14-Year Results of Bilateral versus Single Internal Thoracic Artery Grafts for Left-Sided Myocardial Revascularization in Young Diabetic Patients

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Abstract

Objectives Despite encouraging late outcomes, the use of bilateral internal thoracic artery (BITA) grafting for myocardial revascularization in diabetic patients remains controversial because of an increased risk of sternal wound complications. In the present study, early- and long-term outcomes of the use of left-sided BITA versus single internal thoracic artery (SITA) grafting in young ($<$ 65 years of age) diabetic patients were reviewed retrospectively.
Methods A total of 250 propensity score pair-matched diabetic patients, operated on between February 2000 and December 2011, receiving either BITA ($n = 125$) or SITA ($n = 125$) grafting were analyzed retrospectively. In each group, 104 patients were males, and mean age was 60.1 $\pm$ 5.3 years. Follow-up was 2.1 to 14.8 years (mean, 9.3 $\pm$ 3.5 years) and complete for 100%.
Results Incidence of deep sternal wound infection was 2.4 versus 3.2% ($p = 0.722$). Rethoracotomy due to bleeding occurred in 4.8 versus 3.2% ($p = 0.608$). The 5-, 10-, and 14-year estimates of survival were 93.4, 76.6, and 67.5% (BITA) versus 89.5, 81.5, and 32.8% (SITA); $p = 0.288$. Freedom from reangiography/intervention (60.5 vs. 63.9%) during follow-up was comparable ($p = 0.507$) as well as infarction rate (93.8 vs. 95.1%, $p = 0.833$) and redoes ($p = 0.672$, exclusively valve surgery) were comparable. Freedom from thromboembolic or cerebrovascular events did not show any significant differences (94.0 vs. 94.0%, $p = 0.78$). Multivariate analysis identified poor ejection fraction as predictor for decreased long-term survival. Neither age nor gender or urgency had an influence on long-term mortality.
Conclusion Left-sided BITA grafting may be performed routinely even in diabetic patients without increased incidence of postoperative wound-healing complications. Survival rates after 5, 10, and 14 years were comparable for BITA and SITA grafting.

Keywords
- coronary artery bypass grafts surgery
- CABG
- BITA versus SITA
- diabetes mellitus

Introduction

Several investigations demonstrated superiority of bilateral internal thoracic artery (BITA) grafts to combined arterial and venous conduits for patients who received coronary artery bypass grafting (CABG). Although previous studies documented an evident benefit in long-term survival for BITA compared with single internal thoracic artery (SITA) or saphenous vein bypass grafting in diabetic patients,[1–5] the survival advantage might be limited by the burden of enhanced bleeding and wound complications.[6–8] Particularly, in patients suffering from diabetes, pedicled harvest of both internal thoracic arteries (ITAs) is

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described to increase the risk of postoperative deep sternal wound infections (DSWIs).[9–11]

Since the year 2000, the policy in our department was to perform BITA grafting routinely in a high frequency of isolated CABG cases. Of the whole collective receiving isolated CABG during this period ($n = 7,776$), BITA was performed in 4,942 patients (63.6%) and SITA was performed in 2,834 patients (36.5%); 2,325 patients (29.9%) were diabetics and 5,451 patients (70.1%) did not suffer from diabetes.

Within diabetic patients receiving isolated CABG, frequency of BITA grafting was 61.3% ($n = 1,425$) and frequency of SITA grafting was 38.7% ($n = 900$). BITA grafting in nondiabetics was 64.5% ($n = 3,517$) versus 35.5% ($n = 1,934$) SITA grafting.

ITA preparation technique was done in a pedicled manner predominantly between the years 2000 and 2010. Since 2010, we changed our strategy toward the skeletonized technique, as there exist some new studies which gave evidence about the relatively low development of sternal complications when using the skeletonized approach.

In the present study, early- and long term outcomes of the use of left-sided BITA versus SITA grafting in a subgroup of young (< 65 years of age) diabetic patients were reviewed.

Methods

A total of 250 propensity score pair-matched diabetic patients (exclusively 30-day survivors) operated on between February 2000 and December 2011, receiving either BITA ($n = 125$) or SITA ($n = 125$) grafting were analyzed retrospectively.

Inclusion criteria for diabetic patients were either the presence of insulin dependence or the necessity for oral medication plus diet, dated back at least, or longer than 1 year before the operation.

