ORIGINAL ARTICLE

Impact of diabetes on early and mid-term survival after coronary artery bypass graft surgery in the Hong Kong Chinese population

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Objective To determine the impact of diabetes on early and mid-term survival in the Hong Kong Chinese population undergoing coronary artery bypass graft surgery.

Design Prospective study.

Setting Regional hospital, Hong Kong.

Patients A total of 904 consecutive patients following coronary artery bypass graft surgery from November 1999 to December 2003 were prospectively analysed. Among them, 377 (42%) diabetic and 527 (58%) non-diabetic patients were evaluated.

Main outcome measures Hospital mortality, mid-term mortality, and percutaneous coronary intervention–free survival.

Results The diabetic group had a higher risk score than the non-diabetic group (mean±standard deviation: EuroSCORE 4.7±3.4 and 3.6±3.4, respectively; P<0.001). Hospital mortality was 3.4% in the diabetic group compared to 2.8% in the non-diabetic group (P=0.698). Multiple logistic regression analysis identified left ventricular ejection fraction of less than 30% and preoperative intubation as independent risk factors for early hospital death. There were 81 late deaths and the actuarial survival at 48 months for the diabetic and non-diabetic patients were 86% and 90%, respectively (P=0.298). The angina-free survival and percutaneous coronary intervention–free survival at 48 months for the diabetic and non-diabetic patients yielded no statistically significant difference.

Conclusions Diabetes mellitus was not a predictor of early and mid-term mortality after coronary artery bypass graft surgery in our Chinese population. Furthermore, diabetes did not affect angina recurrence or intervention free–survival up to 4 years.

Introduction

The incidence of diabetes mellitus (DM) and its associated cardiovascular conditions continue to increase in the Hong Kong Chinese population. An estimated one in 10 Chinese in Hong Kong have DM and coronary artery disease remains a leading cause of death in patients with type 2 DM.[1,2] Despite DM being an established risk factor related to significant morbidity and mortality after coronary artery bypass graft (CABG) surgery,[3] in diabetic patients who require revascularisation, the procedure appears to have long-term benefit compared to percutaneous coronary intervention (PCI).[4,5] However, the majority of such studies were carried out in western countries and limited information was available for the Asian population.[3,4,6,7] In addition, the prevalence of DM in Asian CABG patients was consistently higher than that in Caucasians.[3,7-9] Yamamoto et al[8] reported that in Japanese patients, DM was a risk factor for early hospital death but did not affect their long-term survival. The aim of this study was to assess the effect of DM on early and mid-term outcomes after CABG for multiple vessel disease in a Chinese population.

Methods

During the inclusive period November 1999 to December 2003, 904 consecutive patients who underwent isolated CABG surgery at the Department of Cardiothoracic Surgery,

Key words
Coronary artery bypass; Coronary disease; Diabetes mellitus; Survival analysis

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糖尿病對接受冠狀動脈繞道術的香港華人的早期及中期存活率的影響

目的 探討糖尿病對接受冠狀動脈繞道術的香港華人的早期及中期存活率的影響。

設計 前瞻性研究。

安排 香港一所地區醫院。

患者 前瞻性分析於1999年11月至2003年12月期間，連續904位接受冠狀動脈繞道術的病人資料。其中包括377位（42%）糖尿病患者及527位（58%）非糖尿病患者。

主要結果測量 醫院死亡率、中期死亡率，以及未有接受經皮冠狀動脈介入治療的病人的存活率。

結果 與非糖尿病組比較，糖尿病組有較高風險分數：糖尿病組的EuroSCORE平均數±差異為4.7±3.4，非糖尿病組則為3.6±3.4（P<0.001）。醫院死亡率方面，糖尿病組3.4%，非糖尿病組2.8%（P=0.698）。多元迴歸分析顯示左心室射出率少於30%及術前插管為術後早期死亡的獨立風險因素。遲發性死亡共81例，四年的實際生存率，糖尿病組86%，非糖尿病組90%（P=0.298）。術後四年，兩組的心絞痛症狀緩解率及未有接受經皮冠狀動脈介入治療的存活率並無顯著分別。

