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Influence of diabetes and bilateral internal thoracic artery grafts on long-term outcome for multivessel coronary artery bypass grafting☆

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Abstract

Objective: Diabetes mellitus is a major independent risk factor for morbidity and mortality after coronary artery bypass grafting (CABG). The aim of this study was to assess the effect of bilateral (B) internal thoracic artery grafting (ITA) in diabetic patients with multivessel CABG. **Methods**: Between 1985 and 1995, 4382 patients underwent primary isolated multivessel CABG with ITA grafting and concomitant saphenous vein grafting (SVG). Outcome of diabetic and nondiabetic patients undergoing single (S) ITA+SVG ($n=419$ and 2079) and BITA+SVG ($n=214$ and 1594) grafting was obtained at a mean follow-up of 11 ± 3 years. **Results**: Diabetic patients were older, included more women, and had more obesity, hypertension and peripheral vascular disease than nondiabetic patients. Deep sternal wound infection rate was 1.9% for diabetic patients vs 1.2% for nondiabetic patients ($P=0.2$) and 30-day mortality was 1.7 vs 1.8% ($P=0.9$). Cox regression analysis with interaction term and propensity scoring showed that BITA grafting decreased the risk of death (Hazard Ratio= 0.72 [0.57–0.91, 95%CI]) and coronary reoperation (HR=0.38 [0.19–0.77]) in both diabetic and nondiabetic patients, with no significant interaction noted. BITA grafting decreased the risk of myocardial infarction at long-term follow-up in nondiabetic patients (HR=0.72 [0.60–0.86]) but not in diabetic patients. Ten-year freedom rate from myocardial infarction in diabetic patients was 80 and 76% for SITA and BITA grafting patients, respectively. However, survival following myocardial infarction was better for patients who underwent BITA grafting, in both diabetic and nondiabetic subgroups. **Conclusions**: BITA+SVG grafting in diabetic patients improves survival and decrease coronary reoperation compared with SITA+SVG at long-term follow-up. Survival following myocardial infarction is improved with BITA grafting.

Keywords: Coronary artery bypass; Diabetes; Internal thoracic arteries; Long-term follow-up; Myocardial infarction

1. Introduction

Patients with diabetes mellitus have a greater incidence of atherosclerosis and cardiovascular disease, which is associated with increased mortality and morbidity [1]. Diabetes mellitus is an independent risk factor for lesion progression, graft occlusion, and cardiac mortality after coronary artery bypass grafting (CABG) [2–9]. Seven-year follow-up from the Bypass Angioplasty Revascularization Investigation (BARI) trial has shown a survival benefit for diabetic patients randomized to CABG with an internal thoracic artery (ITA) graft compared with percutaneous coronary intervention [1]. Moreover, ITA grafting has consistently shown benefit over saphenous vein grafting (SVG) in terms of long-term patency, survival and freedom from cardiac events [10]. Bilateral ITA (BITA) grafting and complete arterial grafting have been proposed as the procedures of choice for patients with multivessel disease. Data from our group [11] and others [12,13] have shown that BITA patients are likely to experience superior survival, greater freedom from myocardial infarction and coronary reoperation, and better overall event-free survival. However, the enthusiasm for BITA grafting in diabetic patients is hampered by the potential risk of increased early morbidity related to sternotomy, and data on long-term results of diabetic patients following BITA grafting have been scarce.

The aim of this study was to assess the effect of BITA grafting on long-term outcome for patients with multivessel CABG. We studied retrospectively the late clinical outcome of 4382 consecutive patients who underwent isolated CABG at the Montreal Heart Institute between 1985 and 1995.

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2. Materials and methods

The design of this study has been described previously [11]. Briefly, all patients who underwent primary and isolated multivessel CABG with ITA grafting and concomitant SVG grafting from January 1985 to December 1995 were retrospectively reviewed. Patients undergoing single and double CABG, patients who had a concomitant cardiac procedures or reoperation and patients with grafting using the right gastroepiploic artery ($n=65$) were excluded. The late clinical outcome of diabetic and non-diabetic patients undergoing SITA+SVG ($n=425$ and 2122) and BITA+SVG ($n=214$ and 1621) grafting were compared. Diabetes mellitus was reported in patients receiving oral-agent or insulin treatment before the CABG; diabetic patients managed with diet only were not considered. The indication for myocardial revascularization was based on standard angiographic and clinical criteria. The left IMA was harvested as a pedicle and usually grafted on the left anterior descending artery or a diagonal branch; when used, the right IMA was mostly harvested pedicled aiming at the circumflex through the transverse sinus or the right coronary territory or used as a free graft. BITA grafting was performed selectively in patients considered at high risk for deep sternal wound infection, i.e. patients with diabetes, older age, chronic obstructive pulmonary disease, peripheral vascular disease and a body mass index $\geq 30\,kg/m^2$. Otherwise, BITA grafting was performed depending on the preference of the attending surgeon. Demographic variables and major comorbidities were obtained by retrospective review of the institutional discharge summary.

