Table 4
Risk of long-term mortality according to multivariate analysis

| Variable | HR | 95% CI |
|---|---|---|
| Age ≥65 years | 2.65 | 2.36–2.99 |
| Women | 1.06 | 0.94–1.18 |
| Body mass index ≥25 kg/m² | 0.68 | 0.60–0.76 |
| Previous myocardial infarction | 1.18 | 1.06–1.31 |
| History of heart failure | 2.07 | 1.83–2.35 |
| New York Heart Association class IV | 1.21 | 1.01–1.46 |
| Peripheral vascular disease | 1.54 | 1.37–1.74 |
| Renal function | | |
| Serum creatinine ≤179 μmol/L | 1.00 | — |
| Serum creatinine >179 μmol/L | 2.28 | 1.97–2.65 |
| Hemodialysis | 5.20 | 4.36–6.20 |
| Hypertension | 1.23 | 1.09–1.39 |
| Diabetes mellitus | 1.35 | 1.22–1.50 |
| Hyperlipidemia | 0.72 | 0.65–0.80 |
| Family history of coronary artery disease | 0.86 | 0.76–0.97 |
| Smoking | 1.17 | 1.05–1.30 |
| No. of diseased vessels: | | |
| 1 Vessel | 1.00 | — |
| 2 Vessels | 1.14 | 1.01–1.29 |
| 3 Vessels | 1.43 | 1.24–1.64 |
| United States patients | 1.71 | 1.50–1.95 |

Abbreviations as in Table 3.

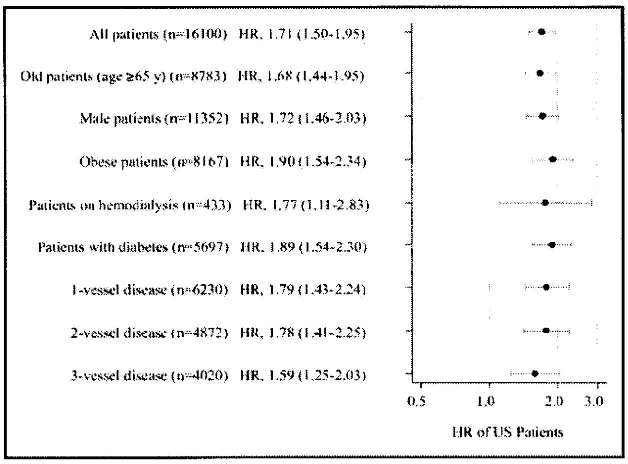


Figure 4. Multivariate analysis with hazard ratio and 95% confidence intervals for long-term mortality in US versus Japanese patients according to patient subgroup.

tively). Figure 2 shows the Kaplan-Meier survival curves for each registry. The crude hazard ratio for the American patients was 1.02 (95% confidence interval 0.93 to 1.13; p = 0.65). This trend did not alter when survival was analyzed according to revascularization procedure (Figure 3).

Several significant predictors of mortality were identified (Table 3). The univariate model showed that the strongest predictors of mortality (p <0.001) in the Japanese group were age >65 years, body mass index >25 kg/m², a history of heart failure, the need for hemodialysis, and the presence of left circumflex artery disease. In the US group, the strongest predictors of mortality were age >65 years and variables associated with an atherosclerotic process, such as a history of MI, a history of heart failure, peripheral vascular disease, renal function, hemodialysis, hypertension, diabetes mellitus, hyperlipidemia, and a family history of CAD.

When the long-term mortality was adjusted for age and gender, the US patients had a significantly greater risk than the Japanese patients (hazard ratio 1.27, 95% confidence interval 1.15 to 1.40; p <0.001). Additional adjustment, using the other long-term predictors listed in the "Methods" section, revealed comparable results (hazard ratio 1.71, 95% confidence interval 1.50 to 1.95; p <0.001; Table 4). A similar trend was seen in all the high-risk subgroups (eg, age ≥65 years, male gender, obesity, use of hemodialysis, diabetes mellitus, multivessel disease; Figure 4).

## Discussion

We used information from 2 well-established registries, CREDO-Kyoto and THIRDBase, to compare the clinical characteristics and outcomes of patients undergoing coronary revascularization in Japan versus the US. The present study involved a large number of patients (>8,000), a high rate of clinical follow-up observation, and an excellent database infrastructure and support system. Although the long-term outcomes were similar with regard to crude mortality, they appeared to favor the Japanese patients after the results were adjusted for confounding factors, including age, gender, and atherosclerotic risk factors.

The 2 registries differed greatly with respect to patient clinical backgrounds. The Japanese patients were older, more likely to be smokers, and more likely to have diabetes mellitus. In contrast, the American patients were more obese and had a greater prevalence of atherosclerotic processes such as MI, peripheral vascular disease, renal insufficiency, and hypertension. This finding agrees with the results of a previous study that compared the risk factors for atherosclerosis among patients of different racial backgrounds.[7,8]

Although smoking is decreasing in the Asian population, this habit remains significantly more prevalent in Japan than in Western countries. The greater prevalence of diabetes mellitus in Japanese patients is in accordance with the rates of this disease recorded by other CAD registries in Japan.[9] However, the adverse cardiovascular events (eg, cardiovascular death or MI) remained extremely low in Japanese patients with diabetes, as shown by our subgroup analysis. In the recent Japanese Primary Prevention of Atherosclerosis with Aspirin for Diabetes (JPAD) study, in which 2,539 patients were followed up for 4.3 years, the overall atherosclerotic event rate in the nonaspirin group was only 17.0/1,000 person-years.[10] In the Western population, patients who have both CAD and diabetes have a poor long-term outcome, especially when multiple vessels are involved.

Our results agree with those from other registries, which have shown a difference in the incidence of CAD-related clinical events among patients living in different countries, highlighting the greater mortality rates in North American populations and lower mortality rates in the Japanese and Chinese populations.[11] The reasons for these differences are not clear. The Japanese lifestyle, especially the daily diet, is now fairly close to that of Europe and the US. However, a number of dietary differences remain—such as a high intake of fish and salt (Japan) versus red meat and sugar (US).

Moreover, patients in Japan versus the US vary considerably with regard to their degree of mixed racial backgrounds, education, workload, and access to medical facilities, and the 2 countries have considerably different social systems. A recent survey of Japanese rural and urban areas showed a decreasing CAD rate despite widespread pursuit of a Western lifestyle; the CAD-related mortality rate has remained approximately ¼ of that encountered in the US.[12] The incidence of CAD in urban men is 100/100,000 in Japan versus 272 to 491/100,000 in the US.[13,14] The better prognosis in Japanese patients has been attributed to differences in the pathogenesis of acute coronary syndromes. Moreover, we speculate that, in Japanese patients, the coronary lesion remains stable after treatment (this was true even in the bare metal stent era) and that atherosclerotic risk factors such as obesity, peripheral vascular disease, and renal failure, which were more prevalent in US patients, contributed more to late mortality than did age.

Given the technical success of PCI and CABG, the focus is now on the optimal use of these techniques to improve survival and reduce symptomatic heart disease. For the best patient care, the interventional cardiologist or cardiothoracic surgeon must be able to predict outcomes, including long-term mortality, and thus define the risks and benefits of revascularization procedures for specific patients. It has increasingly been recognized that nonangiographic variables are more important than angiographic variables in predicting long-term outcomes.[15] Currently, long-term mortality is largely predicted by clinical variables such as age and the presence of congestive heart failure. These variables have been combined into risk scores[3,4]; however, none of these risk scores has directly included ethnic background information. In the Japanese population, postprocedural mortality is significantly low, such as was shown in the present study, and risk–prediction models might not be directly applicable. Our results have also indicated that these predictors differ significantly between the 2 countries, and ethnic information might play a crucial role in predicting the long-term mortality of patients with CAD. Future research involving large-scale registries or clinical studies must take account of differences in outcomes between different regions in the world.

