

## 2015 Young Surgeon's Award Winner: Long-term Prognosis in Patients with Diabetes Mellitus after Coronary Artery Bypass Grafting: A Propensity-Matched Study

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### Abstract

**Introduction:** We aimed to determine the impact of diabetes mellitus (DM) on long-term survival after coronary artery bypass grafting (CABG) in patients with multivessel coronary artery disease. **Materials and Methods:** A retrospective review was conducted for 5720 consecutive patients who underwent isolated first CABG between 1982 and 1999. Outcomes were reviewed to include in-hospital mortality and long-term survival. Mean follow-up was  $13.0 \pm 5.8$  years. To obtain comparable subgroups, 561 diabetic patients were matched with 561 non-diabetic controls based on estimated propensity scores. **Results:** Mean age was  $59.3 \pm 9.1$  years with 4373 (76.5%) males. Amongst 5720 patients, 1977 (34.6%) had DM. Hypertension and dyslipidaemia were the most common cardiovascular comorbidities, present in 2920 (51.0%) and 2664 patients (46.6%) respectively. Emergency surgery was performed in 563 patients (9.8%). In-patient mortality occurred in 115 patients (2.0%), 48 (2.4%) in the DM group and 67 (1.8%) in the non-DM group, ( $P = 0.102$ ). In the unmatched cohort, overall 20-year survival rates were  $30.9 \pm 1.6\%$  in diabetics and  $49.2 \pm 1.0\%$  in non-diabetics ( $P < 0.001$ ). Freedom from cardiac mortality at 20 years was  $56.0 \pm 2.0\%$  in diabetics and  $68.4 \pm 1.0\%$  in non-diabetics ( $P < 0.001$ ). In the propensity-matched group, overall 20-year survival rates were  $35.4 \pm 2.5\%$  in diabetics and  $48.9 \pm 2.9\%$  in non-diabetics ( $P < 0.001$ ). Freedom from cardiac mortality at 20 years was  $57.8 \pm 3.0\%$  in diabetics and  $70.2 \pm 2.9\%$  in non-diabetics ( $P = 0.001$ ). Multivariable Cox regression analysis identified age (hazard ratio (HR): 1.03/year), female gender (HR: 1.43), DM (HR: 1.51), previous myocardial infarction (HR: 1.54) and left ventricular ejection fraction (LVEF)  $< 35\%$  (HR: 2.60) as independent factors influencing long-term cardiac mortality. **Conclusion:** Despite low operative mortality, long-term survival and freedom from cardiac death are significantly lower in patients with DM compared to non-diabetics. Aggressive treatment of DM, cardiovascular comorbidities and smoking cessation are essential to improve long-term survival in diabetic patients.

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**Key words:** Cardiac mortality, Myocardial revascularisation, Survival outcomes

### Introduction

Diabetes mellitus (DM) is a major risk factor for cardiovascular disease, and coronary artery disease is the leading cause of death among adult diabetics. In Singapore, the proportion of people affected by diabetes has increased from 8.2% in 2004 to 11.3% in 2010.<sup>1</sup>

Coronary artery bypass grafting (CABG) is a well-accepted treatment in patients with multivessel coronary artery disease since the 1970s. The major aims of CABG are to improve the quality of life by relieving symptoms of angina and also to increase life expectancy. As coronary artery disease may continue to progress following

revascularisation, CABG is ultimately a useful but palliative treatment of a progressive disease. In general, around 20% of patients undergoing CABG suffer from DM. For patients with diabetes and advanced coronary artery disease, high-level evidence has emerged showing CABG to be superior to percutaneous coronary intervention (PCI) in reducing rates of death and myocardial infarction (MI).<sup>2</sup> Kurlansky et al studied a propensity-matched cohort of diabetic and non-diabetic patients who underwent coronary revascularisation following non-ST-elevation myocardial infarction and reported that diabetic patients benefit from improved long-term survival and reduced major adverse cardiac events with CABG versus PCI.<sup>3</sup>

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Previous studies have demonstrated the adverse effect of DM on both short- and long-term survival after CABG.<sup>4-7</sup> This large retrospective study was conducted to determine the effect of DM on long-term survival outcomes after CABG in our local population.

