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Aortic Valve Replacement and Concomitant Multi-Vessel Coronary Artery Bypass: The Impact of Using the Bilateral Internal Thoracic Arteries on Early and Late Clinical Outcomes

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See Commentary page 204.

Background: The survival benefit of coronary artery bypass grafting (CABG) using the bilateral internal thoracic arteries (BITA) is well known; however, the role of BITA in concomitant aortic valve replacement (AVR) and CABG has not been studied.
Methods: We retrospectively reviewed patients who underwent concomitant AVR and CABG. Cases not using an internal thoracic artery and less than 2 bypass grafts were excluded. We enrolled 114 patients in this study. The mean follow-up duration was 61.5±43.5 months.
Results: Forty patients (35.1%) underwent CABG with a single internal thoracic artery (SITA) and 74 patients (64.9%) underwent CABG with BITA. The preoperative clinical characteristics were not significantly different between the 2 groups, with the exception of a higher prevalence of atrial fibrillation in the SITA group. Postoperative mortality and morbidity were not significantly higher in the BITA group than in the SITA group. In the univariable analysis, the survival of the BITA group was similar to that of the SITA group (p=0.157). Multivariable analysis showed that only mean age was a predictor of death (p=0.042), but using BITA was not an independent predictor (p=0.094). In low-risk patients whose preoperative ejection fraction was >45%, the survival of the BITA group was significantly better than that of the SITA group (p=0.043).
Conclusion: BITA use in concomitant AVR and CABG showed no difference in mortality compared to using SITA. Although its impact on long-term survival was inconclusive, BITA use can be considered for low-risk patients.

Keywords: Aortic valve replacement, Coronary artery bypass

Introduction

The use of the bilateral internal thoracic arteries (BITA) in coronary artery bypass grafting (CABG) has a distinct survival advantage compared to CABG with a single internal thoracic artery (SITA) [1-3]. Recent guidelines recommend using BITA for multi-vessel CABG [4,5]. In patients with aortic stenosis (AS), coronary artery disease (CAD) is more prevalent than in the general population, and performing concomitant CABG and aortic valve replacement (AVR) is recommended for those patients [6]. Using BITA in concomitant CABG and AVR is not standard practice in many centers due to the limited life expectancy of those patients, technical complexity, and concerns regarding the increased risk of early complications [7]. However, it is not known whether BITA use in concomitant AVR and CABG increases operative complications or improves late survival. Therefore, we reviewed our experience with concomitant AVR and CABG in multi-vessel CAD.

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Methods

Study population

We reviewed patients who underwent concomitant AVR and CABG with multi-vessel CAD between July 1996 and June 2014. The inclusion criteria were CABG as a concomitant procedure of AVR and age >18 years. The exclusion criteria were no use of an internal thoracic artery (ITA), previous cardiac surgery, concomitant mitral valve surgery, concomitant aortic surgery, single vessel coronary disease, or less than 2 bypass grafts. In total, 114 patients were included in this study. Forty patients received a SITA graft and 74 patients received a BITA graft. Preoperative, intraoperative, and postoperative data were retrospectively collected from medical records. Follow-up data were obtained from internal and external medical records.

Outcomes, definitions, and follow-up

The study outcomes were early mortality and morbidity and late survival. Early death was defined as death prior to discharge or any death within 30 days postoperatively. CAD was defined as coronary arteries with greater than 70% narrowing. Renal failure was defined as a creatinine level greater than 2.4 mg/dL or the need for dialysis, and postoperative renal failure was defined as a new need for dialysis or hemofiltration. Postoperative stroke was defined as a new central neurological deficit persisting for >24 hours. Prolonged ventilation was defined as ventilation for more than 48 hours postoperatively. The mean follow-up duration was 61.5±43.5 months. The last follow-up period was until January 11, 2016. The survival status of patients lost to follow-up was confirmed by the National Insurance Database. The final survival status was known for all patients.