結論 對於接受冠狀動脈繞道術的香港華人來說，糖尿病並不是早期及中期存活率的一個預測因子。術後四年，糖尿病不影響心絞痛復發及未有接受經皮冠狀動脈介入治療的病人的存活率。

TABLE 1. Baseline clinical characteristics*

Characteristic†	Diabetes (n=377)	Non-diabetes (n=527)	P value
Age (years)	64±9	63±10	0.017
Sex: female	133 (35)	101 (19)	<0.001
Hypertension	298 (79)	314 (60)	<0.001
COAD	54 (14)	65 (12)	0.425
LVEF 30-49%	85 (23)	90 (17)	0.040
LVEF <30%	27 (7)	28 (5)	0.262
Left main >50%‡	163 (43)	218 (41)	0.585
BMI >30 kg/m^2	8 (2)	2 (0.4)	0.022
IABP	16 (4)	26 (5)	0.749
Renal failure§	34 (9)	15 (3)	<0.001
Dialysis dependent	10 (3)	7 (1)	0.213
Carotid disease	51 (14)	59 (11)	0.331
PVD	29 (8)	38 (7)	0.798
Neurological deficit	25 (7)	26 (5)	0.307
EuroSCORE	4.7±3.4	3.6±3.4	<0.001

* Data are shown as mean±standard deviation, or No. (%)

† COAD denotes chronic airway obstructive disease, LVEF left ventricular ejection fraction, BMI body mass index, IABP intra-aortic counterpulsation balloon pump, and PVD peripheral vascular disease

‡ Left main coronary artery stenosis >50%

§ Renal failure defined as preoperative serum creatinine >200 mmol/L

Grantham Hospital, the University of Hong Kong were recruited. Patients with any documentation of DM (even diet-control only) were included. Traditional on-pump CABG and off-pump CABG had been selected according to the surgeon's preference and clinical indications. Insulin dextrose-potassium solution was routinely infused to diabetic patients during the operation and continued for 12 to 24 hours postoperatively, so as to achieve tight serum glucose levels of less than 10 mmol/L. For on-pump CABG, moderate hypothermia down to 30ºC was applied and blood cardioplegia was used to arrest the heart. Postoperatively, every patient had the first dose of 100 mg of aspirin within 8 hours, unless there was excessive bleeding. Patients with aspirin allergy received clopidogrel.

Follow-up information was obtained from hospital records, the Hong Kong Hospital Authority's Clinical Management System, and telephone interviews. Primary endpoints were both the early and mid-term mortality. Early mortality was defined as death within 30 days of the surgery or mortality during the same hospital admission for the operation. Mid-term mortality corresponded to the follow-up period ranging from 2 to 4 years. Secondary endpoints were: (1) the onset of post-CABG angina, and (2) any post-CABG PCI; one patient could therefore contribute two events. Simple coronary artery catheterization without balloon plasty or stenting was not counted as an event. Follow-up was 96% complete.

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (Windows version 11.0; SPSS Inc, Chicago [IL], US). Continuous variables were expressed as mean ± standard deviation and compared by unpaired Student's *t* tests. Additionally, the Chi squared test was used for categorical variables. Multiple logistic regression analysis was performed for independent predictors of early hospital mortality. Actuarial survival analysis was performed by the Kaplan-Meier method and life tables. The log rank test was used to compare survival curves. Odds ratios with 95% confidence intervals were calculated and a P value of less than 0.05 was considered statistically significant.

Results

Baseline clinical (including operation) details are shown in Tables 1 and 2. Diabetic patients were more likely to be female, older, obese, hypertensive, and have renal failure and poor left ventricular function. Their overall operative risk scores were poorer than those of the non-diabetic population; EuroSCOREs were 4.7 versus 3.6, respectively (P<0.001). The operative bypass times and aortic cross-clamped times

were similar in the two groups, as were the on-table estimates of native coronary artery diameters. Early mortality was marginally higher for diabetic patients, but the difference was not statistically significant (Table 2). Multivariate logistic regression analysis of factors affecting early hospital mortality is shown in Table 3; only left ventricular ejection fraction of less than 30% and preoperative ventilation support were independent predictors.