Patient survival during follow-up and the occurrence of acute myocardial infarction, coronary reoperation and percutaneous coronary intervention (PCI) were obtained from institutional database and a governmental centralized health care database in Quebec. Follow-up was complete except for 76 patients (70 nondiabetic patients and 6 diabetic patients) in whom the health insurance number was unavailable. Thus, complete data were available for 4306 (98%) of the 4382 patients. The mean duration of follow-up was longer for nondiabetic patients (11 ± 3 years) than diabetic patients (10 ± 3 years) ($P<0.001$) for an overall mean follow-up of 11 ± 3 years.

3. Statistical analysis

Data are expressed as mean±SD or median (range) for continuous variable and frequency for categorical variable. Survival is expressed as survival±survival standard error. Univariate analysis was performed with Student's t test and Wilcoxon test depending on the distribution of the continuous variable and χ^2 test for categorical variable. Global effect of diabetes and BITA grafting and their interaction were studied by logistic regression and two-way ANOVA. Logistic regression was also used to find predictors of deep sternal wound infection. Survival analysis was performed with the Kaplan–Meier method and the log rank test was used to compare curves. To better account for selection bias in both groups, the influence of BITA grafting and diabetes on outcome was analysed using a stepwise multivariate approach with propensity scoring as previously published [11]. Cox proportional hazard regression models were used to determine the influence of demographic and operative covariates on late survival and event-free survival, and freedom from myocardial infarction, PCI and coronary reoperation. To seek whether BITA grafting had the same influence for long-term outcome in diabetic and nondiabetic population, an interaction term between diabetes and BITA grafting was included in the Cox proportional hazard regression model. Hazard ratio (HR), 95% confidence intervals (CI) and level of statistical significance (P-value) were calculated. A P-value <0.05 was considered statistically significant. The statistical analyses were performed using SAS release 8.2 (SAS Institute, Cary, NC).

4. Results

4.1. Patients characteristics and early results

Diabetic patients were older, more likely to be women, hypertensive, obese and suffer from peripheral vascular disease than nondiabetic patients (Table 1). Diabetic patients had a lower number of ITA grafts and a higher number of SVG grafts performed per patient than nondiabetic patient, but overall both diabetic and nondiabetic patients had same number of total grafts per patient. The rate of deep sternal wound infection was slightly higher for diabetic patient, although the difference was not statistically significant (1.9% for diabetic patients vs 1.2% for nondiabetic patients, $P=0.1524$). Predictors of wound infection were peripheral vascular disease, need for intraaortic balloon pump and subsequent need for thoracic drainage (Table 2). Both diabetic and nondiabetic patients experienced similar operative and early mortalities, and same rate of reoperation for bleeding. The mean hospital length of stay was 2 days higher for diabetic patients compared with nondiabetic patients (11 days vs 9 days), although the median hospital length of stay was similar (8 days).

4.1.1. Diabetes and ITA grafting subgroups

Patient characteristics for the four groups taking into account diabetes and ITA grafting strategy are shown in Table 1. By two-way ANOVA and logistic regression, diabetic patients were older, more likely to be female, hypertensive, dyslipidemic and had greater need for perioperative insertion of an intraaortic ballon pump than nondiabetic patients. Conversely, patients who underwent BITA grafting were younger, less likely to be female, hypertensive or obese than patients who underwent SITA grafting. There was a statistically significant interaction of diabetes and BITA grafting with peripheral vascular disease as diabetic patients who underwent SITA grafting suffered less from peripheral vascular disease than diabetic patients who underwent BITA grafting, and vice versa for nondiabetic patients (post-hoc tests non significant).

By two-way ANOVA, diabetic patients had a slightly higher number of coronary artery bypass grafts and saphenous vein grafts performed than nondiabetic patients.