Surgery

The left ITA was used in all patients. The second conduit was generally chosen based on guidelines at the time of surgery [4,8] and the surgeon's preference. In terms of aortic valve prosthesis, mechanical valves were preferred for patients under 65 years, while bioprosthetic valves were preferred for patients older than 65 years. All procedures were performed using standard median sternotomy. The ITA and gastroepiploic artery were both harvested in a skeletonized fashion. The left ITA and gastroepiploic artery were used as *in situ* grafts. Before cardiopulmonary bypass (CPB), a composite Y graft was constructed using the *in situ* left and right ITA as a free graft. The great saphenous vein and radial artery were harvested using an open technique. CPB was established with single or bicaval venous cannulation. Myocardial protection was achieved by a combination of antegrade and retrograde cold blood cardioplegia. Either a mechanical or bioprosthetic aortic valve was implanted in the supra-annular position. The distal anastomosis of bypass grafts was performed before implantation of the aortic prosthesis. Particularly in CABG with only BITA, distal anastomosis was performed before initiation of CPB (off-pump technique). Other concomitant procedures included Cox-maze III in 5 patients (4.3%).

Statistical analyses

Continuous variables were expressed as means±standard deviations. Categorical variables were expressed as proportions. For further analysis, patients were separated into 2 groups based on BITA or SITA grafting. The chi-square test (Pearson chi-square and the Fisher exact tests) for categorical variables and the Student t-test or Wilcoxon signed-rank test for continuous variables were used to compare data among the 2 groups. The log-rank test was used to compare postoperative morbidities and mortality. The Kaplan-Meier method was used for survival analysis. Cox regression analysis was used to identify significant predictors of mortality. The preoperative variables were initially analyzed using univariable Cox regression, and a multivariable Cox hazard model was made by selecting variables that had a p-value of <0.05 and clinical significance. Results are presented as hazard ratios (HRs) and 95% confidence intervals (CIs). Statistical significance for all analyses was accepted at a p-value less than 0.05. Statistical analyses were performed using R Statistical Software ver. 4.2.0 (R Foundation for Statistical Computing, Vienna, Austria).

Ethics statement

This study was approved by the Institutional Review Board of Samsung Medical Center (IRB approval no., 2015-06-172). The requirement for informed consent from individual patients was omitted because of the retrospective design of this study.

Results

The mean patient age was 69.4±7.6 years, and 41 patients were women (36%). Triple-vessel CAD was present in 65 patients (57%), recent myocardial infarction in 12 patients (11%), the mean preoperative left ventricle ejection fraction was 54.3%±13.4%, and the mean additive EuroScore was 7.9±3.0. Comparisons of preoperative clinical characteristics between the 2 groups are shown in Table 1. The SITA group had a significantly higher prevalence of preoperative atrial fibrillation than the BITA group. Otherwise, there were no significant differences between the 2 groups. The operative data of patients with atrial fibrillation are presented in the Supplementary Table 1.

Mechanical AVR was performed in 24 patients (21.0%). The mean aortic cross-clamp (ACC) time and CPB time were 116.5±40.3 minutes and 169.5±80.5 minutes, respectively. The mean ACC time and CPB time were longer in the SITA group than in the BITA group. The number of anastomosis sites was 3.03±1.09 in the SITA group and 3.55±1.10 in the BITA group (p=0.03). Otherwise, there were no significant differences between the 2 groups (Table 2).

Table 3 shows postoperative complications and mortality results in both groups. Deep sternal wound infection, stroke, renal failure requiring dialysis, bleeding requiring reoperation, low cardiac output syndrome, and prolonged ventilation were not different between the 2 groups. The intensive care unit stay was significantly shorter in the BITA group than in the SITA group, but the total hospital stay was not significantly different between the 2 groups.

Table 1. Preoperative clinical characteristics

Characteristic	Single ITA (N=40)	Bilateral ITA (N=74)	p-value
Age (yr)	70.7±8.6	68.7±6.9	0.20
Female	18 (45.0)	23 (31.1)	0.20
Triple-vessel CAD	19 (47.5)	46 (62.2)	0.19
Unstable angina	9 (22.5)	25 (33.8)	0.30
Recent MI (<21 day)	6 (15.0)	6 (8.1)	0.41
Aortic stenosis	34 (85.0)	66 (89.0)	0.73
Diabetes mellitus	18 (45.0)	38 (43.2)	0.65
Hypertension	30 (75.0)	54 (73.0)	0.99
Dyslipidemia	17 (42.5)	23 (31.1)	0.31
Carotid stenosis	18 (45.0)	29 (39.2)	0.69
COPD	4 (10.0)	8 (11.0)	1.0
Stroke	7 (17.5)	15 (20.3)	0.91
Renal failure	3 (7.5)	6 (8.1)	1.0
Atrial fibrillation	7 (17.5)	2 (2.7)	0.02
Previous PCI	5 (12.5)	4 (5.4)	0.74
NYHA class 3 or 4	11 (27.5)	13 (17.6)	0.32
Preoperative IABP	2 (5.0)	1 (1.4)	0.58
Emergency operation	2 (5.0)	3 (4.1)	1.0
LVEF (%)	56.4±14.4	53.2±12.7	0.22
Additive EuroScore	8.5±3.6	7.6±2.6	0.18