Mid-term results and survival

Follow-up duration ranged from 6 to 56 months. There were 81 'mid-term' deaths among these patients. Actuarial angina-free survivals at 48 months were 79% and 83% for diabetic and non-diabetic patients, respectively (Fig a). Corresponding freedom from PCI rates were 94% and 97% (Fig b). Overall actuarial survival rates (based on all-cause deaths) at 48 months were 86% and 90% for diabetic and non-diabetic patients, respectively (Fig c). None of the above-mentioned differences between the diabetic and non-diabetic patients were statistically significant.

TABLE 2. Operative data and mortality*

Operative details and mortality†	Diabetes (n=377)	Non-diabetes (n=527)	P value
No. of grafts	2.8±0.9	2.7±0.9	0.009
LAD (mm)	1.63±0.24	1.64±0.24	0.463
OM1 (mm)	1.54±0.20	1.57±0.19	0.164
OM2 (mm)	1.56±0.21	1.57±0.23	0.801
PDA (mm)	1.52±0.21	1.53±0.22	0.719
Cross clamp (min)	66.8±22.3	64.4±22.9	0.161
Bypass (min)	108±32.2	104.8±32.3	0.162
Off-pump CABG	47 (12.4)	101 (19.2)	0.008
Early mortality	13 (3.4)	15 (2.8)	0.698
Late mortality	38 (10.1)	43 (8.2)	-

* Data are shown as mean±standard deviation, or No. (%)

† LAD denotes left anterior descending artery, OM1 first obtuse marginal artery, OM2 second obtuse marginal artery, PDA posterior descending artery, and CABG coronary artery bypass graft

TABLE 3. Preoperative factors that might affect early hospital mortality subjected to multivariate logistic regression analysis

Preoperative factor*	Odds ratio (95% confidence interval)	P value
Hypertension	0.89 (0.37-2.13)	0.796
Diabetes mellitus	1.06 (0.46-2.47)	0.892
Dialysis dependent	1.78 (0.19-16.72)	0.615
Preoperative IABP	2.82 (0.77-10.35)	0.119
LVEF <30%	4.75 (1.72-13.12)	0.003
Preoperative ventilation support	6.82 (1.87-23.66)	0.003

* IABP denotes intra-aortic counterpulsation balloon pump, and LVEF left ventricular ejection fraction

Discussion

In the present study in our Chinese population, we determined the impact of DM on survival after CABG surgery. Diabetes is a well-known risk factor for coronary artery disease and cardiovascular death.[10] The reported prevalence of DM among patients undergoing CABG ranges from 12 to 38%.[6,11,12] Hence diabetic CABG patients have been extensively evaluated, and the majority of studies have shown that such patients have a poorer prognosis in terms of postoperative complications as well as early and long-term survival. The adverse impact of DM on the outcome of coronary artery disease patients is related to its atherosclerotic, pro-inflammatory, and pro-thrombotic effects.[10]