Table 1
Effect of diabetes, BITA grafting and interaction for patients characteristics, operative data and postoperative course

	Interaction	Nondiabetic patients			Diabetic patients			Two-way ANOVA	
	Diabetes and BITA	Overall	*SITA*	*BITA*	Overall	*SITA*	*BITA*	Global effect diabetes	Global effect BITA grafting
	P	(*n*=3673)	(*n*=2079)	(*n*=1594)	(*n*=633)	(*n*=419)	(*n*=214)	*P*	*P*
Patients characteristics									
Age, years (mean±SD)	0.6060	60±9	*63±9*	*57±9*	62±8	*64±8*	*58±8*	0.0057	<0.0001
Gender (female)	0.1744	658 (18%)	*480 (23%)*	*178 (11%)*	177 (28%)	*147 (35%)*	*30 (14%)*	<0.0001	0.0004
Hypertension	0.0893	412 (11%)	*248 (12%)*	*164 (10%)*	150 (24%)	*113 (27%)*	*37 (17%)*	0.0019	<0.0001
Unstable angina	0.9889	838 (23%)	*505 (24%)*	*333 (21%)*	154 (24%)	*107 (26%)*	*47 (22%)*	0.0680	0.5444
Prior MI	0.6557	1093 (30%)	*646 (31%)*	*447 (28%)*	192 (30%)	*134 (32%)*	*58 (27%)*	0.0571	0.9801
Preop. PCI	0.9762	50 (1.4%)	*35 (1.7%)*	*15 (0.9%)*	4 (0.6%)	*4 (1.0%)*	*0 (0%)*	0.9739	0.9740
Periop. IABP need	0.9618	247 (7%)	*161 (8%)*	*86 (5%)*	50 (8%)	*37 (9%)*	*13 (6%)*	0.0287	0.4567
CHF	0.5955	46 (1.3%)	*29 (1.4%)*	*17 (1.1%)*	10 (1.6%)	*8 (1.9%)*	*2 (0.9%)*	0.2426	0.8275
PVD	0.0230	228 (6%)	*154 (7%)*	*74 (5%)*	66 (10%)	*41 (10%)*	*25 (12%)*	0.3295	<0.0001
Contrast		*P*=0.3295			*P*=0.4605				
Obesity	0.1420	316 (9%)	*179 (9%)*	*137 (9%)*	153 (24%)	*110 (26%)*	*43 (20%)*	0.1376	<0.0001
Dyslipidemia	0.0653	497 (14%)	*212 (10%)*	*285 (18%)*	96 (15%)	*60 (14%)*	*36 (17%)*	0.0008	0.2104
COPD	0.2190	183 (5%)	*126 (6%)*	*57 (4%)*	37 (6%)	*25 (6%)*	*12 (6%)*	0.1184	0.2520
Operative data									
No. of grafts per patient	0.2945	3.3±0.5	*3.2±0.5*	*3.4±0.6*	3.3±0.6	*3.3±0.5*	*3.4±0.6*	0.0388	<0.0001
3 Grafts		2683 (73%)	*1627 (78%)*	*1056 (66%)*	456 (72%)	*325 (78%)*	*131 (61%)*	-	-
4 Grafts	-	905 (25%)	*417 (20%)*	*488 (31%)*	152 (24%)	*80 (19%)*	*72 (34%)*	-	-
5 Grafts and more	-	85 (2%)	*35 (2%)*	*50 (3%)*	25 (4%)	*14 (3%)*	*11 (5%)*	-	-
No. of ITA grafts per patient	-	1.4±0.5	-	-	1.3±0.5	-	-	-	-
No. of SVG per patient	0.2945	1.9±0.7	*2.2±0.5*	*1.4±0.6*	2.0±0.7	*2.3±0.5*	*1.4±0.6*	0.0388	<0.0001
Postoperative complications									
Reoperation for bleeding	0.9789	170 (5%)	*103 (5%)*	*67 (4%)*	30 (5%)	*21 (5%)*	*9 (4%)*	0.4163	0.9768
Sternal wound infection	0.5645	44 (1.2%)	*25 (1.2%)*	*19 (1.2%)*	12 (1.9%)	*9 (2.2%)*	*3 (1.4%)*	0.5484	0.3072
Mortality									
Operative	0.9736	8 (0.2%)	*5 (0.2%)*	*3 (0.2%)*	2 (0.3%)	*2 (0.5%)*	*0 (0%)*	0.9725	0.9768
30-day	0.8364	67 (1.8%)	*48 (2.3%)*	*19 (1.2%)*	11 (1.7%)	*9 (2.2%)*	*2 (0.9%)*	0.0684	0.7010
Hospital	0.6439	74 (2.0%)	*53 (2.6%)*	*21 (1.3%)*	13 (2.0%)	*11 (2.6%)*	*2 (0.9%)*	0.0347	0.6978
LOS in hospital, days (mean±SD, [range])	0.0103	8 [0-129]	*9 [0-129]*	*9 [0-118]*	8 [0-117]	*11 [0-96]*	*12 [0-117]*	<0.0001	0.2872
Contrast		*P*=0.0415			*P*=0.0509				