Our study was limited because statistical adjustments were made only for the characteristics that were obtainable from both registries. Conditions such as cerebrovascular disease, unstable angina, and chronic obstructive pulmonary disease were excluded from the multivariate analyses because of considerable differences in the definition of such diseases. In addition, more subtle, immeasurable variables were not taken into account. These variables included differences in physician attitudes and approaches to diagnosis, health policies, and social and cultural circumstances. Some of these factors could have had a substantial effect. However, we attempted to nullify the effects of potential confounding variables using a Cox proportional hazards regression model.

Another limitation of our study was that technologic advances could quickly outdate our findings. One such advance was the advent of drug-eluting stents, which dramatically reduced the need for repeat revascularization after stent placement. No clear-cut evidence, however, has yet shown that such stents improve survival.[16] Therefore, we can still draw valid inferences about comparative survival from populations that have bare metal stents.

Finally, other outcome variables such as major adverse cardiac events and cerebrovascular events were not assessed in THIRDBase; thus, our assessment of long-term outcomes was based solely on mortality. The ascertainment of mortality was also different in the 2 registries, and the median follow-up period differed significantly (Japan 3.5 years vs US 5.2 years; Wilcoxon rank sum test $p < 0.001$).

**Acknowledgment:** The authors thank Virginia Fairchild, MB, of the Texas Heart Institute Department of Scientific Publications, for editorial assistance in preparing this report.

### Supplementary Data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.amjcard.2010.01.349.

1. Carulli L, Rondinella S, Lombardini S, Canedi I, Loria P, Carulli N. Review article: diabetes, genetics and ethnicity. *Aliment Pharmacol Ther* 2005;22(Suppl 2):16–19.
2. Health: United States 2005 with Chartbook on Trends in the Health of Americans. Washington, DC: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics, 2005:62–63.
3. Anderson HV, Shaw RE, Brindis RG, McKay CR, Klein LW, Krone RJ, Ho KK, Rumsfeld JS, Smith SC Jr, Weintraub WS. Risk-adjusted mortality analysis of percutaneous coronary interventions by American College of Cardiology/American Heart Association guidelines recommendations. *Am J Cardiol* 2007;99:189–196.
4. Singh M, Gersh BJ, Li S, Rumsfeld JS, Spertus JA, O'Brien SM, Suri RM, Peterson ED. Mayo Clinic risk score for percutaneous coronary intervention predicts in-hospital mortality in patients undergoing coronary artery bypass graft surgery. *Circulation* 2008; 117:356–362.
5. Kimura T, Morimoto T, Furukawa Y, Nakagawa Y, Shizuta S, Ehara N, Taniguchi R, Doi T, Nishiyama K, Ozasa N, Saito N, Hoshino K, Mitsuoka H, Abe M, Toma M, Tamura T, Haruna Y, Imai Y, Teramukai S, Fukushima M, Kita T. Long-term outcomes of coronary-artery bypass graft surgery versus percutaneous coronary intervention for multivessel coronary artery disease in the bare-metal stent era. *Circulation* 2008;118:S199–S209.
6. Kohsaka S, Goto M, Virani S, Lee VV, Aoki N, Elayda MA, Reul RM, Wilson JM. Long-term clinical outcome of coronary artery stenting or coronary artery bypass grafting in patients with multiple-vessel disease. *J Thorac Cardiovasc Surg* 2008;136:500–506.
7. Hutchinson RG, Watson RL, Davis CE, Barnes R, Brown S, Romm F, Spencer JM, Tyroler HA, Wu K. Racial differences in risk factors for atherosclerosis: the ARIC study. Atherosclerosis Risk in Communities. *Angiology* 1997;48:279–290.
8. Kronmal RA, McClelland RL, Detrano R, Shea S, Lima JA, Cushman M, Bild DE, Burke GL. Risk factors for the progression of coronary artery calcification in asymptomatic subjects: results from the Multi-Ethnic Study of Atherosclerosis (MESA). *Circulation* 2007;115:2722–2230.
9. Motomura N, Miyata H, Tsukihara H, Okada M, Takamoto S. First report on 30-day and operative mortality in risk model of isolated coronary artery bypass grafting in Japan. *Ann Thorac Surg* 2008;86: 1866–1872.

10. Ogawa H, Nakayama M, Morimoto T, Uemura S, Kanauchi M, Doi N, Jinnouchi H, Sugiyama S, Saito Y; Japanese Primary Prevention of Atherosclerosis With Aspirin for Diabetes (JPAD) Trial Investigators. Low-dose aspirin for primary prevention of atherosclerotic events in patients with type 2 diabetes: a randomized controlled trial. *JAMA* 2008;300:2134–2141.
11. Tunstall-Pedoe H, Kuulasmaa K, Amouyel P, Arveiler D, Rajakangas AM, Pajak A. Myocardial infarction and coronary deaths in the World Health Organization MONICA project: registration procedures, event rates, and case-fatality rates in 38 populations from 21 countries in four continents. *Circulation* 1994;90:583–612.
12. Statistics and Information Department MsS, Ministry of Health, Labour and welfare. Vital Statistics of Japan 2003 (vol. 1) [Japanese]. Tokyo: Health and Welfare Statistics Association, 2005:1–358.
13. McGovern PG, Jacobs DR Jr, Shahar E, Arnett DK, Folsom AR, Blackburn H, Luepker RV. Trends in acute coronary heart disease mortality, morbidity, and medical care from 1985 through 1997: the Minnesota heart survey. *Circulation* 2001;104:19–24.
14. Rosamond WD, Folsom AR, Chambless LE, Wang CH. Coronary heart disease trends in four United States communities: the Atherosclerosis Risk in Communities (ARIC) study 1987–1996. *Int J Epidemiol* 2001;30(Suppl 1):S17–S22.
15. Cavender MA, Ohman EM. What do you need to know before performing a percutaneous coronary intervention? *Circulation* 2008;118: 609–611.
16. Malenka DJ, Kaplan AV, Lucas FL, Sharp SM, Skinner JS. Outcomes following coronary stenting in the era of bare-metal vs the era of drug-eluting stents. *JAMA* 2008;299:2868–2876.

# Increased Graft Occlusion or String Sign in Composite Arterial Grafting for Mildly Stenosed Target Vessels

Susumu Manabe, MD, Toshihiro Fukui, MD, Tomoki Shimokawa, MD, Minoru Tabata, MD, Yuzo Katayama, MD, Satoshi Morita, MD, PhD, and Shuichiro Takanashi, MD

Department of Cardiovascular Surgery, Sakakibara Heart Institute, and Department of Biostatistics and Epidemiology, Yokohama City University, Tokyo, Japan

*Background.* Composite grafting is a useful technique that avoids the need for aortic manipulation and enables a wide range of target vessels to be revascularized, effectively using the limited arterial grafts available. However, it has not been clarified whether composite grafting can achieve angiographic outcomes equivalent to those obtained with individual grafting for specific target vessels.

*Methods.* We retrospectively reviewed 830 distal arterial graft anastomoses in 256 patients who underwent off-pump coronary artery bypass surgery and also underwent 1-year follow-up coronary angiograms. Four hundred and ten anastomoses using a composite grafting technique were compared with 420 anastomoses using individual grafting.

*Results.* In target vessels with mild stenosis, the incidence of graft occlusion or string sign was significantly higher in composite internal thoracic arteries (ITA) than in individual ITA grafts (composite 20.3% versus individual 7.3%; $p = 0.018$) and showed a higher tendency in composite radial arteries (RA) than in individual RA grafts (59.3% versus 36.4%, $p = 0.09$). In contrast, the incidence was similar between composite and individual ITA grafts (5.7% versus 3.3%, $p = 0.278$) and composite and individual RA grafts (11.5% versus 29.6%, $p = 0.297$) in target vessels with severe stenosis.