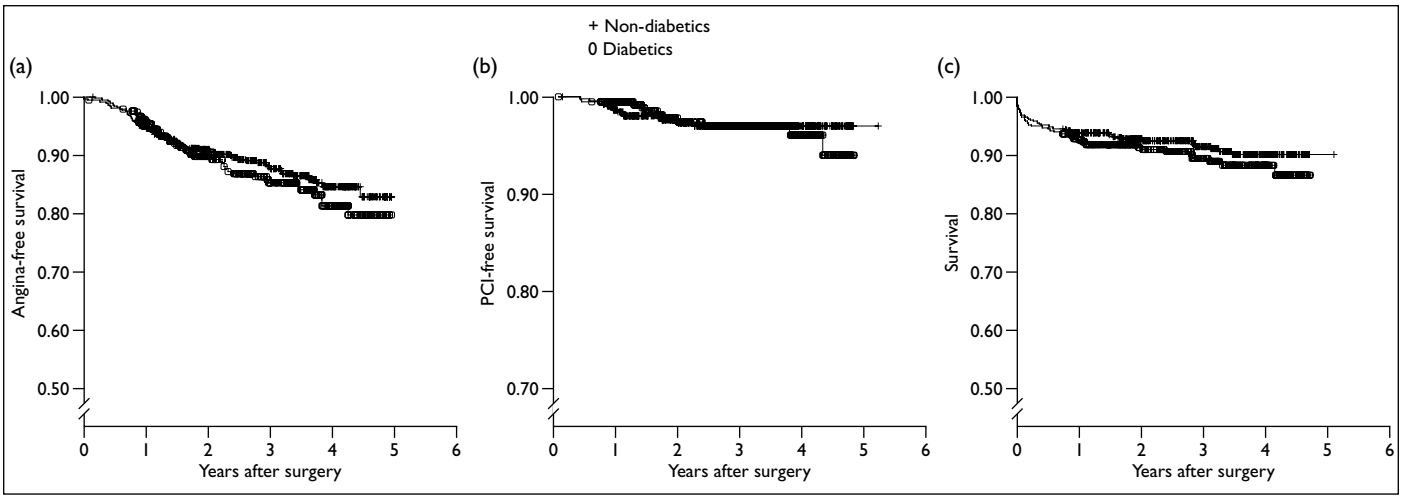

FIG. Effect of diabetes mellitus on (a) angina-free survival, (b) percutaneous coronary intervention (PCI)–free survival, and (c) mid-term actuarial survival in Chinese patients with coronary artery bypass graft

Log rank test: (a) P=0.417, (b) P=0.771, and (c) P=0.298

Carson et al[7] reported one of the largest series of diabetic patients undergoing CABG in the United States, and concluded that it is an important risk factor for 30-day mortality and in-hospital morbidity. Their mortality was 3.7% in diabetic individuals compared to 2.7% in non-diabetics. In a study reported by Thourani et al,[13] mortality in diabetic patients (3.9%) was significantly higher than that in non-diabetics (1.6%), with DM having a direct impact on early postoperative outcomes.

In our study however, DM was not a predictor of early and mid-term mortality after CABG surgery. This finding was consistent with some recent studies that failed to show the adverse effect of DM on survival outcomes in both Caucasian and Asians,[4,8,11,14] which raises questions about the potential influence of this disease on early operative results. Nor did the EuroSCORE committee identify DM as a significant risk factor in adult coronary and heart valves surgery.[15] Recently, it has even been suggested that DM may not be a risk factor for morbidity outcomes following CABG.[16] In fact, Calafiore et al[17] suggested that the 30-day mortality was more influenced by the technical factors related to the surgery than by the disease itself.

Diabetes-related sequelae are associated with the risk of death from CABG, many of which are associated with co-morbidity. The incidences of various co-morbidities in our patients were very similar to those described by others.[3,8] Leavitt et al[4] reported that diabetic patients without renal failure and/or peripheral vascular disease and non-diabetics who undergo CABG have similar long-term survival. Yet, despite our diabetic patients having more co-morbidities and higher risk scores than our non-diabetics (EuroSCORE 4.7 vs 3.6, respectively; P<0.001), we failed to identify DM as a predictor of early hospital mortality after CABG. We only identified poor left ventricular function and preoperative ventilation support as independent predictors for early hospital mortality, though identifying multiple risk factors was not the main aim of this study. Study sample bias, genetic predisposition, and physician referral pattern may all have played a role in our observation. Due to the relatively small sample size in this study, further subdivision into smaller categories (based on different subgroups of DM-related risk factors, such as renal impairment or peripheral vascular diseases) would have rendered statistical analysis difficult and inaccurate.