SITA, single internal thoracic artery grafting; BITA, bilateral ITA grafting; MI, myocardial infarction; PCI, percutaneous coronary intervention; IABP, intraaortic ballon pump; CHF, chronic heart failure; PVD, peripheral vascular disease; COPD, chronic obstructive pulmonary disease; LOS, length of stay.

Table 2
Predictors of deep sternal wound infection

Variable	Odds ratio estimate (95% confidence interval)	*P*-value
BITA	1.26 (0.70–2.27)	0.4430
Diabetes	1.49 (0.77–2.89)	0.2311
PVD	2.24 (1.09–4.61)	0.0290
Perioperative need for IABP	3.03 (1.54–5.99)	0.0014
Postoperative need for thoracic drainage	3.17 (1.30–7.75)	0.0112

BITA, bilateral internal thoracic artery grafting; PVD, peripheral vascular disease; IABP, intraaortic ballon pump.

Patients who underwent BITA grafting had a higher number of coronary artery bypass grafts performed and a lower number of saphenous vein grafts performed than patients who underwent SITA grafting. The rate of sternal wound infection was not significantly higher for diabetic patients who underwent SITA grafting than diabetic patients who underwent BITA grafting. Each group had similar rate of reoperation for bleeding and 30-day mortality. The postoperative hospital length of stay was longer for diabetic patients.

4.2. Late results and survival

Survival of diabetic patients averaged 94, 84 and 73% compared with 96, 91 and 84% in nondiabetic patients at 5, 10 and 15 years after surgery, respectively. The Kaplan–Meier curves of diabetic and nondiabetic patients were statistically different ($P<0.0001$) (Fig. 1). Diabetic patients had significantly worse freedom rates from myocardial infarction ($P=0.0003$; 10-year freedom from myocardial infarction: 79 vs 84% for diabetic and nondiabetic patients, respectively; Fig. 2) and worse event-free survival ($P<0.0001$; 10-year event-free survival: 71 vs 78% for diabetic and nondiabetic patients, respectively) compared with nondiabetic patients. The freedom rate from coronary reoperation and PCI was similar in diabetic and nondiabetic groups ($P=$NS).

4.2.1. Diabetes and ITA grafting subgroups

Survival of diabetic patients who underwent BITA grafting averaged 95, 88 and 79% compared with 93, 85 and 73% in diabetic patients who underwent SITA grafting, 97, 94 and 88% in nondiabetic patients who underwent BITA grafting, and 96, 91 and 84% for nondiabetic patients who underwent SITA grafting at 5, 10 and 15 years after surgery, respectively. The Kaplan–Meier survival curves of these four groups were statistically different ($P<0.0001$) (Fig. 3 for adjusted survival).

The Cox multivariate analysis with propensity score and diabetes–BITA grafting interaction showed that diabetic patients had a decreased survival compared with nondiabetic patients ($P<0.0001$; Table 3). Diabetes has no effect on freedom from percutaneous coronary intervention and coronary reoperation. Conversely, patients who underwent BITA grafting showed better survival and event free survival and higher rates of freedom from coronary reoperation compared with patients who underwent SITA grafting.