*Conclusions.* The angiographic outcomes of composite grafts were closely related to the severity of stenosis of the target coronary artery. In target vessels with mild stenosis, composite grafting resulted in a higher incidence of graft occlusion or string sign than individual grafting did.

(Ann Thorac Surg 2010;89:683–8)


Modern coronary artery bypass graft surgery (CABG) involves several sophisticated procedures developed to handle particular problems or improve the quality of treatment. The aortic "no-touch" technique is considered effective for reducing stroke risk in patients with the atherosclerotic ascending aorta, and multiple arterial grafting is usually preferred because it provides excellent long-term clinical outcomes. Composite grafting plays a crucial role in these procedures, because it eliminates the need for proximal anastomosis to the ascending aorta and conserves extra lengths of an arterial graft for additional grafting.

Although the prevalence of composite grafting is increasing, there have been few studies to support the feasibility of performing composite grafting for a particular target coronary artery. Several studies reported that the clinical and angiographic results of composite grafting were equivalent to those of individual grafting [1–3]. Conversely, some other studies reported that composite grafting may be susceptible to the detrimental effect of flow competition with native coronary artery when used for a mildly stenosed target vessel [4, 5]. The difference in angiographic outcomes between composite and individual grafting in target vessels with mild stenosis has not been clarified. Hence, the purpose of this study was to compare the angiographic outcomes between composite and individual grafts according to the severity of stenosis of the target coronary artery.

## Material and Methods

### Study Design

This was a retrospective cohort study to verify the hypothesis that angiographic outcomes of composite grafts

Accepted for publication Nov 19, 2009.

Address correspondence to Dr Manabe, Department of Cardiovascular Surgery, Sakakibara Heart Institute, Asahicho 3-16-1, Fuchu, Tokyo 183-0003, Japan; e-mail: s-manabe@fb3.so-net.ne.jp.


Published by Elsevier Inc

0003-4975/10/$36.00
doi:10.1016/j.athoracsur.2009.11.053

*Table 1. Patient Characteristics*

| | Total n = 256 | Without Composite n = 108 | With Composite n = 148 | *p* Value* |
|---|---|---|---|---|
| Age, years | 66.3 ± 8.1 | 66.3 ± 8.1 | 66.6 ± 7.3 | 0.776 |
| Male (n) | 85.6% (219) | 85.2% (92) | 85.8% (127) | 1.000 |
| Coronary risk factor (n) | | | | |
| Hypertension | 69.9% (179) | 69.4% (75) | 70.3% (104) | 0.891 |
| Diabetes mellitus | 41.0% (105) | 35.2% (38) | 45.3% (67) | 0.123 |
| Hyperlipidemia | 63.7% (163) | 68.5% (74) | 60.1% (89) | 0.189 |
| Smoking | 57.0% (146) | 57.4% (62) | 56.8% (84) | 1.000 |
| Old cerebral infarction (n) | 7.4% (19) | 4.6% (5) | 9.5% (14) | 0.227 |
| PVD (n) | 6.3% (16) | 3.7% (4) | 8.1% (12) | 0.194 |
| Chronic hemodialysis (n) | 3.5% (9) | 1.9% (2) | 4.7% (7) | 0.310 |

* Comparison between patients with and without composite grafts.

PVD = peripheral vascular disease.

were inferior to those of individual grafts in target vessels with mild stenosis. One-year angiographic outcomes of arterial grafts were reviewed, and incidence of graft occlusion or string sign was compared between composite and individual grafts according to the severity of stenosis of the target coronary artery. Moreover, multivariate analysis was performed to identify the independent predictor of graft occlusion or string sign. The Ethics Committee of Sakakibara Heart Institute approved this study, waived the need for patient consent, and provided approval before the publication of the data.

### *Study Subjects and Data Collection*

Between September 2004 and July 2007, 536 patients underwent isolated CABG in our institute. All patients were scheduled for off-pump CABG. Six patients who were converted to an on-pump CABG were excluded from the study. We routinely performed coronary angiograms 1 year after surgery in patients who have undergone off-pump CABG, regardless of the patient's symptoms. Patients who died, refused angiographic evaluation, were more than 75 years old, or had renal dysfunction (serum creatinine > 1.2 mg/dL) were excluded from the angiographic follow-up. Of the 536 patients, 256 patients (47.8%) underwent 1-year follow-up angiograms and were retrospectively reviewed. Preoperative characteristics of the study patients are shown in Table 1.

In the 256 study patients, there were 1,050 distal anastomoses, an average of 4.1 per patient. Of these, 830 anastomoses were constructed with arterial grafts and 220 were constructed with saphenous vein. All composite grafts were constructed with arterial grafts. Anastomoses constructed with saphenous vein were excluded from the analysis. Among the 830 anastomoses using arterial grafts, 410 anastomoses were constructed with composite graft (composite group) and 420 anastomoses with individual graft (individual group). Both groups included sequential grafting. Graft material and location and stenosis of the target coronary artery are shown in Table 2. Composite grafts were made using an "I" configuration in 37 anastomoses and a "Y" configuration in 373 anastomoses.

One physician initially reviewed all the coronary angiograms, and a consensus was reached after review. For native coronary arteries, mild stenosis was defined as a stenotic lesion producing luminal narrowing of 75% or less, and severe stenosis as narrowing of more than 75%. Distal anastomoses were assessed and classified as patent, focally stenosed, string sign, or occluded. Focally stenosed was defined as a focal stenosis of 90% or greater anywhere within the conduit or at the anastomosis. String sign was defined as luminal narrowing throughout the entire conduit, including stenosis of 90% or more.

### *Operative Strategy*

The surgical procedures and principles of off-pump CABG we used have been previously described [6]. The left-sided coronary arteries were revascularized with arterial grafts in most cases. The left anterior descending artery (LAD) was revascularized exclusively using the

*Table 2. Graft Material and Location and Stenosis of Target Coronary Artery*

| | Composite n = 410 | Individual n = 420 | *p* Value |
|---|---|---|---|
| Graft material | | | <0.001 |
| ITA | 191 (46.6%) | 336 (80.0%) | |
| RA | 211 (51.5%) | 49 (11.7%) | |
| GEA | 8 (2.0%) | 35 (8.3%) | |
| Location of target coronary artery | | | <0.001 |
| LAD | 34 (8.3%) | 223 (53.1%) | |
| D | 127 (31.0%) | 51 (12.1%) | |
| LCX | 234 (57.1%) | 108 (25.7%) | |
| RCA | 15 (3.7%) | 38 (9.0%) | |
| Stenosis of target coronary artery | | | 0.021 |
| Mild, ≤ 75% | 153 (37.3%) | 125 (30.0%) | |
| Severe, > 75% | 257 (62.7%) | 295 (70.2%) | |

D = diagonal branch; GEA = gastroepiploic artery; ITA = internal thoracic artery; LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery; RA = radial artery; RCA = right coronary artery.