## Material and Methods

Following approval from the local institutional review board (reference: 2007/095/C), a retrospective case-note and database review was performed on consecutive patients who had undergone isolated first CABG at our tertiary referral centre. Surgical outcomes were reviewed to include in-hospital mortality and long-term survival. Between August 1982 and December 1999, 5720 patients underwent isolated first CABG at National Heart Centre Singapore (NHCS), of which 1977 patients (34.6%) had existing DM. Patients who underwent reoperative CABG and CABG with concomitant cardiac surgical procedures such as valve replacement, repair of ventricular septal rupture or aneurysmectomy were excluded. Both elective and urgent surgeries were included. The diagnosis of diabetes was based on a history of previously diagnosed DM or current drug therapy for DM.

To obtain comparable subgroups, a one-to-one matched analysis based on estimated propensity scores for patients with DM and non-diabetic controls yielded 2 groups comprising 561 patients each. Information regarding the cause and date of death were obtained from hospital records, supplemented by data from the National Registry of Deaths.

## Statistical Analysis

Statistical analyses were performed with the Statistical Package for Social Science, version 17 (SPSS, Chicago, IL, USA). Continuous variables were expressed as means with standard deviation and were compared using two-tailed t-test. Categorical variables, expressed as percentages, were analysed with  $\chi^2$  or Fisher's exact test. Before performing propensity score matching, we conducted a univariable analysis of potentially confounding baseline covariates associated with diabetes. A propensity score was then estimated with the use of a logistic regression model fit with the 8 factors identified—age, gender, left ventricular ejection fraction (LVEF), presence of hypertension, dyslipidaemia, end-stage renal failure, history of smoking and left internal mammary artery to left anterior descending artery (LIMA-LAD) grafting. Diabetic patients were matched in a 1:1 ratio to patients without diabetes on the basis of propensity score, following a greedy nearest neighbour matching without replacement algorithm. Each matched pair was unique, and data for unmatched patients in either group were not used in subsequent analyses. Survival function and freedom from

morbid events were presented using Kaplan-Meier survival curves and comparisons performed with log-rank test. Cox multivariable regression analysis was used to identify the independent predictors of long-term outcomes. Preoperative and operative variables with a univariate  $P < 0.10$  or those judged to be clinically important were entered into the multivariable Cox model. All two-tailed  $P$  values  $< 0.05$  were taken as significant.

## Surgical Technique

All operations were performed via median sternotomy using moderately hypothermic (30°C to 32°C) cardiopulmonary bypass (CPB) instituted with ascending aortic and dual-stage right atrial cannulation. Aortic cross-clamping and intermittent blood cardioplegia for myocardial protection was applied in all cases. CABG was performed to all major territories as long as there appeared to be viable myocardium and the coronary arteries were not too small ( $< 1.5$  mm) or too heavily calcified. Bypass conduits included the LIMA (grafted to the LAD), saphenous vein grafts and radial artery grafts from the non-dominant arm. Surgical and myocardial preservation techniques remained largely unchanged during the study period.

## Results

Mean age was  $59.3 \pm 9.1$  years with 4373 (76.5%) males. The clinical characteristics of the unmatched study groups are shown in Table 1. Hypertension and dyslipidaemia were the most common cardiovascular risk factors, being present in 2920 (51.0%) and 2664 patients (46.6%) respectively. Amongst 5720 patients, 1977 (34.6%) had existing DM; 563 patients (9.8%) underwent emergency surgery within 24 hours of hospital admission. The most common indications for emergency CABG were angina refractory to medical therapy and high-risk coronary anatomy with critical stenosis. Except for body surface area, all other preoperative and operative variables showed significant differences between the diabetic and non-diabetic patients. Results for multivariable Cox regression analysis of factors affecting long-term freedom from cardiac death in the unmatched cohort are shown in Table 2.

The preoperative and operative data of the propensity-matched pairs are shown in Table 3. The number of distal anastomoses was higher in the diabetic group than in the non-diabetic group ( $3.6 \pm 0.9$  vs  $3.4 \pm 1.0$ ,  $P = 0.009$ ). There was a trend towards a larger proportion of patients with a previous MI in the DM group ( $P = 0.064$ ). Other variables were not significantly different between the 2 groups. Inpatient mortality occurred in 115 patients (2.0%), 48 in the DM group (2.4%) and 67 in the non-DM group (1.8%), ( $P = 0.102$ ).