Propensity score pair match was built by means of the following variables: age, gender, number of grafts (mean 3.3 ± 0.83 vs. 3.2 ± 0.99; $p = 0.921$), ejection fraction (EF), elective, urgent/emergent operations, preoperative infarction, preoperative percutaneous coronary intervention (PCI), or preoperative stent.

In each group, 104 patients were males, and mean age was 59.3 ± 5.3 versus 60.1 ± 5.3 years. EF > 50% was 63.2 versus 67.2% ($p = 0.595$), and elective operations were performed in 94.4 versus 92.0% ($p = 0.617$). Follow-up was 2.1 to 14.8 years (mean, 9.3 ± 3.5 years) and complete for 100%. Ethics vote was achieved from the local ethic committee of the Technical University Munich (No.: 5839/13).

Statistical Analysis

Demographic and clinical data are presented as frequency distribution and simple percentages. Values of continuous variables are expressed as mean ± standard deviation. Quantitative and qualitative or binary variables were compared using Student *t*-test and chi-square test. In patient cohorts, univariate analysis of selected preoperative and postoperative discrete variables was accomplished by the chi-square test with the appropriate degrees of freedom or the Fisher exact test to assess the equality of proportions. An odds ratio (OR) with a 95% confidence interval (CI) was given for each variable. Conditional logistic regression models with ordinal variables were used to determine the independent effects of selected demographic/clinical variables on hospital complications and mortality. Nonparametric estimates and curves of overall survival, freedom from cardiac and cerebrovascular death, and MACCEs (Major Adverse Cardiac and Cerebrovascular Events) were generated with the Kaplan–Meier method. All analyses were performed with Statistical Package for Social Science version (SPSS Inc., Chicago, Illinois, United States). A p-value < 0.05 was considered to indicate statistical significance.

Results

Demographic data are depicted in ►**Table 1**.

Mean age was 59.3 ± 5.3 versus 60.1 ± 5.3 years. EF > 50% was 63.2 versus 67.2% ($p = 0.595$), elective operations were performed in 94.4 versus 92.0% ($p = 0.617$), and both groups were comparable in terms of having preoperative myocardial infarction, PCI ORs STENTING. Portion of insulin-dependent diabetics (IDD) versus non-IDD (NIDD) did not differ significantly between both groups.

Perioperative Results

Number of grafts was 3.3 ± 0.83 versus 3.2 ± 0.99 (mean) ($p = 0.921$).

Incidence of DSWI revealed 2.4 versus 3.2% ($p = 0.722$). Incidence of superficial sternal wound infection was 3.2 versus 1.6% ($p = 0.684$). Rethoracotomy due to bleeding occurred in 4.8 versus 3.2% ($p = 0.608$).

Long-Term Results

The 5-, 10-, and 14-year estimates of survival were 93.4 (95% CI: 91.1–99.7), 76.6 (95% CI: 71.76–87.7), and 67.5% (95% CI: 53.0–85.2) (BITA) versus 89.5 (95% CI: 86.5–97.4), 81.5 (95% CI: 76.9–92.6), and 32.8% (95% CI: 5.38–71.2) (SITA); $p = 0.288$ (►**Table 2**).

Table 1 Demographic data

	BITA	SITA	p-Value
Males	$n = 104$	$n = 104$	0.728
Mean age (y)	59.3 ± 5.3	60.1 ± 5.3	0.964
EF > 50%	63.2%	67.2%	0.595
Elective operations	94.4%	92.0%	0.617
Noninsulin-dependent diabetics	$n = 80$	$n = 75$	
Insulin-dependent diabetics	$n = 45$	$n = 50$	0.602
Preoperative infarction	30.6%	39.5%	0.183
Preoperative PCI	20.0%	20.0%	1.000
Preoperative stent	19.1%	18.0%	0.860

Abbreviations: BITA, bilateral internal thoracic artery; EF, ejection fraction; PCI, percutaneous coronary intervention; SITA, single internal thoracic artery.

