Survival Benefit of Exclusive Use of In Situ Arterial Conduits Over Combined Use of Arterial and Vein Grafts for Multiple Coronary Artery Bypass Grafting

Hiroshi Nishida, MD; Yasuko Tomizawa, MD; Masahiro Endo, MD; Hiromi Kurosawa, MD

Background—The purpose of this study was to evaluate mortality after coronary artery bypass grafting (CABG) comparing the use of only in situ arterial grafts with the use of arterial and venous conduits.

Methods and Results—From April 1985 to March 1999, 1159 patients with multivessel disease underwent elective, isolated, primary, multiple CABG with at least one in situ arterial conduit. Patients who were on chronic dialysis, had active malignant disease, or had free arterial conduits were excluded. The long-term results were compared between 532 patients who had CABG using only in situ arterial conduits (group A; mean follow-up, 7.8 years) and 627 patients who underwent CABG using in situ arterial conduits and saphenous vein grafts (group B; mean follow-up, 10.3 years). Actuarial survival and freedom from cardiac death were determined by the Kaplan-Meier method. Propensity score was included in the Cox multivariable regression model for adjustment of selection bias. Survival at 10 years after surgery was 81.4% in group A and 76.9% in group B (P=0.11). Freedom from cardiac death at 10 years was 93.4% in group A and 90.4% in group B. Hazard ratio for cardiac death was significantly lower in group A (0.61; 95% confidence interval, 0.38 to 1.00; P=0.05).

Conclusions—Our data suggest that the exclusive use of in situ arterial grafts in CABG achieves significantly better long-term survival compared with combined use of arterial and vein grafts. (Circulation. 2005;112[supp I]:I-299–I-303)

Key Words: arteries ▪ surgery ▪ grafting ▪ coronary ▪ bypass
TABLE 1. Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, % female</td>
<td>12</td>
<td>18</td>
<td>0.0058</td>
</tr>
<tr>
<td>Age, y</td>
<td>60.7±9.7</td>
<td>60.7±9.0</td>
<td>0.9860</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>65.6</td>
<td>64.4</td>
<td>0.6780</td>
</tr>
<tr>
<td>Hyperlipidemia, %</td>
<td>76.5</td>
<td>73.1</td>
<td>0.1776</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>47.4</td>
<td>37.0</td>
<td>0.0004</td>
</tr>
<tr>
<td>Smoking, %</td>
<td>76.7</td>
<td>73.4</td>
<td>0.1931</td>
</tr>
<tr>
<td>Double/Triple/LMT, n</td>
<td>157/297/78</td>
<td>118/375/134</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Previous MI, %</td>
<td>65.0</td>
<td>62.8</td>
<td>0.1931</td>
</tr>
<tr>
<td>BMI &lt;25, %</td>
<td>64.7</td>
<td>53.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BSA ≥1.60 m², %</td>
<td>74.1</td>
<td>63.6</td>
<td>0.0001</td>
</tr>
<tr>
<td>LVEF</td>
<td>51.3±13.0</td>
<td>53.7±14.6</td>
<td>0.004</td>
</tr>
<tr>
<td>LVEF &lt;35, %</td>
<td>11.5</td>
<td>11.8</td>
<td>0.85</td>
</tr>
</tbody>
</table>

LMT indicates left main trunk lesion; MI, myocardial infarction; BMI, body mass index; BSA, body surface area; and LVEF, left ventricular ejection fraction.

CABG with at least 1 in situ arterial conduit. The in situ arterial grafts included the left and right internal thoracic arteries (LITA and RITA) and the right gastroepiploic artery (RGEA). Patients who were on long-term dialysis, had active malignant disease, or had free arterial conduits were excluded. Of the 1159 patients, 532 underwent CABG using only in situ arterial conduits (group A) and 627 patients underwent CABG using in situ arterial conduits and saphenous vein grafts (group B). During the study period, surgical techniques,2,3,6 including harvesting and preservation of graft material, were consistent.