Table 1. Preoperative and Operative Data of 5720 Patients Undergoing First CABG

| Variable                             | All Patients*<br>n = 5720 (%) | Diabetic*<br>n = 1977 (%) | Non-Diabetic*<br>n = 3743 (%) | P Value |
|--------------------------------------|-------------------------------|---------------------------|-------------------------------|---------|
| <b>Demographics</b>                  |                               |                           |                               |         |
| Age (years)                          | 59.3 ± 9.1                    | 60.9 ± 8.4                | 58.4 ± 9.3                    | <0.001  |
| Gender (male)                        | 4373 (76.5)                   | 1327 (67.1)               | 3046 (81.4)                   | <0.001  |
| BSA (m <sup>2</sup> )                | 1.71 ± 0.17                   | 1.71 ± 0.18               | 1.71 ± 0.17                   | 0.204   |
| BMI (kg/m <sup>2</sup> )             | 23.2 ± 2.6                    | 23.0 ± 2.5                | 23.3 ± 2.7                    | <0.001  |
| Obesity (BMI >25 kg/m <sup>2</sup> ) | 1142 (20.0)                   | 346 (17.5)                | 842 (22.5)                    | <0.001  |
| <b>Comorbidities</b>                 |                               |                           |                               |         |
| History of smoking                   | 1424 (24.9)                   | 567 (28.7)                | 857 (22.9)                    | <0.001  |
| End-stage renal failure              | 134 (2.3)                     | 67 (3.4)                  | 67 (1.8)                      | <0.001  |
| Hypertension                         | 2920 (51.0)                   | 1415 (71.6)               | 1505 (40.2)                   | <0.001  |
| Hyperlipidaemia                      | 2664 (46.6)                   | 1186 (60.0)               | 1478 (39.5)                   | <0.001  |
| <b>LVEF category</b>                 |                               |                           |                               |         |
| LVEF >50%                            | 3021 (52.8)                   | 884 (44.7)                | 2137 (57.1)                   | <0.001  |
| LVEF 35% to 50%                      | 2027 (35.4)                   | 803 (40.6)                | 1224 (32.7)                   | <0.001  |
| LVEF <35%                            | 672 (11.8)                    | 290 (14.7)                | 382 (10.2)                    | <0.001  |
| Previous myocardial infarction       | 2532 (44.3)                   | 1054 (53.3)               | 1478 (39.5)                   | <0.001  |
| Left main coronary artery disease    | 678 (11.8)                    | 184 (9.3)                 | 494 (13.2)                    | <0.001  |
| Emergency surgery                    | 563 (9.8)                     | 249 (12.6)                | 314 (8.4)                     | <0.001  |
| Duration of cardiopulmonary bypass   | 73.9 ± 65.5                   | 62.8 ± 64.5               | 77.8 ± 65.5                   | <0.001  |
| Duration of aortic cross-clamping    | 41.0 ± 37.5                   | 34.1 ± 35.1               | 43.5 ± 38.0                   | <0.001  |
| LIMA to LAD grafting                 | 4181 (73.1)                   | 1542 (78.0)               | 2639 (70.5)                   | <0.001  |
| Number of bypass grafts              | 3.4 ± 1.0                     | 3.5 ± 0.9                 | 3.4 ± 1.0                     | 0.004   |

BMI: Body mass index; BSA: Body surface area; CABG: Coronary artery bypass graft; LAD: Left anterior descending artery; LIMA: Left internal mammary artery; LVEF: Left ventricular ejection fraction

\*Values for continuous variables are expressed as mean ± standard deviation.

Survival data was available for all 5605 patients (98.0%) surviving to hospital discharge. The mean duration of follow-up was 13.0 ± 5.8 years (range, 0.1 to 24.7 years). During the follow-up period in the unmatched cohort, 1072 diabetic (54.2%) and 1589 non-diabetic patients (42.5%) died ( $P < 0.001$ ). Overall 20-year survival rates were 30.9

± 1.6% in diabetics and 49.2 ± 1.0% in non-diabetics ( $P < 0.001$ , Fig. 1A). The most common causes of non-cardiac death were malignancy (27.8%), pneumonia (18.6%) and stroke (15.7%). Death from cardiac causes occurred in 523 diabetic (26.5%) and 867 non-diabetic patients (23.2%), ( $P = 0.006$ ). Freedom from cardiac mortality at 20 years was