There was a statistically significant interaction of diabetes–BITA and freedom from myocardial infarction as nondiabetic patients who underwent BITA grafting had significantly better freedom from myocardial infarction than nondiabetic patients who underwent SITA grafting

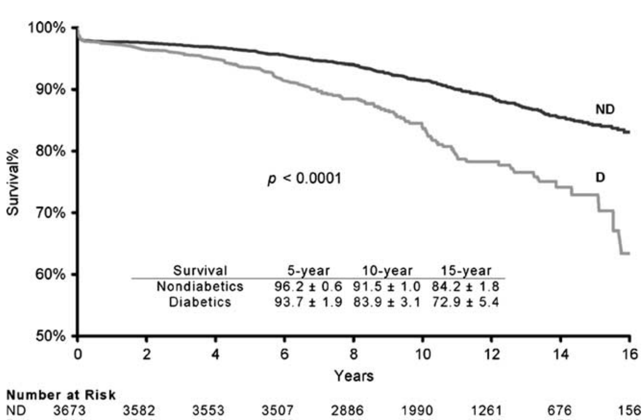

Fig. 1. Kaplan–Meier survival of diabetics (D) and nondiabetics (ND) patients undergoing primary elective coronary artery bypass for multivessel coronary artery bypass grafting (CABG) using single internal thoracic artery or bilateral ITA grafting.

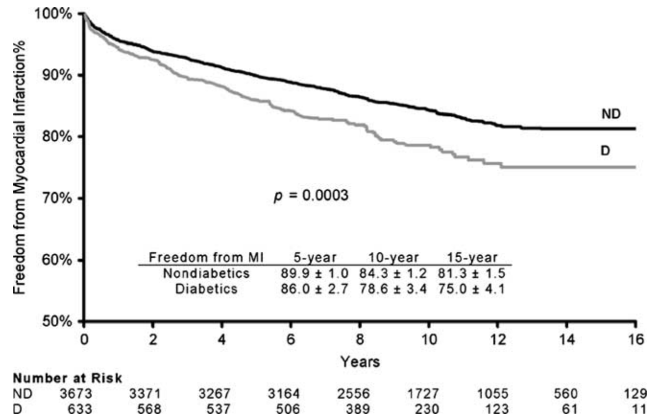

Fig. 2. Freedom from myocardial infarction for diabetics (D) and nondiabetics (ND) patients undergoing primary elective coronary bypass graft for multivessel coronary artery bypass grafting (CABG) using single internal thoracic artery or bilateral ITA grafting.

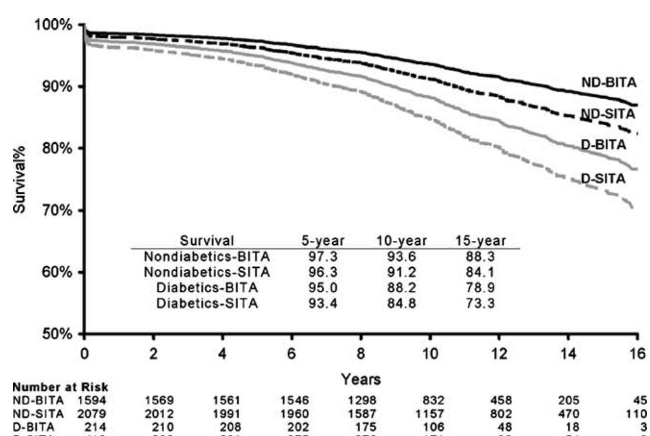

Fig. 3. Survival of diabetics (D) and nondiabetics (ND) patients undergoing primary elective coronary artery bypass for multivessel coronary artery bypass grafting (CABG) using single internal thoracic artery (SITA) vs bilateral ITA grafting (BITA), with correction with propensity score and confounding variables, for illustrative purposes. No confidence interval or log rank test were obtained.

Table 3
Cox regression multivariate analysis with propensity score for BITA grafting interaction with diabetes for long-term outcomes

	Interaction		Diabetes		BITA grafting	
	HR (95%CI)	*P*	HR (95%CI)	*P*	HR (95%CI)	*P*
Primary outcome						
Death	1.06 (0.66–1.70)	0.8086	1.80 (1.41–2.29)	<0.0001	0.72 (0.57–0.91)	0.0053
Secondary outcomes						
Myocardial infarction	1.68 (1.14–2.48)	0.0088	-	-	-	-
In nondiabetic patients	-	-	-	-	0.72 (0.60–0.86)	0.0003
In diabetic patients	-	-	-	-	1.21 (0.85–1.72)	0.2995
Percutaneous coronary intervention	1.32 (0.57–3.03)	0.5149	1.05 (0.62–1.80)	0.8496	0.89 (0.64–1.25)	0.5024
Coronary reoperation	1.41 (0.25–8.05)	0.6989	1.03 (0.43–2.47)	0.9448	0.38 (0.19–0.77)	0.0076
Any event	1.22 (0.87–1.70)	0.2557	1.26 (1.04–1.53)	0.0176	0.77 (0.66–0.89)	0.0004

These multivariate models were adjusted for the following covariables: age, gender, hypertension, unstable angina, prior myocardial infarction, preoperative percutaneous coronary intervention (except for the outcome percutaneous coronary intervention), perioperative intraaortic balloon pump need, chronic heart failure, peripheral vascular disease, obesity, dyslipidemia and chronic obstructive pulmonary disease.