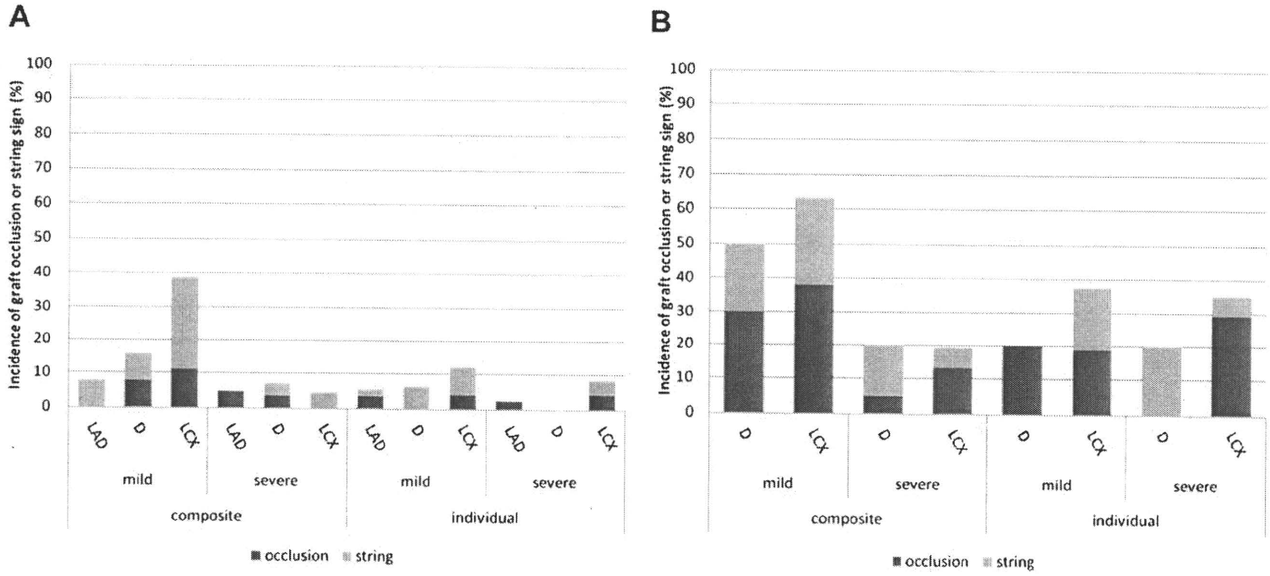


*Fig 1. The incidence (%) of graft occlusion (dark gray shaded bar) or string sign (light gray shaded bar) according to graft material or location of target coronary artery. (A) internal thoracic artery (ITA). (B) Radial artery (RA). (D = diagonal artery; LAD = left anterior descending artery; LCX = left circumflex artery.)*

internal thoracic artery (ITA), and the left ITA was preferably used. The right ITA was revascularized to the LAD only when the left ITA was required to bypass a remote anastomosis site of the left circumflex artery. The most frequently used arrangement for diagonal artery and left circumflex artery was composite grafting with right ITA and radial artery (RA). In this arrangement, the right ITA was used as an in-situ graft for the diagonal artery, and the RA was anastomosed proximally to the right ITA and distally to the left circumflex artery. The right coronary artery was grafted with saphenous vein or gastroepiploic artery in most cases. Use of the gastroepiploic artery was usually limited to patients with severe stenosis of the right coronary artery.

### *Statistical Analysis*

Categorical variables are reported as percentages. To compare categorical variables, the $\chi^2$ test was used to compare among three groups and the Fisher's exact test was used to compare between two groups. Student's $t$ test was used to compare continuous variables. Multivariate analysis was performed to identify independent risk factors for graft occlusion or string sign. A generalized estimating equation method was used to account for within-patient correlation. Covariates included in the generalized estimating equation models were age, sex, hypertension, diabetes mellitus, hyperlipidemia, smoking history, peripheral vascular disease, graft material (ITA or non-ITA), target coronary artery (LAD or non-LAD), stenosis rate of target coronary artery (mild or severe), composite grafting, and sequential grafting. Odds ratios are presented with 95% confidence intervals. Statistical significance was accepted at $p$ less than 0.05. All statistical analyses was performed with SPSS statistical software (SPSS version 17.0; SPSS Japan, Tokyo, Japan).

## Results

Incidence of graft occlusion or string sign was compared between composite grafts and individual grafts according to graft material, location of target coronary artery, and stenosis of target coronary artery (Table 3). There were significant differences between composite and individual

*Table 3. Incidence of Graft Occlusion or String Sign in Composite and Individual Grafts*

| | Composite | Individual | $p$ Value |
|---|---|---|---|
| Graft material | | | |
| ITA | 11.0% (21/191) | 4.5% (15/336) | 0.006 |
| RA | 34.6% (73/211) | 32.7% (16/49) | 0.868 |
| GEA | 12.5% (1/8) | 22.9% (8/35) | 1.000 |
| Location of target coronary artery | | | |
| LAD | 5.9% (2/34) | 3.1% (7/223) | 0.339 |
| D | 15.0% (19/127) | 7.8% (4/51) | 0.228 |
| LCX | 30.8% (72/234) | 17.6% (19/108) | 0.052 |
| RCA | 13.3% (2/15) | 26.3% (10/38) | 0.472 |
| Stenosis of target coronary artery | | | |
| Mild, ≤ 75% | 40.5% (62/153) | 13.6% (17/125) | <0.001 |
| Severe, > 75% | 12.8% (33/257) | 7.8% (23/295) | 0.065 |
| ≤ 50% | 66.7% (14/21) | 57.1% (4/7) | 0.674 |
| > 50%, ≤ 75% | 36.4% (48/132) | 11.0% (13/118) | <0.001 |
| > 75%, ≤ 90% | 15.1% (23/152) | 6.9% (13/188) | 0.020 |
| > 90% | 9.5% (10/105) | 9.3% (10/107) | 1.000 |

D = diagonal branch; GEA = gastroepiploic artery; ITA = internal thoracic artery; LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery; RA = radial artery; RCA = right coronary artery.

*Table 4. Incidence of Graft Occlusion or String Sign According to Severity of Target Coronary Artery*

| | Composite | Individual | *p* Value |
|---|---|---|---|
| ITA | | | |
| Mild, ≤ 75% | 20.3% (14/69) | 7.3% (7/96) | 0.018 |
| Severe, > 75% | 5.7% (7/122) | 3.3% (8/240) | 0.278 |
| ≤ 50% | 14.3% (1/7) | 60.0% (3/5) | 0.222 |
| > 50%, ≤ 75% | 21.0% (13/62) | 4.4% (4/91) | 0.003 |
| > 75%, ≤ 90% | 5.6% (4/72) | 3.2% (5/157) | 0.473 |
| > 90% | 6.0% (3/50) | 3.6% (3/83) | 0.672 |
| RA | | | |
| Mild, ≤ 75% | 59.3% (48/81) | 36.4% (8/22) | 0.090 |
| Severe, > 75% | 11.5% (25/130) | 29.6% (8/27) | 0.297 |
| ≤ 50% | 93.0% (13/14) | 50.0% (1/2) | 0.242 |
| > 50%, ≤ 75% | 50.7% (34/67) | 35.0% (7/20) | 0.308 |
| > 75%, ≤ 90% | 23.4% (18/77) | 40.0% (6/15) | 0.206 |
| > 90% | 13.2% (7/53) | 16.7% (2/12) | 0.667 |

ITA = internal thoracic artery; RA = radial artery.

grafts in ITA grafts and in the presence of mild stenosis of target coronary artery.

Incidence of graft occlusion or string sign in ITA and RA graft according to severity of target coronary artery is shown in Table 4. In target vessels with severe stenosis, there were no differences in the incidence of graft occlusion or string sign between composite and individual grafts in ITA (composite 5.7% versus individual 3.3%, $p = 0.278$) and RA (11.5% versus 29.6%, $p = 297$). But in target vessels with mild stenosis, the incidence of graft occlusion or string sign was significantly higher for composite grafts than for individual grafts in ITA (20.3% versus 7.3%, $p = 0.018$) and showed a lower tendency in RA (59.3% versus 36.4%, $p = 0.09$). The incidence of graft occlusion or string sign according to graft material, location and stenosis of the target coronary artery, and graft configuration is shown in Figure 1. The incidences of graft occlusion and string sign were particularly high when composite grafts were used for a mildly stenosed target vessel, irrespective of the graft material or location of the target coronary artery.

The results of multivariate analysis are shown in Table 5. The independent predictors of graft occlusion or string sign in total were non-ITA graft, mild stenosis of the target coronary artery, and peripheral vascular disease. Composite grafting was an independent predictor of graft occlusion or string sign only when grafted to the target vessels with mild stenosis.