Our criteria for the use of an all-arterial graft are as follows.3 We aim for complete arterial grafting with exclusive use of in situ arterial conduits whenever possible anatomically. Anatomic consideration includes the relationship between the target coronary artery and the reach of each in situ arterial conduit, and the relationship between the degree of the proximal stenosis and the size of the in situ arterial conduits. The only limiting factors are too small a graft size, too mild a proximal stenosis, and the impossibility of proper design of graft placement. The presence of diabetes mellitus, advanced age, or left ventricular dysfunction is not thought to be a contraindication for this approach.

Grafts were selected on the basis of the in situ arterial graft size. Preoperative angiography for ITA and RGEA graft selection was performed routinely at the end of diagnostic coronary angiography at our institution. Isosorbide dinitrate was routinely administered as a vasodilator at angiographic examination. Briefly, an angiogram was performed unilaterally on the LITA, and the distal diameter of the ITA was measured at the level of the sixth intercostal space because the sizes of RITA and LITA at this position are recognized to be almost the same. The distal diameter of the RGEA was measured at approximately two thirds of the way along the greater curvature of the stomach. The use of small grafts was avoided, and the lower limit was a distal diameter of 1.6 mm for the ITA and 1.7 mm for RGEA.

Comparing the baseline patient characteristics (Table 1), the mean age was similar in both groups. Compared with group B, group A had fewer female patients (P=0.0058), a higher proportion of diabetic patients (P=0.0004), and a lower frequency of triple-vessel disease and left main trunk disease (P<0.0001). Mean left ventricular ejection fraction (LVEF) was significantly lower in group A (P=0.004), but the proportion of patients with left ventricular dysfunction (LVEF <35%) was similar between groups (11.5% [61 of 532] in group A and 11.8% [74 of 627] in group B). Mild obesity was significantly more prevalent in group A (P<0.0001), and body size was significantly larger in group A as well. These facts support the hypothesis that arterial graft size is proportional to body size to some extent. The proportions of patients with hypertension, hyperlipidemia, smoking history, and previous myocardial infarction were not significantly different between the 2 groups.

TABLE 2. Major Graft Combinations

<table>
<thead>
<tr>
<th>Group A (n=532)</th>
<th>Group B (n=627)</th>
</tr>
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<tbody>
<tr>
<td>LITA sequential only</td>
<td>8 (2%)</td>
</tr>
<tr>
<td>LITA and RITA</td>
<td>185 (35%)</td>
</tr>
<tr>
<td>LITA and RGEA</td>
<td>159 (30%)</td>
</tr>
<tr>
<td>LITA and RITA &amp; RGEA</td>
<td>178 (33%)</td>
</tr>
<tr>
<td>RITA and RGEA</td>
<td>2 (0.3%)</td>
</tr>
</tbody>
</table>

LITA indicates left internal thoracic artery; RITA, right internal thoracic artery; RGEA, right gastroepiploic artery.

Surgical Procedures
We have consistently used the skeletonization technique since 1970 in the dissection of the ITA.2,3,6 The RGEA is isolated from the stomach by ligation of individual branches and surrounding adipose tissues with 4-0 nylon or 3-0 nylon sutures. Hemoclips and staples were not used during dissection.

The mean number of distal anastomoses per patient was 2.39 ±0.66 in group A and was significantly less than 2.82 ±0.76 in group B (P<0.001). This difference may be partly due to a lower frequency of triple-vessel disease in group A (Table 1). The major graft combinations are summarized in Table 2. In group A, combinations of bilateral ITAs, LITA, and RGEA, as well as 3 as arterial conduits were used at almost equal frequencies (33%). In group B, the combination of ITA and venous conduits was used in 74% of the cases. Sequential arterial grafting was performed in 24% of group A and in 11% of group B patients.

Early Result Assessment
Hospital mortality was assessed as early result. Hospital mortality included not only death within 30 days after operation, but also any death that occurred before discharge from hospital (mean, 30.7 days; range, 0 to 138 days after operation).