($P=0.0003$; 10-year freedom from myocardial infarction: 88 vs 83%, respectively; Fig. 4), and diabetic patients who underwent BITA grafting had a worse freedom from myocardial infarction than diabetic patients who underwent SITA grafting ($P=$NS; 10-year freedom from myocardial infarction: 76 vs 80%, respectively; Fig. 4 for adjusted survival). However, survival following myocardial infarction was better for patients who underwent BITA grafting, in both diabetic and nondiabetic subgroups (Fig. 5 for adjusted survival).

5. Discussion

The major findings of this retrospective study are that diabetic patients who underwent BITA+SVG grafting for multivessel coronary artery disease showed better overall survival compared with diabetic patients who underwent SITA+SVG. Diabetic patients who underwent BITA+SVG grafting had higher rates of myocardial infarction at long-term follow-up compared with diabetic patients who underwent SITA+SVG, but the difference is not statistically significant. However, survival of patients who underwent BITA grafting was significantly improved following myocardial infarction.

The Bypass Angioplasty Revascularization Investigation (BARI) trial has shown that patients with treated diabetes randomized to an initial strategy of percutaneous coronary angioplasty had significantly higher 7-year mortality than patients randomized to an initial strategy of CABG [1]. The benefit of CABG was restricted to patients receiving at least one ITA graft during CABG. At 4-year mean follow-up, angiography of BARI patients showed that treated diabetes does not appear to adversely affect patency of ITA grafts and SVG [9]. Detre et al. [14] recently suggested that the benefit of CABG in BARI-eligible diabetic patients may be related to a protective effect on mortality after myocardial infarction, although the incidence of Q-wave myocardial infarction was similar in CABG and angioplasty groups.

5.1. Early results

In an earlier report, Cosgrove et al. [15] studied the risk of BITA grafting and identified diabetes and advanced age, but not BITA grafting, as risk factors for wound complications. They concluded that 'special consideration should be given

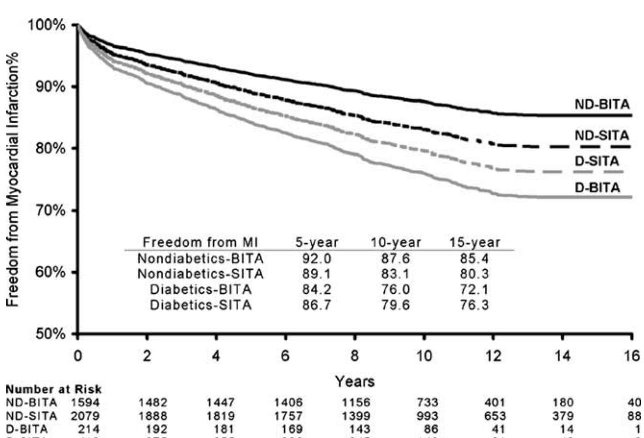

Fig. 4. Freedom from myocardial infarction for diabetics (D) and nondiabetics (ND) patients undergoing primary elective coronary bypass graft for multivessel coronary artery bypass grafting (CABG) using single internal thoracic artery (SITA) vs bilateral ITA grafting (BITA), with correction with propensity score and confounding variables, for illustrative purposes. No confidence interval or log rank test were obtained.

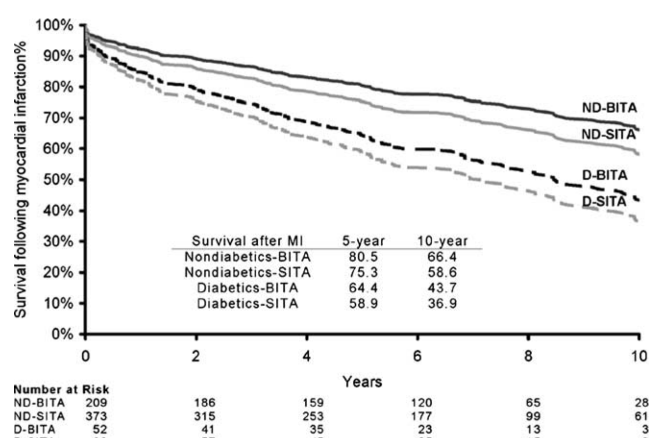

Fig. 5. Survival following myocardial infarction for diabetics (D) and nondiabetics (ND) patients undergoing primary elective coronary bypass graft for multivessel coronary artery bypass grafting (CABG) using single internal thoracic artery (SITA) vs bilateral ITA grafting (BITA), with correction with propensity score and confounding variables, for illustrative purposes. No confidence interval or log rank test were obtained.