Table 2. Multivariable Cox Regression Analysis for Predictors of Late Cardiac Mortality in 5720 Patients Undergoing First CABG

| Variable                    | Hazard Ratio (HR) | 95% CI        | P Value |
|-----------------------------|-------------------|---------------|---------|
| Age                         | 1.022             | 1.015 – 1.030 | <0.001  |
| Female gender               | 1.162             | 1.003 – 1.347 | 0.045   |
| Obesity                     | 1.225             | 1.063 – 1.412 | 0.005   |
| Diabetes mellitus           | 1.378             | 1.195 – 1.588 | <0.001  |
| End-stage renal failure     | 2.765             | 1.904 – 4.014 | <0.001  |
| History of smoking          | 1.183             | 1.022 – 1.371 | 0.025   |
| LVEF 35% to 50%             | 1.425             | 1.231 – 1.650 | <0.001  |
| LVEF <35%                   | 2.925             | 2.448 – 3.494 | <0.001  |
| Non-usage of LIMA-LAD graft | 1.578             | 1.389 – 1.796 | <0.001  |

CABG: Coronary artery bypass graft; LAD: Left anterior descending artery; LIMA: Left internal mammary artery; LVEF: Left ventricular ejection fraction

Table 3. Preoperative and Operative Data of 1122 Propensity-Matched Patients Undergoing First CABG

| Variable                             | All Patients*<br>n = 1122 (%) | Diabetic*<br>n = 561 (%) | Non-Diabetic*<br>n = 561 (%) | P Value |
|--------------------------------------|-------------------------------|--------------------------|------------------------------|---------|
| <b>Demographics</b>                  |                               |                          |                              |         |
| Age (years)                          | 60.4 ± 7.2                    | 60.4 ± 7.2               | 60.5 ± 7.3                   | 0.885   |
| Gender (male)                        | 862 (76.8)                    | 431 (76.8)               | 431 (76.8)                   | 1.000   |
| BSA (m <sup>2</sup> )                | 1.72 ± 0.16                   | 1.73 ± 0.17              | 1.71 ± 0.16                  | 0.122   |
| BMI (kg/m <sup>2</sup> )             | 23.1 ± 2.4                    | 23.2 ± 2.3               | 23.1 ± 2.4                   | 0.463   |
| Obesity (BMI >25 kg/m <sup>2</sup> ) | 217 (19.3)                    | 111 (19.7)               | 106 (18.9)                   | 0.734   |
| <b>Comorbidities</b>                 |                               |                          |                              |         |
| History of smoking                   | 312 (27.8)                    | 156 (27.8)               | 156 (27.8)                   | 1.000   |
| End stage renal failure              | 2 (0.2)                       | 1 (0.2)                  | 1 (0.2)                      | 1.000   |
| Hypertension                         | 774 (69.0)                    | 387 (69.0)               | 387 (69.0)                   | 1.000   |
| Hyperlipidaemia                      | 565 (50.4)                    | 286 (51.0)               | 279 (49.7)                   | 0.676   |
| <b>LVEF category</b>                 |                               |                          |                              |         |
| LVEF >50%                            | 617 (55.0)                    | 312 (55.6)               | 305 (54.4)                   | 0.771   |
| LVEF 35% to 50%                      | 394 (35.1)                    | 197 (35.1)               | 197 (35.1)                   | 0.771   |
| LVEF <35%                            | 111 (9.9)                     | 52 (9.3)                 | 59 (10.5)                    | 0.771   |
| Previous myocardial infarction       | 557 (49.6)                    | 294 (52.4)               | 263 (46.9)                   | 0.064   |
| Left main coronary artery disease    | 187 (16.7)                    | 84 (15.0)                | 103 (18.4)                   | 0.128   |
| Emergency surgery                    | 106 (9.5)                     | 56 (10.0)                | 50 (8.9)                     | 0.534   |
| Duration of cardiopulmonary bypass   | 63.7 ± 63.2                   | 65.2 ± 64.5              | 62.4 ± 62.1                  | 0.523   |
| Duration of aortic cross-clamping    | 35.0 ± 34.4                   | 36.2 ± 34.4              | 34.0 ± 34.4                  | 0.373   |
| LIMA to LAD grafting                 | 957 (85.3)                    | 482 (85.9)               | 475 (84.7)                   | 0.555   |
| Number of bypass grafts              | 3.5 ± 1.0                     | 3.6 ± 0.9                | 3.4 ± 1.0                    | 0.009   |

BMI: Body mass index; BSA: Body surface area; CABG: Coronary artery bypass graft; LAD: Left anterior descending artery; LIMA: Left internal mammary artery; LVEF: Left ventricular ejection fraction

\*Values for continuous variables are expressed as mean ± standard deviation.