Recent animal studies show that diabetic myocardial tissue has different membrane ionic homeostatic activities, which may be protective for ischaemic and reperfusion injury.[18] This cannot explain the survival findings of our study, because there is still no direct evidence of ischaemic preconditioning of the heart in human DM patients. Conversely, DM has been repeatedly associated with increased mortality in patients suffering from acute myocardial infarction.[19] It is therefore doubtful that DM had any clinically protective effect, and speculations that DM could have increased survival in our patients seem unwarranted.

Our study found that the calibre of native coronary vessels was similar in diabetic and non-diabetic patients, but we did not set out to evaluate this particular issue. Also, it is very difficult to quantify the quality of the entire length of native coronary vessels for the purpose of accurate statistical analysis. Our average cardiopulmonary bypass and aortic cross-clamped times, however, were no different between the two patient groups, which may indirectly reflect on the general quality of the native coronary vessels in our patients. Studies have shown that diabetic native coronary arteries are inferior in quality to those of non-diabetics undergoing coronary artery revascularisation.[5,7,9] Mosseri et al[20] observed that even before coronary disease becomes evident in diabetic patients, their arteries are smaller in diameter than those of the general population. This important aspect cannot be overlooked. Our number of patients having off-pump CABG was significantly less than those having on-pump traditional surgery. Surgeon's preference was one reason for this observation, but the quality of the native coronary vessels (including vessel calibre and the distal run-off) was also a major consideration.

In contrast to other studies,[21,22] our results showed that angina-free survival and PCI-free survival were not significantly different between the diabetic and non-diabetic groups in our Chinese population. Schwartz et al[9] noted that vessels grafted in patients with DM were on average smaller and more diffusely diseased. Nevertheless the disease did not appear to affect the patency of CABG grafts adversely over an average of 4-year follow-up, which was also consistent with our experience. Järvinen et al[22] found that the diabetics and non-diabetics experienced similar freedom from anginal symptoms at 1 year, and Choi et al[23] found that DM was not a risk factor for 1-year angiographic occlusion after off-pump CABG.

There is increasing evidence that ethnicity might also influence atherosclerosis and coronary heart disease, and that it should be included as a risk factor when assessing potential risks associated with any surgical or medical intervention.[24-26] Currently there are no published data regarding outcomes after CABG in Chinese versus other ethnic groups. Slater et al,[27] however, reported findings from one of the first investigations to compare acute and mid-term outcomes in four different ethnic groups (whites, blacks, Hispanics, and Asians) undergoing percutaneous coronary stenting. He found no differences in unadjusted acute and 1-year adverse event rates between Asian or Hispanic patients and Caucasians.

Limitations

Our study has several limitations that need to be clearly addressed. First, the number of patients was relatively small, which reduced its statistical power. Second, postoperative complications of these CABG patients were not detailed, as they have been reported in many previous papers.[3,6,7] Third, our diabetic patients were not divided into insulin-dependent and non–insulin-dependent subgroups. Despite our attempt to retrieve such data from the Hospital Authority Clinical Management System database, we could not confidently separate our DM patients into these categories. Some studies have suggested that insulin-dependent diabetic patients undergoing CABG are at higher risk than non–insulin-dependent patients.[8,28,29] Fourth, patients' haemoglobin A_{1c} levels were not detailed, although more and more researchers indicate that stricter blood glucose control before and immediately after CABG surgery does not improve clinical outcomes.[29] Moreover, we were not able to ascertain whether optimal glycaemic control was a factor contributing to favourable outcome in our diabetic patients.

Conclusions

Our Chinese CABG population had a higher incidence of DM compared to Caucasian series. In contrast to many other CABG studies in DM patients, our Chinese patients did not show any significant increase in early and mid-term mortality, despite having significantly higher surgical risk scores. Our results have important implications for diabetic patients undergoing surgical revascularisation. The choice of initial revascularisation strategy should not be based on a history of DM, rather the decision should rely on other factors such as angiographic suitability and the clinical context. Further studies are warranted to address late outcomes of DM patients undergoing CABG in the Asia-Pacific region. A large-scale multi-national trial to study the impact of race and ethnicity on outcomes in DM patients undergoing CABG operations seems warranted to resolve these conflicting observations.

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