to diabetic patients and elderly patients before BITA grafting'. We have previously demonstrated using sternal radionuclide tomography that ITA dissection as a pedicle caused an important but transient decrease in the sternal blood supply, which is more severe after BITA than SITA mobilization [16]. Moreover, the ratio of hypoperfused to total sternal area was similar both in non-diabetic and in diabetic patients.

Skeletonization of the ITA appears to lower the risk of deep sternal wound infection in patients with diabetes undergoing BITA grafting by preserving sternal and anterior intercostal branches and their collaterals [17]. In the present paper, the ITA were harvested pedicled in both diabetic and nondiabetic patients with a low rate of sternal wound infection. Hirotani et al. [18] shown that the incidence of chest wound infection in diabetic patients differed significantly according to whether patients were treated with insulin (11%) or not (3.9%), but did not differ whether patients underwent SITA vs BITA grafting. In a cohort of diabetic patients who underwent skeletonized BITA grafting, Lev-Ran et al. [19] reported chronic lung disease, obesity, reoperation and renal insufficiency as risk factors for sternal infection.

In the present report, diabetic and nondiabetic patients who underwent SITA and BITA grafting had similar rates of sternal wound infection and reoperation for bleeding despite mobilization of the ITA graft as a pedicle. Predictors of wound infection were PVD, need for IABP and subsequent thoracic drainage, which may identify patients with poor sternal wound healing and increased risk of catheter-related bacteriemia or thoracic cavity colonization. Surprisingly, neither diabetes nor ITA grafting strategy were identified as predictors of wound infection which could be due to the low rate of deep sternal wound infection in our cohort.

5.2. Survival

Diabetes is an important risk factor for late mortality after CABG [2–9], even in high-risk subgroups such as patients with low ejection fraction, advanced age and urgent surgery [4]. Lytle et al. [12] have shown that BITA grafting produces improved outcomes for patients with or without pharmacologically treated diabetes compared with SITA grafting. Hirotani et al. [18] reported no beneficial effect in either survival, cardiac death or cardiac event-free survival at 5-year follow-up in diabetic patients having one vs two ITA grafts. In a larger study using skeletonized ITA grafts for multivessel disease, Endo et al. [20] demonstrated that diabetic patients with preserved ejection fraction benefited from BITA grafting compared to SITA grafting for 10-year survival and freedom from cardiac event, but the benefit disappeared in diabetic patients with reduced ejection fraction.

Insulin requirement has been reported as a poor prognosis factor for long-term mortality in diabetic patients [3,8]. However, recent reports by Calafiore et al. [21] and others [2,18] have shown that preoperative treatment of diabetes did not affect early mortality or 5-year survival in patients undergoing CABG for multivessel disease. We have previously demonstrated that BITA grafting is superior to SITA grafting for long-term survival and freedom from cardiac event at more than 10-year follow-up [11]. In the present study, we specifically looked at diabetic patient population and demonstrated that the survival benefit remained despite an overall poorer prognosis than nondiabetic patients.

5.3. Myocardial infarction

In general population, the relative risk of myocardial infarction and sudden death is 50% greater in diabetic men and 150–300% greater in diabetic women, compared to their age-matched nondiabetic counterpart [5]. Diabetic patients without previous MI have the same [22] or a lower [23] risk of MI as nondiabetic patients without previous MI.

In an earlier report, we have shown a higher recurrence rate of angina in patients with BITA grafts which was thought to be related to the presence of more severe coronary artery disease and higher rates of diabetes and reoperation for CABG in that group, three significant risk factors for a poorer prognosis [7]. We now report that (1) the incidence of myocardial infarction in diabetic patients is higher than nondiabetic patients; (2) diabetic patients undergoing BITA grafting experience higher rates of myocardial infarction than diabetic patients undergoing SITA grafting; and (3) survival following myocardial infarction is improved in patients who underwent BITA grafting.