## Comment

### *Comparison of Composite and Individual Grafting*

The present study revealed that the angiographic outcomes of composite grafts were closely related to the severity of stenosis of the target coronary artery. Several previous studies reported that the patency rate of composite grafts was equal to that of individual grafts [1–3]. However, none of them examined the patency rate in relation to stenosis of the target coronary artery. Suboptimum angiographic results of composited grafting for mildly stenosed target vessels have been reported by several studies. Pevni and colleagues [4] reported that a lower stenosis rate of the target coronary arteries was associated with a higher occlusion rate of composite ITA grafts. Gaudino and associates [5] reported that the threshold of stenosis for graft occlusion in a target coronary artery was higher in composite RA grafts than in individual RA grafts. Nakajima and associates [7] reported that 75% stenosis in the right coronary artery was an independent predictor of competitive flow and graft occlusion. From a practical standpoint, whether there is a difference in angiographic outcomes between composite and individual grafts for particular target vessels has been considered important, but none of these studies compared angiographic outcomes of composite and individual grafting. The present study is the first to demonstrate a higher incidence of graft failure in composite grafting for mildly stenosed target vessels. Moreover, in target vessels with mild stenosis, composite grafting has been shown to be an independent predictor of graft occlusion or string sign. Based on these results, we do not recommend composite grafting in target vessels with mild stenosis.

### *Mechanism of Graft Failure in Composite Grafts*

The precise mechanism of graft failure in composite grafts has not been completely clarified. Arterial grafts are known to narrow diffusely or occlude when they are used in low-flow conditions [6, 8]. The susceptibility of composite grafting to low-flow conditions when used in target vessels with mild stenosis has been suggested by several studies. Studies examining the blood flow of composite grafts reported flow reduction of approximately 20% for composite grafting compared with the

*Table 5. Multivariate Analysis of Risk Factors for Graft Occlusion or String Sign*

| Risk Factors | Odds Ratio | 95% CI | *p* Value |
|---|---|---|---|
| Total | | | |
| Non-ITA | 4.88 | 2.74–8.69 | <0.001 |
| Mild stenosis | 3.61 | 2.29–5.70 | <0.001 |
| Composite grafting | 1.37 | 0.70–2.68 | 0.362 |
| Peripheral vascular disease | 2.65 | 1.21–5.82 | 0.015 |
| For mildly stenosed target vessels | | | |
| Non-ITA | 5.80 | 2.64–12.71 | <0.001 |
| Composite grafting | 2.73 | 1.17–6.40 | 0.021 |
| For severely stenosed target vessels | | | |
| Non-ITA | 4.26 | 1.83–9.90 | <0.001 |
| Composite grafting | 0.72 | 0.27–1.91 | 0.509 |
| Peripheral vascular disease | 4.55 | 1.69–12.23 | 0.003 |

CI = confidence interval; ITA = internal thoracic artery.

sum of 2 individual grafts [9, 10]. Furthermore, the flow through a composite graft is strongly influenced by native coronary flow. Markwirth and colleagues [11] reported that in composite grafts anastomosed to a patent but stenosed target vessel, the graft flow is lower by 40% than that in grafts anastomosed to occluded target vessels. Nakajima and coworkers [7] reported the incidence of flow competition in composite grafts was as high as 14.6%. These findings suggest that composite grafting may be susceptible to the detrimental effect of flow competition with native coronary artery, resulting in a low-flow condition. This supposition is in agreement with the finding in the present study that mild stenosis of the target coronary artery is related to the incidence of graft occlusion or string sign in composite grafts.

### *Study Limitations*

This study has several limitations. First, all data were retrospectively collected, which may have led to information bias. Second, a follow-up angiogram was performed in only 47.8% of the patients who underwent off-pump CABG during this study period. The angiogram was performed according to a protocol and was not symptom-directed. Third, composite grafting included both I and Y configurations. According to our data, there were no differences in patency rate between these configurations. Fourth, in some graft designs, the number of anastomoses was too small to perform statistical analysis. The number of gastroepiploic arteries was too small to draw any conclusion. The number of individual RA grafts was relatively small, which may have involved a wide variation of the data. Fifth, the graft occlusion and string sign may include intraoperative graft failure, because we did not perform early postoperative angiography in all patients.

In conclusion, the angiographic outcomes of composite grafts were closely related to the severity of stenosis of the target coronary artery. In target vessels with mild stenosis, angiographic outcomes of composite grafts were inferior to those of individual grafts.

## References

1. Calafiore AM, Contini M, Vitolla G, et al. Bilateral internal thoracic artery grafting: long-term clinical and angiographic results of in situ versus Y grafts. J Thorac Cardiovasc Surg 2000;120:990–8.
2. Kim KB, Cho KR, Chang WI, Lim C, Ham BM, Kim YL. Bilateral skeletonized internal thoracic artery grafting in off-pump coronary artery bypass: early result of Y versus in situ grafts. Ann Thorac Surg 2002;74(Suppl):1371–6.
3. Fukui T, Takanashi S, Hosoda Y, Suehiro S. Total arterial myocardial revascularization using composite and sequential grafting with the off-pump technique. Ann Thorac Surg 2005;80:579–85.
4. Pevni S, Hertz I, Medalion B, et al. Angiographic evidence for reduced graft patency due to competitive flow in composite arterial T-grafts. J Thorac Cardiovasc Surg 2007;133: 1220–5.
5. Gaudino M, Alessandrini F, Pragliola C, et al. Effect of target artery location and severity of stenosis on mid-term patency of aorta-anastomosed radial artery grafts. Eur J Cardiothorac Surg 2004;25:424–8.
6. Fukui T, Takanashi S, Hosoda Y, Suehiro S. Early and midterm results of off-pump coronary artery bypass grafting. Ann Thorac Surg 2007;83:115–9.
7. Nakajima H, Kobayashi, J, Tagusari O, Bando K, Niwaya K, Kitamura S. Competitive flow in arterial composite grafts and effect of graft arrangement in off-pump coronary revascularization. Ann Thorac Surg 2004;78:481–6.
8. Tokuda Y, Song MH, Oshima H, Usui A, Ueda Y. Predicting midterm coronary artery bypass graft failure by intraoperative transit time flow measurement. Ann Thorac Surg 2008; 86:532–6.
9. Affleck DG, Barner HB, Bailey MS, et al. Flow dynamics of the internal thoracic and radial artery T-graft. Ann Thorac Surg 2004;78:1290–4.
10. Royse AG, Royse CF, Groves KL, Yu G. Blood flow in composite arterial grafts and effect of native coronary flow. Ann Thorac Surg 1999;68:1619–22.
11. Markwirth T, Hennen B, Scheller B, Schafers HJ, Wendler O. Flow wire measurements after complete arterial coronary revascularization with T-grafts. Ann Thorac Surg 2001;71: 788–93.

## INVITED COMMENTARY

This report by Manabe and colleagues [1] provides a 1-year angiographic follow-up of coronary revascularization using composite grafting, which was compared with revascularization using individual grafting, and composite grafting in target vessels with mild stenosis is not recommended.

Greater freedom from reinterventions and enhanced long-term survival rates have been demonstrated when bilateral internal thoracic arteries (ITAs) are used rather than a single ITA graft in surgical revascularization for multi-vessel coronary disease. The superiority of one method in comparison to another has not been established for bilateral ITA grafting in an individual or composite configuration. A recent study by Kim and colleagues [2] demonstrated that perfusion improvements were similar for both bilateral individual ITA and composite grafts in terms of reversibility scores at 5 years postoperatively.

Revascularization of stenotic coronary lesions that induce myocardial ischemia can improve a patient's functional status and outcome. However, the benefit of revascularization is less clear for mildly stenotic coronary lesions that do not induce myocardial ischemia. Coronary angiography remains the most accurate morphologic assessment of lumen of the coronary arteries. However, angiographically, the degree of stenosis is a poor tool for gauging the functional significance of a specific coronary stenosis. Fractional flow reserve (ie, the ratio of maximal blood flow in a stenotic artery to normal maximal flow) is an index of the physiologic significance of a coronary stenosis, and this can easily be measured during coronary angiography. The combination of anatomic assessment and precise functional information is indispensable in tailoring the revascularization in angiographically dubious stenoses [3].