56.0 ± 2.0% in diabetic and 68.4 ± 1.0% in non-diabetic patients ( $P < 0.001$ ) (Fig. 1B). The most common causes of cardiac death were MI (51.2%) and congestive cardiac failure (41.9%).

During the follow-up of the propensity-matched group, 310 diabetic (55.3%) and 228 non-diabetic patients (40.6%) died ( $P < 0.001$ ). Overall 20-year survival rates were 35.4 ± 2.5% in diabetics and 48.9 ± 2.9% in non-diabetics ( $P$

<0.001) (Fig. 2A). Death from cardiac causes occurred in 157 diabetic (28.0%) and 118 non-diabetic patients (21.0%), ( $P = 0.007$ ). Freedom from cardiac mortality at 20 years was 57.8 ± 3.0% in diabetics and 70.2 ± 2.9% in non-diabetics ( $P = 0.001$ ) (Fig. 2B). Fatal stroke occurred in 24 patients, 17 (3.0%) in the DM group and 7 patients (1.2%) in the non-DM group ( $P = 0.039$ ). Multivariable Cox regression analysis (Table 4) identified age, female

Table 4. Multivariable Cox Regression Analysis for Predictors of Late Cardiac Mortality in 1122 Propensity-Matched Patients Undergoing First CABG

| Variable                       | Hazard Ratio (HR) | 95% CI        | P Value |
|--------------------------------|-------------------|---------------|---------|
| Age                            | 1.025             | 1.006 – 1.045 | 0.010   |
| Female gender                  | 1.425             | 1.037 – 1.958 | 0.029   |
| Diabetes mellitus              | 1.508             | 1.179 – 1.930 | 0.001   |
| History of smoking             | 1.321             | 0.995 – 1.754 | 0.054   |
| Previous myocardial infarction | 1.542             | 1.170 – 2.032 | 0.002   |
| LVEF <35%                      | 2.595             | 1.795 – 3.753 | <0.001  |

CABG: Coronary artery bypass graft; LVEF: Left ventricular ejection fraction

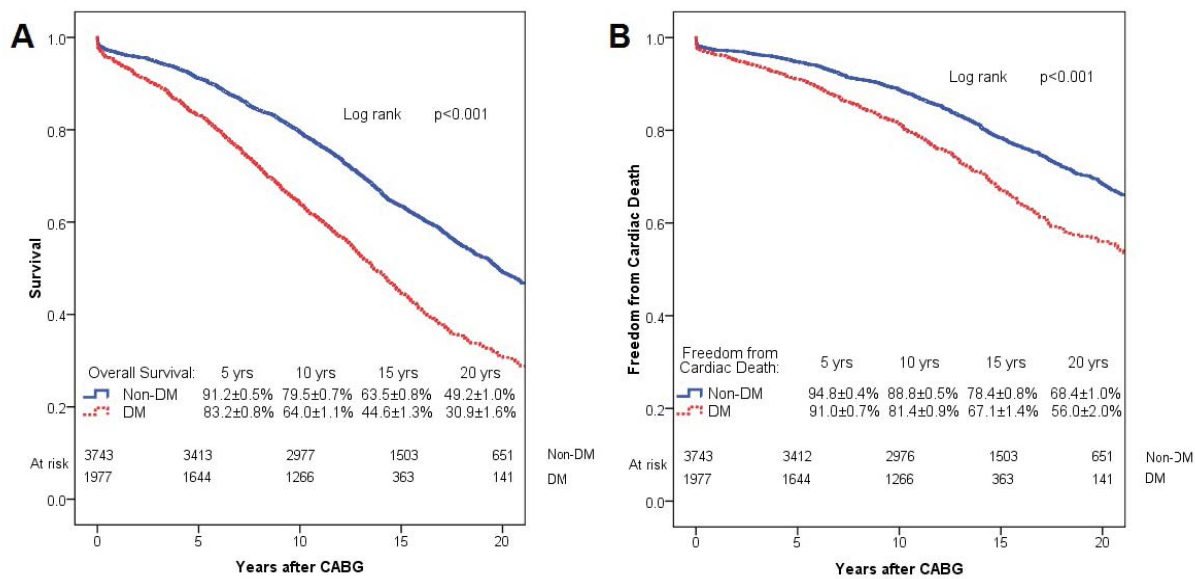


Fig. 1. Kaplan-Meier estimate of A) overall survival and B) freedom from cardiac death, in 5720 patients undergoing first CABG, including operative deaths.