The tremendous impact of diabetes on survival and myocardial infarction rate could be partly explained by the unfavorable demographics of diabetic patients. However, multivariate analysis with propensity score used in this report identified diabetes as a predictor of death and myocardial infarction. Diabetes is known to affect every physiological system as well as the coronary vasculature and several mechanisms have been postulated. Diabetes is associated with a more diffuse atherosclerotic disease and a higher rate of native vessel disease progression [2,4,5] explained by the diabetes associated dyslipidemia, reno-vascular hypertension, hyperglycemia, hyperinsulinemia, impaired fibrinolysis and hypercoagulability [23,24]. Furthermore, the combination of lipid-rich atherosclerotic plaque and enhanced intraluminal thrombosis in diabetic patients may increase the likelihood of infarction [5]. Elevated blood viscosity due to high level of plasma proteins and increased red cells aggregation in diabetes could contribute to infarct extension by increasing shear forces on atherosclerotic plaques and by impending collateral coronary blood flow [5]. Platelet and endothelial dysfunction in diabetes result in increased production of procoagulant thromboxane A2 and von Willebrand factor, and deficient production of vasorelaxing prostacyclin [25]. The hyperpolarizing mechanism, present in endothelial cells of normal arteries and implicated in coronary vasodilatation, is also impaired in diabetics [5].

Diabetic cardiovascular autonomic neuropathy could lead to myocardial infarction by increasing heart rate and myocardial oxygen demand at rest, increasing coronary vascular tone at the site of coronary stenosis with decreased myocardial blood flow, reducing coronary perfusion pressure during orthostatic hypotension and eliminating early warning signs of ischemia [5].

Diabetes is an independent risk factor for atherosclerotic lesion progression and coronary bypass graft occlusion [2]. However, late graft patency in diabetic patients is similar to nondiabetic patients [1–3]. CABG greatly reduces the risk of death after spontaneous Q-wave myocardial infarction in diabetic patients [14], but the overall incidence of myocardial infarction is similar in diabetic and nondiabetic patients [1,8].

5.4. Selection of diabetic patients for BITA grafting

In the present study, selection criteria favoring SITA grafting over BITA grafting were insulin-dependent diabetes, chronic obstructive pulmonary disease, older age, and serious comorbidities affecting long-term survival such as diffuse coronary artery disease, severe peripheral vascular disease, and dialysis-dependent renal insufficiency. BITA grafting was performed selectively in patients considered at low risk for deep sternal wound infection. In this cohort, diabetic patients undergoing BITA grafting are significantly younger, less likely to be female, hypertensive or obese than patients who underwent SITA grafting.

6. Limitations

This study reported the retrospective experience of a single tertiary center. Statistical methods such as propensity score and multivariate analysis were used to improve the comparability of the groups and reduce the influence of selection bias. Some significant risk factors for coronary artery disease were not available, such as smoking, angina functional class and left ventricular ejection fraction.

In this retrospective study, some myocardial infarction could have been missed especially in diabetic patients in whom silent myocardial infarction are more prevalent [5]. In BARI, 46% of spontaneous Q-wave myocardial infarction was silent [1,14].

We did not separate diabetic patients by their preoperative treatment (oral therapy, insulin therapy) because the aim of this study was to assess the impact of diabetes and not the preoperative treatment of diabetes.

7. Conclusion

BITA+SVG grafting in diabetic patients improves survival and decrease coronary reoperation compared with SITA+SVG at long-term follow-up. Survival following myocardial infarction during long-term follow-up is significantly improved in patients who underwent BITA grafting. BITA grafting should be offered to every diabetic patient except if there are numerous other comorbidities expected to severely decrease life expectancy.

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Appendix A. Conference discussion

Dr A. Calafiore (*Chieti, Italy*): I think that with your research you were able to confirm some of the findings we were able to demonstrate in our previous presentation. There is increasing evidence today that bilateral internal mammary grafting has some kind of protective effect on survival and freedom from major ischemic events also in diabetics. Surely, long-term results are not worse than those obtained with a single internal mammary artery. I congratulate you for your study and I think that your data support more and more the use of mammary grafting.

Dr Stevens: I believe that bilateral internal thoracic artery grafting should be offered to every diabetic patient except if there are numerous other comorbidities expected to severely decrease life expectancy.