Published by Elsevier Inc

0003-4975/10/$36.00
doi:10.1016/j.athoracsur.2009.12.039

# Angiographic outcomes of right internal thoracic artery grafts in situ or as free grafts in coronary artery bypass grafting

Toshihiro Fukui, MD, PhD,[a] Minoru Tabata, MD, MPH,[a] Susumu Manabe, MD, PhD,[a] Tomoki Shimokawa, MD, PhD,[a] Satoshi Morita, MD, PhD,[b] and Shuichiro Takanashi, MD[a]

**Objective:** We sought to compare early and 1-year angiographic results of various coronary artery bypass grafting configurations with the right internal thoracic artery in combination with the left internal thoracic artery.

**Methods:** We reviewed the records of 705 patients who underwent bilateral internal thoracic artery grafting between September 2004 and November 2008. The right internal thoracic artery was used as an in situ graft in 547 patients and as a free graft in 158 patients. We compared operative and postoperative variables and early and 1-year angiographic patency rates of the right internal thoracic artery between the groups.

**Results:** The operative mortality and incidence of postoperative complications were not significantly different between groups. The overall patency rates of the right internal thoracic artery were 98.8% at early angiography and 94.3% at 1-year postoperative follow-up. There were no significant differences in patency rate between in situ and free right internal thoracic artery grafts (98.6% vs 99.3% early and 95.3% vs 89.8% at 1 year). The best patency rate of the right internal thoracic artery was achieved with in situ grafting to the left anterior descending system (99.4% early and 98.5% at 1 year).

**Conclusions:** Patency rates of in situ and free right internal thoracic artery grafts were similar in early and 1-year angiographic studies. Among various configurations, the best patency of the right internal thoracic artery was obtained with in situ grafting to the left anterior descending coronary artery. (J Thorac Cardiovasc Surg 2010;139:868-73)

Internal thoracic artery (ITA) grafts are the most reliable conduits for revascularization of diseased coronary arteries because of their long-term durability.[1] The use of bilateral ITA grafts has been shown to provide better survival and economic benefits than the use of single ITA grafts.[2] Furthermore, the patency rate and survival benefits were satisfactory when bilateral ITAs were used for the left coronary system.[3] There are, however, many different arrangements of the bilateral ITA in left-sided myocardial revascularization. In particular, the right ITA has been flexibly used as an in situ or free graft in combination with an in situ left ITA.[4] An in situ right ITA can be used for anterior territory (the left anterior descending coronary artery [LAD] and diagonal branch) along the front of the ascending aorta or lateral territory (obtuse marginal or posterolateral branch) through the transverse sinus. A free right ITA can be used as a composite graft or aortocoronary bypass graft.[5]

There is little information available on angiographic studies comparing these various configurations with bilateral ITA grafting. The aim of this study was to examine the early and 1-year angiographic results of various strategies with right ITA grafts in combination with in situ left ITA grafts. Furthermore, we sought to evaluate the serial angiographic outcomes of right ITA grafts.

From the Department of Cardiovascular Surgery,[a] Sakakibara Heart Institute, Tokyo, Japan, and the Department of Biostatistics and Epidemiology,[b] Yokohama City University Medical Center, Yokohama, Japan.

Disclosures: None.

Received for publication March 9, 2009; revisions received May 1, 2009; accepted for publication May 31, 2009; available ahead of print July 27, 2009.

Address for reprints: Toshihiro Fukui, MD, Department of Cardiovascular Surgery, Sakakibara Heart Institute, 3-16-1 Asahi-cho, Fuchu City, Tokyo 183-0003, Japan (E-mail: tfukui-cvs@umin.ac.jp).

0022-5223/$36.00



doi:10.1016/j.jtcvs.2009.05.033

## MATERIALS AND METHODS

### Patient Population

Between September 2004 and November 2008, a total of 827 patients underwent isolated coronary artery bypass grafting at Sakakibara Heart Institute. Of these patients, 705 (85.2%) underwent bilateral ITA grafting. Preoperative characteristics of these 705 patients are shown in Table 1. We used bilateral ITA for patients who needed revascularization of both the LAD and left circumflex artery territories. The right ITA was used as an in situ graft in 547 patients (77.6%) and as a free graft in 158 patients (22.4%). Our grafting strategy of right ITA is described in Table 2. When the right ITA was used as an inflow of other grafts (radial artery or saphenous vein graft), an end-to-end anastomosis was performed between grafts. We applied multiple sequential grafting with the free right ITA in patients with a limited number of grafts. When we anastomosed the free right ITA to the ascending aorta, we routinely used intraoperative epiaortic echocardiography to detect a disease-free area of the aorta. When we anastomosed the free right ITA proximally to another graft (left ITA, radial artery, or saphenous vein graft), we created a Y-composite graft.

### Operation

The operative technique used for off-pump coronary artery bypass grafting has been described previously.[6] All arterial grafts were harvested in a skeletonized fashion with an ultrasonic scalpel (Harmonic Scalpel; Ethicon Endosurgery, Cincinnati, Ohio). We bypassed all significantly diseased coronary vessels (at least 50% diameter reduction) larger than 1 mm in diameter. We performed long segmental reconstruction when the LAD was diffusely diseased and its branches, such as septal and diagonal arteries,

**Abbreviations and Acronyms**
ITA = internal thoracic artery
LAD = left anterior descending coronary artery

were affected by severe atheromatous plaques. An arteriotomy was extended proximally and distally to the intact segment of the LAD. Additionally, we performed endarterectomy when the atheromatous plaque was circumferential or too hard to pass a needle. The left ITA was anastomosed to the LAD in a long on-lay patch fashion with 7-0 and 8-0 polypropylene running sutures. The detailed indication, technique, and outcomes of long segmental reconstruction of the LAD have been described previously.[7] Although the sequential grafting to a proximal and a distal LAD could achieve the same objective, we prefer this method and have had excellent outcomes.[7]

## Angiography

Early postoperative angiography was performed in 579 patients (82.1%) who gave us informed consent. Median time of early postoperative angiography was 10 days after surgery (range 1–20 days). If a patient had symptoms during follow-up, diagnostic angiography was performed at that time. For patients who did not have symptoms within 1 year after surgery, follow-up angiography was performed at 1 year. The follow-up postoperative angiography was performed for 336 patients (47.7%) at a median of 12.2 months after surgery (range 2–21 months). Of these patients, 312 patients (44.3%) underwent both early and 1-year angiographic studies.

We compared the preoperative, intraoperative, postoperative, and angiographic variables between patients with in situ right ITA grafts and those with free right ITA grafts. All data were collected prospectively and reviewed retrospectively. The institutional review board approved this retrospective study and waived the need for written consent.

Nonelective operations included both emergency and urgent cases according to the definition of the Society of Thoracic Surgeons database. Operative death was defined as death occurring within 30 days after surgery. Low-output syndrome was defined as the postoperative need for any dose of adrenaline or more than 5 $\mu g\ kg^{-1}\ min^{-1}$ of dopamine or dobutamine. Perioperative myocardial infarction was defined as a positive result for new Q waves in an electrocardiogram or a peak creatine kinase MB level of greater than 10% of total creatine kinase. Respiratory failure was defined as requirement for prolonged ventilation (>48 hours) or presence of pneumonia. A postoperative cerebrovascular accident was defined as a new stroke or intracranial bleeding and was confirmed by computed tomography. In patients with preoperative stroke, postoperative stroke was defined as a worsening of the neurologic deficit with new radiologic findings.