Values are presented as mean±standard deviation or number (%).
ITA, internal thoracic artery; CAD, coronary artery disease; MI, myocardial infarction; COPD, chronic obstructive pulmonary disease; PCI, percutaneous coronary intervention; NYHA, New York Heart Association; IABP, intra–aortic balloon pump; LVEF, left ventricular ejection fraction; EuroScore, European System for Cardiac Operative Risk Evaluation.

Table 2. Operative data

Variable	Single ITA (N=40)	Bilateral ITA (N=74)	p-value
Mechanical AVR	8 (20.0)	16 (21.6)	0.84
Cox-maze III procedure	4 (10.0)	1 (1.4)	0.09
No. of vein grafts	1.3±0.7	0.3±0.4	<0.001
No. of anastomosis site	3.03±1.09	3.55±1.10	0.03
CPB time (min)	211.0±113.6	149.0±49.0	0.005
ACC time (min)	135.0±45.7	107.0±34.3	0.01
Postoperative EF (%)	52.0±14.6	51.7±11.3	0.90

Values are presented as number (%) or mean±standard deviation.
ITA, internal thoracic artery; AVR, aortic valve replacement; CPB, cardiopulmonary bypass; ACC, aortic cross-clamp; EF, ejection fraction.

Table 3. Postoperative morbidity and mortality

Complication	Single ITA (N=40)	Bilateral ITA (N=74)	p-value
Postoperative morbidity			
Deep sternal wound infection	1 (2.5)	3 (4.1)	0.69
Stroke	3 (7.5)	2 (2.7)	0.54
Renal failure (requiring dialysis)	5 (12.5)	3 (4.1)	0.09
Bleeding requiring reoperation	3 (7.5)	6 (8.1)	0.54
Low cardiac output syndrome	3 (7.5)	1 (1.4)	0.08
Prolonged ventilation >48 hr	7 (17.5)	4 (5.4)	0.08
Intensive care unit stay (hr)	135.7±165.8	87.6±125.3	0.04
In-hospital stay (day)	18.32±20.0	22.04±78.0	0.46
Early death	4 (10.0)	2 (2.7)	0.09
Late death	13 (32.5)	20 (28.9)	0.40

Values are presented as number (%) or mean±standard deviation.
ITA, internal thoracic artery.

There were 6 (5.2%) early and 33 (28.9%) late deaths. There were more early deaths in the SITA group than in the BITA group, but this difference was not statistically significant. Kaplan-Meier survival curve analysis revealed that the 5-year survival rates of the SITA and BITA groups were 68.3% and 83.1%, respectively (p=0.15). The overall survival in the BITA group was similar to that in the SITA group (Fig. 1). In the multivariable analysis, mean age was an independent predictor of death (p=0.042). However, the use of BITA was not an independent predictor of survival (p=0.094) (Table 4).

There were 83 patients (73%) whose preoperative ejection fraction was >45%. Thirty-two patients had CABG with SITA and 51 patients had CABG with BITA (Supplementary Table 2). In those with an ejection fraction >45%, the overall survival rate in the BITA group was higher compared to the SITA group (p=0.043) (Fig. 2). Fifty-eight patients (51%) did not have diabetes mellitus (Supplementary Table 3). Twenty-two patients had CABG with SITA and 36 patients had CABG with BITA. In patients who did not have diabetes mellitus, the overall survival rate in the BITA group was not significantly higher than in the SITA group (p=0.07) (Fig. 3).