Late Result Assessment
Follow-up was conducted annually in June according to a standardized protocol. Charts of patients who were followed-up at our hospital were thoroughly reviewed, whereas survey sheets were mailed to the other patients. When there was no reply, we attempted to contact either the patient or the contact person registered in the chart or database by telephone. When all these efforts failed, survival was confirmed at the City Office of the patient’s latest mailing address, after obtaining permission from the Ministry of Justice. The rate of complete postoperative follow-up was 98.3% (523 of 532 patients) in group A and 98.7% (619 of 627 patients) in group B, and the follow-up period averaged 7.8 years in group A and 10.3 years in group B. Late death was defined as any death that occurred after discharge from hospital.

End Point Measures
All-cause death and cardiac death were measured as end points. All-cause death indicated death resulting from any cause. Cardiac death was restricted to death from myocardial infarction, arrhythmia, heart failure, or sudden death. All sudden deaths were classified as cardiac death except when the cause was clearly noncardiac, such as stroke. The date of censoring was the date of closure of annual follow-up for living patients, the date of repeat CABG for patients who underwent repeat CABG during follow-up, and the last date of survival confirmation for patients lost to follow-up. For calculation of cardiac death-free rate, the date of non-cardiac death was the date of censoring.

Statistical Analysis
The analyses were performed with the SAS System (SAS Institute Inc.). The data are presented as frequency or mean ± standard deviation. Characteristics of the patient groups were compared by χ² test.
or Fisher’s exact probability test for the comparison of dichotomous variables. Unadjusted long-term survival curves were estimated by the Kaplan-Meier method, and univariate comparison between 2 curves was assessed by the Cox-Mantel method.

To determine the effects of various predictors and operative mode, multivariate Cox proportional hazard model analysis and propensity score-matched multivariate analysis were performed. All-cause death and cardiac death were used as dependent variables. As independent variables, we examined the operative modality (group A versus group B) and various independent covariates including sex (male versus female), age (continuous), hypertension (yes versus no), hyperlipidemia (yes versus no), diabetes (yes versus no), smoking habit (yes versus no), number of diseased vessel (double, triple, left main trunk), previous myocardial infarction (yes versus no), body mass index (25< versus ≥25 kg/m²), body surface area (1.60< versus ≥1.60 m²), and left ventricular ejection fraction (40< versus ≥40%). In the calculation of propensity score, we used the above-mentioned covariates except for operative modality. After calculating the propensity scores, we stratified each group according to the propensity score and performed Cox analysis for each stratum using operation groups and propensity score as covariates. Two-tailed values of $P<0.05$ were considered to indicate statistical significance.

Results

Early Result

There were 4 hospital deaths (0.8%: 1 sudden cardiopulmonary arrest, 1 low cardiac output, 1 multiorgan failure, 1 healthcare-associated Staphylococcus aureus infection) in group A, and 10 hospital deaths (1.6%: 1 paralysis of bilateral phrenic nerves, 1 coronary spasm, 2 ventricular fibrillation, 2 respiratory failure, 1 massive bleeding from respiratory tract, 1 bleeding caused by removal of drainage tube by himself due to intensive care unit syndrome) in group B. The difference was not statistically significant ($P=0.19$).

Late Result

After discharge from the hospital, there were 29 cardiac deaths (0.70% per patient-year), including 7 sudden deaths (0.17% per patient-year) and 51 noncardiac deaths (1.23% per patient-year) in group A. In group B, there were 70 cardiac deaths (1.08% per patient-year), including 24 sudden deaths (0.37% per patient-year) and 101 noncardiac deaths (1.55% per patient-year).

Survival Rate Calculated With Kaplan-Meier Method

Actuarial all-cause death-free curve and freedom from cardiac death including early death were determined by the Kaplan-Meier method. The all-cause death-free rate at 10 years after surgery was 81.4% in group A and 76.9% in group B (Figure 1). Cardiac death-free rate at 10 years was 93.4% in group A and 90.4% in group B (Figure 2).