Patent graft was defined as a graft without occlusion, significant stenosis (>90%), or string sign. String sign was defined as luminal narrowing throughout the entire conduit, including stenosis of 90% or greater. Grafts with competitive flow or reverse flow were considered patent unless they had occlusion, significant stenosis, or string sign. Competitive flow and reverse flow were defined according to the classification by Nakajima and colleagues.[8] Competitive flow was defined as a situation in which the target vessel was barely opacified from the ITA graft injection and the bypass graft was filled by retrograde flow from the native coronary injection. Reverse flow was defined as a situation in which the distal anastomotic site was not opacified from the ITA graft injection at all but was filled clearly by retrograde flow from the native coronary injection.

Early and 1-year patency rates were calculated by dividing the number of patent grafts by the total number of grafts. If patients with early nonpatent grafts underwent 1-year angiography, those nonpatent grafts were also counted as 1-year nonpatent grafts.

## Statistical Analysis

All statistical analyses were performed with StatView 5.0 software (SAS Institute Inc, Cary, NC). Continuous variables are reported as the mean ± SD if normally distributed. Otherwise, they are reported as median.

**TABLE 1. Preoperative characteristics of patients with right internal thoracic artery as in situ or free graft**

| | All (n = 705) | In situ (n = 547) | Free (n = 158) | *P* value |
|---|---|---|---|---|
| Age (y, mean ± SD) | 67.9 ± 9.4 | 68.2 ± 9.2 | 66.7 ± 10.0 | .0837 |
| Sex (no. female) | 125 (17.7%) | 90 (16.5%) | 35 (22.2%) | .1250 |
| Body surface area (m², mean ± SD) | 1.7 ± 0.2 | 1.7 ± 0.2 | 1.6 ± 0.2 | .0119 |
| Unstable angina (no.) | 225 (31.9%) | 177 (32.4%) | 48 (30.4%) | .7090 |
| Canadian Cardiovascular Society class (mean ± SD) | 2.2 ± 0.9 | 2.3 ± 0.9 | 2.2 ± 0.8 | .5474 |
| Ejection fraction (%, mean ± SD) | 55.7 ± 12.1 | 55.8 ± 11.9 | 55.7 ± 12.3 | .9380 |
| Diseased vessels (mean ± SD) | 2.8 ± 0.4 | 2.8 ± 0.4 | 2.9 ± 0.3 | .0118 |
| Left main disease (no.) | 240 (34.0%) | 190 (34.7%) | 50 (31.6%) | .5309 |
| Creatinine (mg/dL, mean ± SD) | 1.2 ± 1.4 | 1.1 ± 1.2 | 1.4 ± 1.9 | .0257 |
| Congestive heart failure (no.) | 95 (13.5%) | 65 (11.9%) | 30 (19.0%) | .0299 |
| Previous myocardial infarction (no.) | 344 (48.8%) | 263 (48.1%) | 81 (51.3%) | .5385 |
| Hypertension (no.) | 469 (66.5%) | 365 (66.7%) | 104 (65.8%) | .9071 |
| Diabetes mellitus (no.) | 341 (48.4%) | 250 (45.7%) | 91 (57.6%) | .0109 |
| Insulin (no.) | 79 (11.2%) | 54 (9.9%) | 25 (15.8%) | .0517 |
| Hyperlipidemia (no.) | 433 (61.4%) | 337 (61.6%) | 96 (60.8%) | .9199 |
| Smoking (no.) | 427 (60.6%) | 327 (59.8%) | 100 (63.3%) | .4820 |
| Previous stroke (no.) | 88 (12.5%) | 64 (11.7%) | 24 (15.2%) | .3018 |
| Peripheral vascular disease (no.) | 65 (9.2%) | 45 (8.2%) | 20 (12.7%) | .1235 |
| Chronic obstructive pulmonary disease (no.) | 28 (4.0%) | 18 (3.3%) | 10 (6.3%) | .1358 |
| Nonelective (no.) | 88 (12.5%) | 81 (14.8%) | 7 (4.4%) | .0003 |
| Previous percutaneous coronary intervention (no.) | 200 (28.4%) | 152 (27.8%) | 48 (30.4%) | .5916 |
| Reoperation (no.) | 9 (1.3%) | 5 (0.9%) | 4 (2.5%) | .1195 |



ACD

TABLE 2. Strategy for using either in situ or free right internal thoracic artery graft

| Target | Reasons | No. |
|---|---|---|
| In situ | | 547 |
| Left anterior descending artery | Unstable left main or bifurcation disease | 124 |
| Diagonal branch | Larger than other lateral vessels; inflow of radial artery graft as Y graft | 262 |
| Circumflex artery | Single major lateral vessel | 128 |
| Inflow for another graft | Diseased aorta | 33 |
| Free | | 158 |
| Diagonal branch | Multiple grafting | 26 |
| Circumflex artery | Multiple grafting | 132 |

Continuous variables were compared with the Student $t$ test, whereas discrete variables were compared with the $\chi^2$ test or Fisher exact test.

## RESULTS

### Clinical Outcomes

Preoperative characteristics of both groups are shown in Table 1. Mean body surface area was significantly larger in the in situ right ITA group than in the free right ITA group ($P = .0119$). The mean number of diseased vessels was significantly larger in the free right ITA group than in the in situ right ITA group ($P = .0118$). Preoperative creatinine levels were significantly higher in the free right ITA group than in the in situ right ITA group ($P = .0299$). The free right ITA group contained a significantly larger number of patients with histories of congestive heart failure and diabetes mellitus than did the in situ right ITA group ($P = .0299$ and $P = .0109$, respectively). More patients in the in situ right ITA group underwent emergency or urgent operations than in the free right ITA group ($P = .0003$).

Operative and postoperative variables are listed in Table 3. There was no significant difference in the mean number of distal anastomoses per patient between the groups ($P = .9290$). The number of distal anastomoses of the right ITA, however, was higher in the free ITA group than in the in situ ITA group ($P < .0001$).

Long segmental reconstruction of the LAD was carried out with the left ITA in 288 patients (40.9%). The operative time in the free right ITA group was significantly longer than that in the in situ right ITA group ($P = .0007$). The operative mortality was not significantly different between the groups ($P = 0.6569$). The incidence of postoperative complications was also not significantly different between the groups.

During the follow-up period, among the 705 patients there were 10 patients with recurrent angina, 12 with congestive heart failure, and 1 with stroke.

### Angiographic Outcomes

The follow-up angiographic studies included patients without symptoms (n = 326) and those with symptoms (n = 10). Among the 10 patients with symptoms, percutaneous coronary intervention was performed in 5 cases. Of these 5 patients, 2 patients needed percutaneous coronary intervention for new coronary lesions. The other 3 patients needed percutaneous coronary intervention for stenosis of the gastroepiploic artery graft. Five patients who did not undergo percutaneous coronary intervention had stenosis of small native coronary arteries that were not an indication for intervention. None of these 10 patients were found to have a lesion related to the right ITA graft.

The overall patency rates of the right ITA were 98.8% at early angiography and 94.3% at 1-year angiography. The patency rates of the left ITA were 99.1% in the early study and 97.0% in the 1-year study. There were no significant differences in the early ($P = .7732$) and 1-year ($P = .1288$) patency rates between the left and right ITAs. Patency rates of various configurations of the right ITA at both early and 1-year angiographic studies are listed in Table 4.

In early examinations, there was no significant difference in the patency rate between in situ and free right ITAs ($p > .9999$). In the in situ right ITA group, the patency rate of the right ITA graft when used as an inflow to other grafts was significantly lower than when used as a direct graft to coronary arteries ($P = .0149$). In the free right ITA group, the site of proximal anastomoses (composite or aorta) did not affect the patency rate ($P > .9999$). In 1-year examinations, there was also no significant difference in the patency rate between in situ and free right ITAs ($P = .1792$). In the in situ right ITA group, the patency rate of the right ITA anastomosed to the anterior territory was superior to that of other grafting methods ($P < .0001$). In the free group, there was no significant difference in the patency rate between sites of proximal anastomoses ($P > .9999$).