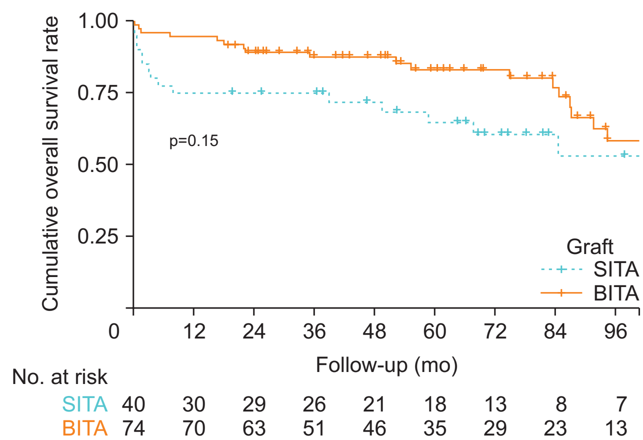

Fig. 1. Cumulative overall survival of concomitant aortic valve replacement and coronary artery bypass grafting in patients with bilateral internal thoracic artery (BITA) or single internal thoracic artery (SITA) grafts. A p-value represents the difference between the cumulative survival of the 2 groups over the 10-year study period.

Discussion

The impact of BITA on long-term survival after CABG is well known [1-3]. Current guidelines for CABG recommend using BITA in young patients [4,5]. However, BITA grafts are only used in 30% of CABG patients in Japan, 10% in Europe, and 4% in the United States [9,10]. Furthermore, even fewer surgeons use BITA in concomitant AVR and CABG than in CABG only. This is likely due to the fact that patients with both AS and multi-vessel CAD may have a shorter life expectancy than those with AS or multi-vessel CAD alone. The use of BITA may prolong surgery and increase the risk of sternal wound infection [7]. However, our group has been aggressive in using BITA in CABG patients, including those patients requiring concomitant valve surgery.

Some authors have advocated for BITA during CABG, even in elderly patients [11,12]. Many studies have reported that the postoperative morbidity and mortality of CABG using BITA were comparable to those of CABG using SITA. Currently accepted relative contraindications for BITA use are morbid obesity, uncontrolled diabetes, and chronic pulmonary obstructive disease [12-14]. We always harvest the ITA in a skeletonized fashion. In this study, the risk of surgical complications, including deep sternal wound infection, was not significantly higher in the BITA

Table 4. Univariable and multivariable analyses of predictors of survival

Variable	Univariable analysis	Multivariable analysis	
	p-value	HR (95% CI)	p-value
Mean age (yr)	0.000	1.063 (0.940–1.002)	0.042
Female	0.314	-	-
Triple-vessel CAD	0.413	-	-
Unstable angina	0.279	-	-
Recent MI (<21 day)	0.023	-	-
Aortic stenosis	0.274	-	-
Diabetes mellitus	0.011	-	-
Hypertension	0.185		
Dyslipidemia	0.199	-	-
Carotid stenosis	0.376	-	-
COPD	0.870	-	-
Stroke	0.795	-	-
Renal failure	0.039	-	-
Atrial fibrillation	0.114	-	-
Previous PCI	0.062	-	-
NYHA class 3 or 4	0.324	-	-
Preoperative IABP	0.000		
Emergency operation	0.013	-	-
Mechanical AVR	0.003	0.162 (0.123–1.420)	0.162
LVEF	0.225	-	-
Bilateral ITA	0.157	0.565 (0.290–1.101)	0.094

HR, hazard ratio; CI, confidence interval; CAD, coronary artery disease; MI, myocardial infarction; COPD, chronic obstructive pulmonary disease; PCI, percutaneous coronary intervention; NYHA, New York Heart Association; IABP, intra–aortic balloon pump; AVR, aortic valve replacement; LVEF, left ventricular ejection fraction; ITA, internal thoracic artery.

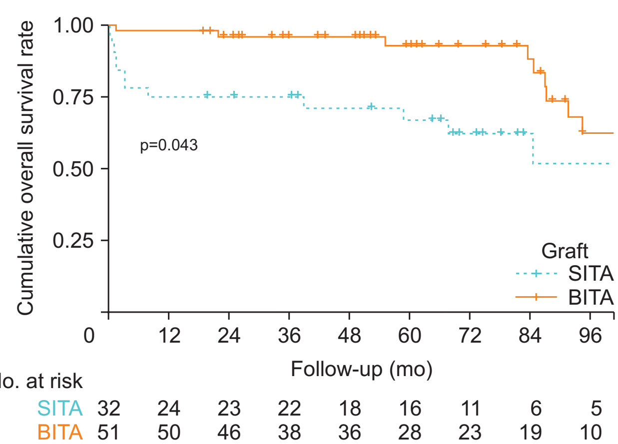

Fig. 2. Cumulative overall survival of concomitant aortic valve replacement and coronary artery bypass grafting in patients who had an ejection fraction >45% with bilateral internal thoracic artery (BITA) or single internal thoracic artery (SITA) grafts. A p-value represents the difference between the cumulative survival of the 2 groups over the 10-year study period.