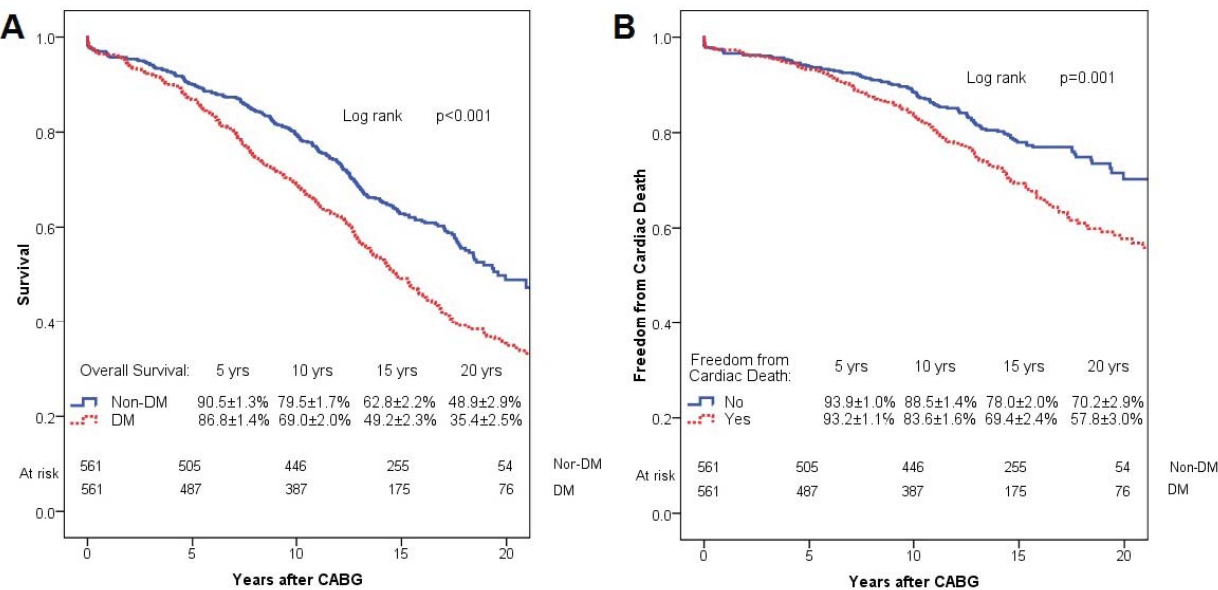


Fig. 2. Kaplan-Meier estimate of A) overall survival and B) freedom from cardiac death, in 1122 propensity-matched patients undergoing first CABG, including operative deaths.

gender, the presence of DM, previous MI and severely impaired LVEF (<35%) as factors influencing long-term freedom from cardiac death.

Discussion

As the unmatched groups in our study population had significant differences in most of the preoperative and

intraoperative variables, we studied the influence of diabetes on the long-term survival outcomes after CABG by matching a large number of diabetic and non-diabetic patients according to 8 important clinical characteristics, to make the study groups as comparable as possible. After propensity-matching, apart from the number of bypass grafts received, the 2 propensity-matched groups were comparable. Although statistically significant, in the setting



of complete revascularisation of all ischaemic territories, the minor difference in the number of bypass grafts received was unlikely to be clinically significant.