Univariate Analyses

Comparing the all-cause death-free rate between group A and group B, the probability value of univariate analysis calculated by the Cox-Mantel method was 0.07. For the cardiac death-free rate, the probability value calculated by the Cox-Mantel method was also 0.07.

Cox Proportional Hazard Model

Multivariate Cox proportional-hazard model analysis was used to calculate hazard ratios (HR) with 95% confidence intervals (CIs) for all-cause death (Table 3) and cardiac death (Table 4).

The hazard ratios in group B for all-cause death (early and late) (versus group A: HR, 1.39; 95% CI, 1.03 to 1.89; $P=0.028$), older age (HR, 1.04; 95% CI, 1.03 to 1.06; $P<0.001$), lower body mass index (HR, 1.45; 95% CI, 1.09 to 1.92; $P=0.012$), and left ventricular ejection fraction less than 40% (HR; 2.33, 95% CI, 1.69 to 3.13, $P<0.001$) were significantly higher than in group A.

The hazard ratios in group B for cardiac death (early and late) (versus group A: HR, 1.64; 95% CI, 1.01 to 2.70; $P=0.047$) and left ventricular ejection fraction less than 40% (HR; 4.35, 95% CI, 2.70 to 7.14, $P<0.001$) were higher than in group A. Small body surface area was almost a significant predictor of a higher cardiac death-free rate (HR, 1.69; 95% CI, 0.99 to 2.86; $P=0.054$).
TABLE 3. Simple Cox Analysis: Independent Risk Factors for All-Cause Death

<table>
<thead>
<tr>
<th></th>
<th>P Value</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group B</td>
<td>0.028</td>
<td>1.39</td>
<td>1.03–1.89</td>
</tr>
<tr>
<td>Sex, female</td>
<td>0.75</td>
<td>0.93</td>
<td>0.57–1.45</td>
</tr>
<tr>
<td>Age</td>
<td>&lt;0.001</td>
<td>1.04</td>
<td>1.03–1.06</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.793</td>
<td>1.04</td>
<td>0.78–1.39</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>0.558</td>
<td>0.91</td>
<td>0.67–1.24</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.081</td>
<td>1.28</td>
<td>0.97–1.70</td>
</tr>
<tr>
<td>Smoking</td>
<td>0.203</td>
<td>1.27</td>
<td>0.88–1.84</td>
</tr>
<tr>
<td>Triple vessel or LMT</td>
<td>0.158</td>
<td>1.17</td>
<td>0.94–1.47</td>
</tr>
<tr>
<td>Old MI</td>
<td>0.162</td>
<td>1.27</td>
<td>0.91–1.77</td>
</tr>
<tr>
<td>BMI (&lt;25)</td>
<td>0.012</td>
<td>1.45</td>
<td>1.09–1.92</td>
</tr>
<tr>
<td>BSA (&lt;1.60 m²)</td>
<td>0.920</td>
<td>1.02</td>
<td>0.72–1.44</td>
</tr>
<tr>
<td>LVEF (&lt;40%)</td>
<td>&lt;0.001</td>
<td>2.33</td>
<td>1.69–3.13</td>
</tr>
</tbody>
</table>

LMT indicates left main trunk lesion; MI, myocardial infarction; BMI, body mass index; BSA, body surface area; LVEF, left ventricular ejection fraction.

Propensity Score-Matched Multivariate Analysis

In the multivariate analysis using the Cox model with propensity score matching, the HR for all-cause death (early and late) was not significantly higher in group B (HR, 1.28; 95% CI, 0.95 to 1.72; P=0.108). The hazard ratio for cardiac death (early and late) was almost significantly higher in group B (HR, 1.64; 95% CI, 1.00 to 2.63; P=0.053).

Discussion

The present study demonstrated the advantage of all-arterial grafting with in situ arterial conduits over mixed usage of arterial and venous grafts in terms of better cardiac survival. Taking into account the present findings and our previous results,2,3,6 we now confidently perform all-arterial CABG as the routine technique whenever possible, even in off-pump surgery.