Table 2 Long-term results

Long-term follow-up	BITA 5 y	BITA 10 y	BITA 14 y	SITA 5 y	SITA 10 y	SITA 14 y	*p*-Value
Survival	93.4% (95% CI: 91.1–99.7)	76.6% (95% CI: 71.7–87.7)	67.5% (95% CI: 53.0–85.2)	89.5% (95% CI: 86.5–97.4)	81.5% (95% CI: 76.9–92.6)	32.8% (95% CI: 5.4–71.2)	0.288
Freedom from reangiography/intervention			60.5%			63.9%	0.507
Number of postoperative angiographics/interventions			$n = 41$			$n = 28$	0.103
Freedom from myocardial infarction			93.8%			95.1%	0.833
Freedom from reoperation			98.4%			98.4%	0.672
Freedom from major bleeding			99.2%			100%	0.563
Freedom from thromboembolic events			94.4%			96.0%	0.780

Abbreviations: BITA, bilateral internal thoracic artery; CI, confidence interval; SITA, single internal thoracic artery.

Cardiac-related deaths were SITA 30.8% ($n = 8$) and BITA 30.0% ($n = 9$). Noncardiac-related deaths were SITA 46.2% ($n = 12$) and BITA 46.7% ($n = 14$); $p = 0.954$. Freedom from reangiography/intervention (60.5 vs. 63.9%), during follow-up was comparable ($p = 0.507$), as well as number of postoperative interventions (BITA: 32.8%, $n = 41$, SITA: 22.4%, $n = 28$; $p = 0.103$), infarction rate (93.8 vs. 95.1%; $p = 0.833$), and redoes ($p = 0.672$, exclusively valve surgery) were comparable (►**Table 2**).

Freedom from major bleeding (BITA 99.2% vs. SITA 100%; $p = 0.563$) and freedom from thromboembolic or cerebrovascular events (94.0 vs. 94.0%; $p = 0.78$) did not show any significant differences (►**Table 2**).

Multivariate analysis identified poor EF as predictor for decreased long-term survival. Neither age nor gender or urgency had an influence on long-term mortality. Outcome differences and differences in the development of DSWI between the subgroups of IDD and NIDD are given in ►**Table 3**.

The development of DSWI was higher, but without statistically significant difference in IDD patients receiving BITA compared with those receiving SITA. For the subgroup of patients with NIDD, none of measured parameters differs significantly between patients receiving BITA or SITA.

A 30-day mortality in all 7,776 patients with isolated CABG operated on during the same time frame (2000–2011) was 3.3% ($n = 254$) and 4.7% for diabetics ($n = 110$) versus 2.7% ($n = 144$) for nondiabetics. DSWI/mediastinitis occurred in 19 (9 BITA and 10 SITA) of 5,451 nondiabetic patients (0.4%) and in 17 (10 BITA and 7 SITA) of 2,325 (0.7%) diabetic patients. None of the patients with mediastinitis died during 30-day follow-up.

Table 3 Results of BITA versus SITA in insulin-dependent versus noninsulin-dependent patients

	BITA Insulin dependent $n = 45$	SITA Insulin-dependent $n = 50$	*p*-Value	BITA Noninsulin dependent $n = 80$	SITA Noninsulin dependent $n = 75$	*p*-Value
Deep sternal wound infection	$n = 3$	$n = 0$	0.106	$n = 0$	$n = 4$	0.053
Superficial sternal wound infection	$n = 4$	$n = 1$	0.190	$n = 0$	$n = 1$	0.484
Rethoracotomy due to bleeding	$n = 3$	$n = 1$	0.259	$n = 3$	$n = 3$	0.464
Freedom from myocardial infarction	$n = 44$	$n = 50$	0.474	$n = 76$	$n = 71$	1.000
Freedom from reangiography/intervention	$n = 30$	$n = 39$	0.254	$n = 54$	$n = 58$	0.210
Freedom from major bleeding	$n = 44$	$n = 50$	0.474	$n = 80$	$n = 75$	
Freedom from thromboembolic events	$n = 44$	$n = 48$	1.000	$n = 74$	$n = 72$	0.497
Survival (y)						
5	97.7%	88.0%	0.156	91.0%	90.0%	0.781
10	82.5%	81.9%		75.1%	81.2%	
14	69.2%	51.8%		70.4%	71.4%	

Abbreviations: BITA, bilateral internal thoracic artery; SITA, single internal thoracic artery.

A 30-day mortality in all diabetic patients receiving BITA during the years 2000 to 2011 was 3.9% ($n = 56$) and 6% ($n = 54$) in diabetic patients receiving SITA. A 30-day mortality in all nondiabetic patients receiving BITA during this period was 2.4% ($n = 84$) and 3.1% ($n = 60$) in nondiabetic patients receiving SITA.