In-hospital mortality after CABG was similar (2.0%) in diabetic and non-diabetic patients with multivessel coronary artery disease (2.4% in diabetics vs 1.8% in non-diabetics,  $P = 0.102$ ). After matching with relevant clinical factors for coronary artery disease, a similar inpatient mortality rate of 2.1% was observed in the propensity-matched cohort (DM vs non-DM,  $P = 1.000$ ). Our in-hospital mortality compares favourably to the results of a large study reported by Carson et al<sup>5</sup> which included 146,786 patients undergoing isolated CABG. In this study, 30-day mortality was higher in both diabetic and non-diabetic patients (3.7 and 2.7%, respectively) and diabetes was found to be an independent predictor of 30-day mortality (odds ratio (OR): 1.23). Similar to the findings by other authors,<sup>8,9</sup> in-hospital mortality was not significantly different between diabetic and non-diabetic patients. In contrast, some retrospective studies have found diabetes to be an independent predictor for early postoperative death.<sup>5,6,10,11</sup>

Beyond the initial 5 years of follow-up after CABG, cardiac mortality was evidently higher in diabetic patients than in non-diabetic patients, as demonstrated by the divergence in the survival curves (Fig. 2B). This may be explained by the ongoing deleterious effects of diabetes on the cardiovascular system which include endothelial dysfunction, pro-inflammatory and prothrombotic effects, which in turn perpetuate atherosclerosis and progression of coronary artery disease in native vessels, especially distal to the bypass grafts. These effects cannot be prevented by revascularisation of coronary arteries alone. Our overall survival rates at 20 years ( $35.4 \pm 2.5\%$  in diabetics and  $48.9 \pm 2.9\%$  in non-diabetics) compare favourably to that described in another report (DM 23%, non-DM 42%,  $P < 0.01$ ). From the same study, the median life expectancy following CABG was 13.7 years in diabetic patients and 17.9 years in non-diabetic patients.<sup>12</sup>

The overall 20-year survival rates in the propensity-matched group were  $35.4 \pm 2.5\%$  in diabetics and  $48.9 \pm 2.9\%$  in non-diabetics ( $P < 0.001$ ). In the unmatched group, the overall 20-year survival rates were  $30.9 \pm 1.6\%$  in diabetics and  $49.2 \pm 1.0\%$  in non-diabetics ( $P < 0.001$ ). In the propensity-matched group, freedom from cardiac mortality at 20 years was  $57.8 \pm 3.0\%$  in diabetics and  $70.2 \pm 2.9\%$  in non-diabetics ( $P = 0.001$ ). In the unmatched cohort, freedom from cardiac mortality at 20 years was  $56.0 \pm 2.0\%$  in diabetic patients and  $68.4 \pm 1.0\%$  in non-diabetic patients ( $P < 0.001$ ). Compared to the propensity-matched groups, analysis of the unmatched cohort appeared to underestimate the overall survival rate (30.9% vs 35.4%) and freedom from cardiac death (56.0% vs 57.8%) of diabetic patients.

These differences in results were most probably due to the baseline differences between diabetic and non-diabetic patients. Patients with diabetes had a higher prevalence of comorbidities which were associated with a worse prognosis. As a result, the survival outcomes of diabetic patients based on unmatched data were confounded and erroneously worse than what they should be. The use of propensity score matching in this study allowed for correction of these biases arising from the use of non-randomised data.

Diabetic patients face an increased risk of postoperative wound infections following CABG and it has been demonstrated that strict perioperative glucose control lowers the risk of postoperative wound infection in these patients.<sup>5,13-15</sup> Apart from DM, other predictors of late cardiac-related mortality identified in our study (age, smoking and history of MI) have been reported previously.<sup>16</sup> Diabetic patients have a higher incidence of perioperative and late postoperative stroke. In our study, the incidence of fatal stroke during follow-up was 2.5 times higher ( $P = 0.039$ ) in diabetic patients compared to non-diabetics. In an analysis of data from the FREEDOM trial, Domanski et al<sup>17</sup> reported that renal insufficiency (hazard ratio (HR): 3.57), baseline low-density lipoprotein  $\geq 105$  mg/dl (HR: 3.28) and baseline diastolic blood pressure (each 1 mm Hg increase reduces stroke hazard by 5%; HR: 0.95), were independent late stroke predictors in diabetic patients undergoing CABG for multivessel coronary artery disease.