In 1986, Loop et al7 first described the beneficial impact of single ITA grafting to the left anterior descending artery (LAD) over saphenous vein grafting in terms of long-term survival and freedom from cardiac events. Since the 1990s, several reports,1,8 including ours,2,6 demonstrated the clinical advantage of bilateral ITA grafting over single ITA grafting. Furthermore, 2 recent meta-analyses have clearly shown better survival in the bilateral ITA group versus the single ITA group.4,5 In another words, these reported findings of “more arterial grafts, better long-term results” indicate a disadvantage to using the saphenous vein in CABG in the long term. In the recent PCI era, almost all CABG patients have triple-vessel disease with or without left main lesion and thus require multiple bypass. Therefore, if the saphenous vein graft is avoided, even use of bilateral ITAs is not adequate to revascularize 3 major coronary regions; the LAD, left circumflex, and right coronary regions. To overcome this limitation of bilateral ITA usage, the following 3 approaches have been proposed.

First, use of various types of composite graft is proposed.9 In addition to the incidental evidence suggesting incomplete relief of ischemia after T-grafting,10 however, Legare et al11 demonstrated that composite arterial grafting may be associated with an increase in risk-adjusted patient morbidity when compared with conventional artery bypass grafting in 498 propensity score-matched case analyses, although a difference in mortality was not demonstrable. Therefore, in situ arterial grafts should be used as-is rather than as a free graft. In this report, we excluded the patients who received free arterial conduits to eliminate the possible effect of composite graft comprising originally in situ arterial conduit and radial artery graft.

The second proposal is a sequential bypass technique to increase distal anastomoses with one in situ arterial conduit. Ochi et al12 demonstrated excellent early and mid-term results of sequential grafting with the ITA and RGEA. Ishida et al13 reported that although sequential bypass grafting with RGEA is feasible with excellent early and long-term results, careful anatomical consideration of both the RGEA graft size and the degree of proximal coronary stenosis is necessary. Furthermore, revascularization of 2 or more independent coronary artery regions, such as the LAD and left circumflex regions, is not desirable from the standpoint of diversification of risk.

The third proposal is to use a third in situ arterial conduit, the RGEA, in addition to bilateral ITAs. We14 and others14,15 have reported that CABG with exclusive use of 3 in situ arterial conduits is technically feasible and associated with excellent long-term results. We set no contraindication to the usage of in situ arterial conduits except graft size. The size of the RGEA is critical, especially when the degree of proximal stenosis is less than 90%.16 From the anatomical relationship of each in situ arterial conduit and coronary artery, bilateral ITAs are the conduits of choice for the left coronary artery regions such as the LAD and left circumflex artery. The RGEA is the graft conduit for the right coronary artery, as long as the relationship between RGEA size and proximal stenosis of the target lesion is acceptable. If the RGEA is inappropriate, either the radial artery or the saphenous vein is indicated.

There are several limitations of this study. First, the probability value for cardiac death is 0.05 and barely significant. Longer follow-up and a larger number of cases are
necessary to obtain definitive results. Second, in contrast to the Cox hazard model in which confounding factors become a serious problem as the number of covariates increases, multivariate analysis with propensity score matching corrects the selection bias, and inclusion of more covariates is better for this method. We shall expand the propensity score-matched analysis by including extensive covariates, such as predialysis chronic renal failure, calcified aorta, and peripheral vascular disease, for the data in this report and also our previous studies.2,3,6

In conclusion, the results of this propensity score-matched multivariate analysis indicate that the exclusive use of in situ arterial conduits in CABG provides better long-term cardiac survival than CABG using a combination of saphenous vein graft and in situ arterial conduits. Therefore, our findings clearly support total in situ arterial coronary artery bypass grafting without the saphenous vein in selected patients with multivessel disease.

Acknowledgments
We are grateful to both Dr Teresa Nakatani for assistance in preparing the manuscript and Etsuko Yoshida, MS, for assistance in statistical analyses.

References
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Circulation. 2005;112:I-299-I-303
doi: 10.1161/CIRCULATIONAHA.104.524074

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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