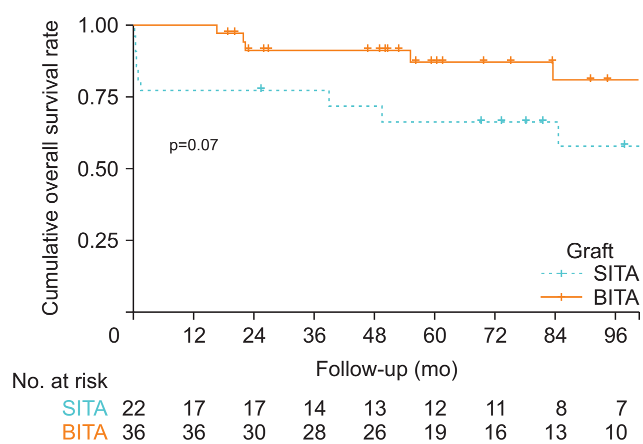

Fig. 3. Cumulative overall survival of concomitant aortic valve replacement and coronary artery bypass grafting in patients who did not have diabetes mellitus with bilateral internal thoracic artery (BITA) or single internal thoracic artery (SITA) grafts. A p-value represents the difference between the cumulative survival of the 2 groups over the 10-year study period.

group than in the SITA group. However, BITA was not a predictor of long-term survival in this study. We think that this may have been due to the inclusion of many patients who had multiple comorbidities. However, in low-risk subgroups, such as patients with preserved systolic function or patients without diabetes, the use of BITA was a significant predictor of long-term survival. Therefore, we believe that patients who have both aortic valve disease and multi-vessel CAD with a reasonably long life expectancy should be considered as candidates for CABG with BITA.

CABG with BITA can prolong surgery because right and left ITA harvesting cannot be done at the same time. Furthermore, an ITA graft is a smaller graft than a saphenous vein graft. Therefore, the time for anastomosis is longer than required for a saphenous vein. Although the entire surgical procedure time is important, the time required for CPB and ACC is more important than the complete procedure time. We performed distal anastomosis with an off-pump technique to reduce the time required for CPB and ACC. We believe this is particularly useful for concomitant valve surgery and CABG using BITA. In addition, in CABG with BITA, a composite graft was made on the left ITA, an *in situ* graft, and it was used without proximal anastomosis. This can be expected to help reduce complications in patients in whom proximal anastomosis is difficult due to calcification of the aortic wall when using a free graft.

Our study had several limitations. First, it was a retrospective analysis of observationally collected data and there might therefore have been selection bias in choosing BITA or SITA. Furthermore, the 2 groups had different degrees of heterogeneity. To address this, we performed a multivariable analysis to adjust for the heterogeneity of the groups. Second, the timing of the distal anastomosis depended on the type of graft used during surgery. It is thought that research using the same surgical method, regardless of the type of graft, is needed. Third, our study results do not support the routine use of BITA in patients with both aortic valvulopathy and multi-vessel CAD. However, our results show, at the very least, non-inferiority of concomitant AVR and CABG with BITA compared to concomitant AVR and CABG with SITA. Fourth, the small number of patients and the relatively short follow-up limited the statistical power. To fully understand the long-term effects of BITA, a larger study population and long-term follow-up are needed.

In conclusion, concomitant AVR and CABG with BITA did not increase postoperative complications or mortality compared to SITA use. The use of BITA may improve long-term survival in low-risk patients. Therefore, BITA use in patients with aortic valve disease and multi-vessel CAD can be a viable option if life expectancy is not expected to be limited.

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Conceptualization: YHC. Data curation: MYK. Formal analysis: MYK. Methodology: MH, MYK, YHC. Writing–original draft: MH, MYK. Writing–review & editing: all authors. Final approval of the manuscript: all authors.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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Supplementary materials

Supplementary materials can be found via https://doi.org/10.5090/jcs.22.122. **Supplementary Table 1**. Operative data of patients with atrial fibrillation. **Supplementary Table 2**. Preoperative clinical characteristics of subgroup (EF >45%). **Supplementary Table 3**. Preoperative clinical characteristics of subgroup (non-DM group).

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