Our study shows that diabetic patients have worse long-term survival and lower freedom from cardiac death after CABG than non-diabetic patients. The poorer survival of diabetics than non-diabetics is due to both non-cardiac deaths and excessive cardiovascular mortality. This finding concurs with most published studies.<sup>4,9,10,18</sup> In a large study of 39,235 patients with a mean follow-up of  $5.9 \pm 3.2$  years, patients with insulin-dependent DM had more than double (HR: 2.04; 95% CI, 1.72 to 2.42) the long-term risk of all-cause death after CABG compared with patients without diabetes. The long-term risk of death in patients with non-insulin-dependent DM was only slightly increased (HR: 1.11; 95% CI, 1.05 to 1.18).<sup>19</sup> In another study following 856 diabetic patients who had undergone CABG up to 10 years, the relative risk of death or having an acute myocardial infarction (AMI) was 1.8 (95% CI, 1.5 to 2.2) in insulin-treated patients and 1.4 (95% CI, 1.2 to 1.7) in patients on oral medication. No increased risk of late death or AMI was observed in diet-treated patients with diabetes compared with patients without diabetes.<sup>20</sup> However, in 1 retrospective report of 767 diabetic patients with multivessel disease undergoing isolated first CABG, there was no significant difference in long-term survival in diabetic and non-diabetic patients who survived beyond the first 30 postoperative days.<sup>6</sup> In a study from China

examining the economic impact of diabetic patients who underwent CABG, costs for diabetic patients at 2 years follow-up were approximately S\$2142 higher than for non-diabetic patients ( $P < 0.001$ ).<sup>9</sup>

Data from large registries has shown that arterial grafts significantly improve survival in CABG patients, especially if a LIMA-LAD graft was constructed.<sup>21,22</sup> Other authors have shown a better long-term outcome in diabetic patients if one or two internal thoracic artery grafts were used.<sup>23,24</sup> Compared with single internal mammary artery (IMA) grafting, bilateral IMA grafting in a propensity score-matched cohort of 828 patients with diabetes showed improved long-term survival without any increase in perioperative morbidity or mortality, in particular, sternal wound infections.<sup>25</sup> Although LIMA-LAD grafts could potentially improve outcomes for patients with diabetes, and 85% of our matched sample received them, the associated survival advantage conferred upon diabetic patients was not large enough to render the survival rates of diabetic and non-diabetic patients similar.

During the study period, the proportion of patients receiving LIMA-LAD grafting (73.1%) was much lower than our current institutional practice. With increasing evidence in the last decade demonstrating the long-term graft patency and survival benefit associated with LIMA-LAD grafting, this technique is now performed as frequently as possible in our patients undergoing isolated CABG, with current utilisation rates approaching 100%. In a study of long-term graft patency in diabetic patients, late angiographic evaluation of 269 patients (83/269, (30.9%) diabetic) at a mean of  $7.7 \pm 1.5$  years after CABG showed that the proportion of complete graft occlusion was significantly lower in radial artery grafts (4.8%) than in saphenous vein grafts (25.3%) ( $P = 0.0004$ ). The authors concluded that the use of the radial artery should be strongly considered in diabetic patients undergoing coronary bypass surgery, especially with high-grade target vessel stenosis.<sup>26</sup> One-year rates of vein graft failure were similar in patients with and without diabetes but among diabetics, it tended to be higher in those who received insulin compared with those who did not.<sup>7</sup>

### Strengths and Limitations

The strengths of this study include its large sample size, extensive period of clinical follow-up and completeness of long-term survival data. As this is a retrospective observational study, inherent biases in data collection were inevitable. We did not investigate the difference in outcomes between patients with insulin dependent and non-insulin dependent DM. This study was also not designed to investigate the incidence of coronary re-interventions

(PCI, redo-CABG), hospital readmissions or bypass graft patency. During the follow-up period of this study, treatment for coronary artery disease has changed and so has the risk profile of the patient population. Patients undergoing CABG today tend to be older and sicker with a wider range of medical comorbidities. The results of this study form an important baseline for future comparison, although they may no longer be generalisable to our patient population today.

### Conclusion

This study reports the long-term survival and freedom from cardiac death of 5720 patients (1977 diabetics), who underwent isolated first CABG for multivessel coronary artery disease. Propensity score matching of 1122 patients (561 pairs) was performed to yield comparable groups. In conclusion, in-hospital mortality after CABG was low at 2% and did not differ significantly between diabetics and non-diabetics. In contrast, long-term survival was significantly impaired in diabetic patients, due to an excess of both cardiac and non-cardiac mortality. Aggressive treatment of DM, coexisting cardiovascular risk factors and cessation of smoking are essential measures to improve long-term survival in diabetic patients.

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