Discussion

Although there is evidence about beneficial long-term outcome after CABG using both ITAs,[1–5] frequency of BITA grafting in Europe is still approximately 12%. The National U.S. Database of the Society of Thoracic Surgeons reports that < 4% of patients, who underwent CABG currently receive the benefits of BITA grafting.[12] BITA frequency in young patients, < 50 years, thus in exactly clientele in whom best long-term benefit is ascribed to, currently amounts less than 5% in the United States.[12–14] Restriction of BITA performance, in particular, among diabetic patients is mainly based on the fear of enhanced postoperative complications such as increased bleeding, DSWIs, or prolonged duration of surgery. Thus, most surgeons recommend this strategy for younger patients who do not suffer from evident risk factors for sternal infections (diabetes mellitus, obesity, and chronic obstructive pulmonary disease).

Even advocates of BITA grafting often perform patient selection toward younger and healthier patients or exclude patients with enhanced risk profiles from this surgical approach. Cons of BITA grafting are mainly based on studies which detected increased bleeding complications or DSWI, in particular, when BITA harvest was performed in a pedicled manner in diabetic patients.[7–11]

Deo et al[10] demonstrated within a large cohort of 126,235 diabetics (122,465 SITA and 3,770 BITA) that the risk of DSWI might be reduced by skeletonized technique of ITA harvest. Using this strategy, diabetic patients were exposed to the same risk for DSWI independent whether SITA or BITA grafting was performed. Incidence of DSWI in the study by Deo et al was 3.1% for BITA grafting and 1.6% for LITA grafting, comparable to our own results.

To avoid misleading results concerning higher early mortality or complications such as mediastinitis/sepsis in our selected cohort of exclusively 30-day survivors, an additional analysis of all 7,776 patients with isolated CABG operated on during the same time frame (2000–2011) was performed. The 30-day mortality in this huge collective was, as expected, higher for diabetic patients compared with nondiabetics (4.7 vs. 2.7%) Occurrence of DSWI/mediastinitis was low (0.4% in nondiabetic vs. 0.7% in diabetic patients). None of the patients with mediastinitis died during 30-day follow-up.

The 30-day mortality in all diabetic patients receiving BITA was lower than in those receiving SITA (3.9 vs. 6.0%) but was comparable in all nondiabetic patients receiving BITA (2.4%) or SITA (3.1%).

The only randomized investigation was published by Taggart et al[15]: a multicenter study which involved 1,554 patients with SITA grafting and 1,548 patients with BITA grafting, certainly only around 50% of this cohort suffered from diabetes. Perioperative complication rate as well as results during 1-year follow-up was comparable between both groups concerning mortality, myocardial infarctions, and necessity of redos. A slight increase of the need of sternal reconstructions was detected in the BITA group (0.6% SITA vs. 1.9% BITA).

As Albes[16] rightly mentioned within his recent comment: "*Conflicts, Compromises, and Common Sense*": long-term patency advantage is the one and only reason for using the ITA. One of our previous investigations[17] entitled: "*Patency of internal thoracic artery compared with vein grafts-postoperative angiographic findings in 1189 symptomatic patients within 12 years*," clearly demonstrated the superior long-term patency of ITA grafts.

In the context of BITA grafting in diabetics, one of the most important studies was performed by Dorman et al[3]: A 30-year follow-up of a propensity score pair-matched cohort, involving exclusively diabetic patients who received either SITA ($n = 414$) or BITA grafts ($n = 414$). This well-designed and valuable study gave evidence about superior survival after BITA revascularization, without enhanced postoperative mortality and morbidity. Thus, ITA harvesting was performed in a pedicled manner, the incidence of DSWI was nearly similar within the BITA and SITA groups. Gatti et al[11] performed BITA grafting in a high frequency of around 60% (from 1989 to 2012) and around 80% (since 2012), similar to our strategy. The only restriction of this approach was hemodynamic instability, inferior quality, or iatrogenic injury of the graft. Main difference between our own and the study by Gatti et al[11] seems to be the fact that the latter involved exclusively insulin-dependent patients suffering from severe diabetes-associated comorbidities such as renal failure and peripheral vascular disease. The incidence of DSWI in patients without diabetes mellitus merely was 3.6 (SITA) versus 5.7% (BITA) within Gatti et al's collective, therefore, higher than our population. Sternal wound healing complications among IDD occurred in 14.4%, whereby the authors performed a strongly divided analysis between superficial sternal wound infections and DSWI. Osteomyelitis/mediastinitis occurred in 8%, although the skeletonized technique was used and, whenever possible, the in situ revascularization method was preferred.

