorac Cardiovasc Surg*. 2018;155:172–179.
  19. Moshkovitz Y, Sternik L, Paz Y, Gurevitch J, Feinberg MS, Smolinsky AK, Mohr R. Primary coronary artery bypass grafting without cardiopulmonary bypass in impaired left ventricular function. *Ann Thorac Surg*. 1997;63:S44–S47.
  20. Jarral OA, Saso S, Athanasiou T. Off-pump coronary artery bypass in patients with left ventricular dysfunction: a meta-analysis. *Ann Thorac Surg*. 2011;92:1686–1694.
  21. Varma P, Kundan S, Ananthanarayanan C, Panicker VT, Pillai VV, Sarma PS, Karunakaran J. Demographic profile, clinical characteristics and outcomes of patients undergoing coronary artery bypass grafting—retrospective analysis of 4,024 patients. *Indian J Thorac Cardiovasc Surg*. 2014;30:272–277.
  22. Minale C, Nikol S, Zander M, Uebis R, Effert S, Messmer BJ. Controversial aspects of coronary endarterectomy. *Ann Thorac Surg*. 1989;48:235–241.
  23. Sellke FW, Laham RJ, Edelman ER, Pearlman JD, Simons M. Therapeutic angiogenesis with basic fibroblast growth factor. *Ann Thorac Surg*. 1998;65:1540–1544.
  24. Thourani VH, Weintraub WS, Stein B, Gebhart SS, Craver JM, Jones EL, Guyton RA. Influence of diabetes mellitus on early and late outcome after coronary artery bypass grafting. *Ann Thorac Surg*. 1999;67:1045–1052.
  25. Cohen Y, Raz I, Merin G, Mozes B. Comparison of factors associated with 30-day mortality after coronary artery bypass grafting in patients with versus without diabetes mellitus. Israeli Coronary Artery Bypass (ISCAB) Study Consortium. *Am J Cardiol*. 1998;81:7–11.
  26. Rutledge R, Applebaum RE, Kim BJ. Mediastinal infection after open heart surgery. *Surgery*. 1985;97:88–92.
  27. Nashef SA, Roques F, Sharples LD, Nilsson J, Smith C, Goldstone AR, Lockowandt U. EuroSCORE II. *Eur J Cardiothorac Surg*. 2012;41:734–745.
  28. Borde D, Gandhe U, Hargave N, Pandey K, Khullar V. The application of European system for cardiac operative risk evaluation II and Society of Thoracic Surgeons risk-score for risk stratification in Indian patients undergoing cardiac surgery. *Ann Card Anaesth*. 2013;16:163–166.
  29. Varma PK. A small step in the right direction. *Ann Card Anaesth*. 2013;16:167–168.
  30. Fukui T, Uchimuro T, Takanashi S. EuroSCORE II with SYNTAX score to assess risks of coronary artery bypass grafting outcomes. *Eur J Cardiothorac Surg*. 2015;47:66–71.
  31. Popovic B, Maureira P, Juilliere Y, Danchin N, Voilliot D, Vanhuyse F, Villemot JP. Bilateral vs unilateral internal mammary revascularization in patients with left ventricular dysfunction. *World J Cardiol*. 2017;9:339–346.
  32. Samady H, Elefteriades JA, Abbott BG, Mattera JA, McPherson CA, Wackers FJ. Failure to improve left ventricular function after coronary revascularization for ischemic cardiomyopathy is not associated with worse outcome. *Circulation*. 1999;100:1298–1304.
  33. Murray CJL, Frenk J, Tandon A, Lauer J. *Overall Health System Achievement for 191 Countries*. Geneva: World Health Organization; 2000. (GPE Discussion Paper Number 28).
  34. Agarwal GR, Krishna N, Jose R, Padmanabhan M, Jayant A, Varma PK. Early outcomes in patients undergoing off-pump coronary artery bypass grafting. *Indian J Thorac Cardiovasc Surg*. 2019;35:168–174.