This strategy only partly echos our own, insofar as we performed the pedicled technique until the year 2010. Since 2010, we changed our strategy toward the skeletonized technique, as there exist new studies which gave evidence about the lower development of sternal complications when using the skeletonized approach. In our experience, the skeletonized technique is more challenging, more time consuming, and bears a higher risk of graft injury.

Several authors emphasize that the use of BITA offers long-term survival benefits compared with SITA grafting.[1–5,11,18] Long-term survival, freedom from MACCE in our investigation are comparable to other previous series which address results of diabetic patients after BITA grafting.[1–5,11,18]

Although the cohort analyzed during the long-term follow-up of Gatti et al[11] was relatively small ($n = 188$), the authors could demonstrate excellent results in terms of mortality and freedom from cardiac events which compare favorable to the results of the present study. Interestingly, we could not detect significant differences between IDD and NIDD, neither in terms of perioperative complications nor in terms of long-term survival.

Simple comparison in terms of survival rates and incidence of MACCE seems to be problematic as study designs are varying widely. Mortality within the randomized series of Taggart et al,[15] for example, was low (1.2% BITA vs. 1.2% SITA). More than 40% of all operations were performed off-pump, whereas Gatti et al[11] as well as our group mostly performed on-pump procedures.

Taggart et al[15] did not present different categories for emergent/urgent surgery. Some authors include or exclude emergent operations, a fact that must result in different outcomes. In this context, the encouraging long-term results of Gatti et al[11] of diabetic patients with a mean EuroSCORE II of 11 $\pm$ 10.8 receiving exclusively BITA conduits present an important contribution to the literature. The mean follow-up period covers 5.7 $\pm$ 3.6 years (range, 0.2–13.9 years), was complete for 100% of the collective and analysis, and included all cardiac or cerebrovascular events, sudden death, recurrent angina, myocardial infarctions, low cardiac output, interventions, and redos.

The 1-, 5-, and 10-year survival rates (including hospital mortality) in the mentioned study were 92.5% (95% CI: 88.8–96.3%), 77.7% (95% CI: 71–84.4%), and 57.7% (95% CI: 45.1–66.2%), respectively, a dimension that constitutes similar results to the present study. Cardiac-related deaths were 23 (mainly myocardial infarction/myocardial failure) and non-cardiac-related deaths were 32 (mostly malignancy or pneumonia).

Advanced age ($p = 0.013$), chronic pulmonary disease ($p = 0.004$), renal failure ($p = 0.009$), and left ventricular dysfunction ($p = 0.035$) were identified as independent predictors for inferior survival, a phenomenon that only partially conforms our results insofar as multivariate analysis solely identified poor EF but not advanced age as a predictor for decreased long-term survival. Freedom from severe cardiac or cerebrovascular events after 1, 5, and 10 years in the study by Gatti et al[11] amounted to 96.1% (95% CI: 93.2–98.9%), 83.6% (95% CI: 77.4–89.7%), and 55.4% (95% CI: 44.7–66.1%), respectively. Percutaneous interventions were necessary in three cases, results, which compare thoroughly to our own. Nevertheless, the aspiration of superior long-term survival after BITA grafting did not come true in our series until 14 years after surgery. The tendency toward better survival and lower MACCE after 14 years at best allows cautious interpretation, as the number of patients at risk after this long time frame is very small.

Limitations

The retrospective character and the small number of patients ($n = 250$) involved in the long-term follow-up might be regarded as a substantial limitation of this series. Moreover, we do not provide the angiographic data/quality of anastomoses in this collective. Another that much larger series consisting of patients ($n = 1,189$) who were operated during an overlapping time period and received reangiography due to each angina equivalent clearly demonstrated superior patency of BITA grafts.[17]

Conclusion

BITA grafting, even in diabetic patients, is not associated with increased perioperative complications. Long-term results are encouraging good, but do not differ between patients receiving BITA or SITA grafting during a 14-year follow-up period. In this cohort of young diabetic patients, BITA shows no benefit over SITA plus vein grafts in the long term.

Note
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