When we compared the patency rates between the anterior and posterior routes in patients with in situ right ITA, there was no difference in early patency rate between these configurations ($P = .2735$). The 1-year patency rate of the anterior route, however, was superior to that of the posterior route ($P = .0042$).

Nonpatent right ITA grafts at any time are listed in Table 5. Among 21 nonpatent grafts, 16 grafts (76.1%) were anastomosed to the coronary artery with low stenosis rate (50%–75%).

TABLE 3. Operative and postoperative data of patients with right internal thoracic artery as in situ or free graft

| | All (n = 705) | In situ (n = 547) | Free (n = 158) | *P* value |
|---|---|---|---|---|
| Anastomoses per patient (mean ± SD) | 4.2 ± 1.2 | 4.2 ± 1.2 | 4.2 ± 1.1 | .9290 |
| Anastomoses of right internal thoracic artery per patient (mean ± SD) | 1.1 ± 0.5 | 1.0 ± 0.3 | 1.7 ± 0.7 | <.0001 |
| Grafts per patient (mean ± SD) | | 3.3 ± 0.6 | 3.1 ± 0.5 | <.0001 |
| Long segment reconstruction of left anterior descending artery (no.) | 288 (40.9%) | 218 (39.9%) | 70 (44.3%) | .3625 |
| Operative time (min, mean ± SD) | 282.3 ± 59.1 | 278.3 ± 57.9 | 296.3 ± 61.2 | .0007 |
| Transfusion (no.) | 257 (36.5%) | 192 (35.1%) | 65 (41.1%) | .1952 |
| Intubation (h, mean ± SD) | 10.1 ± 16.2 | 10.4 ± 17.3 | 9.0 ± 11.1 | .3359 |
| Intensive care unit stay (d, mean ± SD) | 2.0 ± 8.2 | 2.1 ± 9.2 | 1.7 ± 1.6 | .5414 |
| Operative death (within 30 d, no.) | 7 (1.0%) | 5 (0.9%) | 2 (1.3%) | .6569 |
| Reexploration for bleeding (no.) | 6 (0.9%) | 4 (0.7%) | 2 (1.3%) | .6208 |
| Low output syndrome (no.) | 12 (1.7%) | 10 (1.8%) | 2 (1.3%) | >.9999 |
| Perioperative myocardial infarction (no.) | 12 (1.7%) | 9 (1.6%) | 3 (1.9%) | .7366 |
| Severe ventricular arrhythmia (no.) | 5 (0.7%) | 2 (0.4%) | 3 (1.9%) | .0774 |
| Atrial fibrillation (no.) | 186 (26.4%) | 147 (26.9%) | 39 (24.7%) | .6542 |
| Hemodialysis required (no.) | 14 (2.0%) | 10 (1.8%) | 4 (2.5%) | .5282 |
| Stroke (no.) | 8 (1.1%) | 6 (1.1%) | 2 (1.3%) | >.9999 |
| Mediastinitis (no.) | 12 (1.7%) | 7 (1.3%) | 5 (3.2%) | .1534 |

ACD

We also analyzed the subgroup of 312 patients (44.3%) who underwent both early and 1-year angiographic studies. In this subgroup of patients, there were no significant differences in the patency rate at early (*P* > .9999) and 1-year (*P* = .0711) angiography between in situ and free right ITA groups. Among patients with in situ right ITA grafts (n = 257), 4 patients had nonpatent right ITA in the early study and 10 patients had nonpatent right ITA in the 1-year study. Six patients had newly developed nonpatency of right ITA graft at the 1-year study. Four of these 6 patients had a low stenosis rate (50%–75%) in the target coronary artery.

On the other hand, among patients with a free right ITA (n = 55), there was 1 patient whose right ITA was not patent in the early study and 6 patients whose right ITAs were not patent in the 1-year study. Five patients had newly developed nonpatent free right ITA grafts at the 1-year study. These 5 patients had a low stenosis rate (50%–75%) of the target coronary artery.

## DISCUSSION

The right ITA is frequently used as a second or third arterial graft, as well as the radial artery or gastroepiploic artery.[9]

TABLE 4. Cumulative angiographic patency rates of in situ and free right internal thoracic artery grafts

| | Early (n = 579) | 1 y (n = 336) |
|---|---|---|
| Total | 98.8% (572/579) | 94.3% (317/336) |
| In situ | 98.6% (438/444) | 95.3% (264/277) |
| Anterior | 99.4 % (307/309) | 98.5% (197/200) |
| Lateral | 98.1% (105/107) | 89.3% (50/56) |
| Inflow | 92.9% (26/28) | 81.0% (17/21) |
| Free | 99.3% (134/135) | 89.8% (53/59) |
| Composite graft | 99.1% (105/106) | 89.8% (44/49) |
| Aorta | 100% (29/29) | 90% (9/10) |

All figures represent percentages of patent grafts, with numbers of patent grafts and total grafts given in parentheses.

Because the right ITA is anatomically the same as the left ITA, a longer patency duration would be expected than with other arterial grafts. Because the length of the right ITA when it is used as an in situ graft is sometimes not sufficient for revascularization for lateral vessels, however, several configurations have been proposed,[10] such as an in situ graft to the LAD and a free graft with proximal anastomoses to the aorta or an in situ left ITA. Although there have been many reports describing the feasibility and efficacy of each technique, little has been reported about angiographic patency rates comparing several configurations simultaneously. This study demonstrated that clinical and angiographic outcomes were not significantly different between in situ and free right ITA grafts at early and 1-year follow-up. Additionally, in situ right ITA grafting to the LAD system had a superior patency rate to other types of right ITA grafting at early and 1-year angiography.

When the right ITA is used as an in situ graft, it can be useful for revascularization of anterior or lateral vessel for single anastomosis. When the in situ right ITA is anastomosed to the LAD or diagonal branch, it is directed anterior to the aorta.[11] In such cases, the right ITA should be wrapped in thymic tissue and covered with mediastinal fat to prevent injury at reopening.[12] We used an in situ right ITA for revascularization of the anterior territory in 70.7% of patients. An in situ right ITA has sufficient length to reach anterior vessels in almost all patients. It is useful for unstable left main and bifurcation disease when combined with the use of an in situ left ITA for lateral vessels. When the right ITA is anastomosed to the circumflex artery territory, it is passed through the transverse sinus.[13] In such cases, care should be taken not to twist the graft. We used an in situ right ITA for lateral territory in 23.2% of patients. It is useful for revascularization of single major lateral vessel when it is long enough. In this study, the patency rate at 1-year

ACD

TABLE 5. Occluded right internal thoracic artery grafts

| Inflow | Target vessel | Degree of native coronary stenosis | Occluded grafts |
|---|---|---|---|
| In situ | | | |
| Right ITA | Left anterior descending artery | 50% | 1 |
| | Diagonal branch | 50% | 1 |
| | | 90% | 2 |
| | Circumflex artery | 50% | 2 |
| | | 75% | 3 |
| | | 90% | 2 |
| | Inflow of other grafts | 75% | 4 |
| Free | | | |
| Left ITA | Diagonal branch | 90% | 1 |
| | Circumflex artery | 75% | 2 |
| Radial artery | Diagonal branch | 75% | 1 |
| | Circumflex artery | 50% | 1 |
| Aorta | Circumflex artery | 50% | 1 |

*ITA*, Internal thoracic artery.

angiography was superior when an in situ right ITA was used for anterior territory relative to when it was used for lateral territory.

A free right ITA graft is useful for revascularization of lateral or posterior vessels for single or multiple sequential anastomoses. It can reach the posterior descending artery with composite grafting when its proximal anastomosis is carried out on the left ITA.[14] Multiple sequential grafting to lateral vessels with the free right ITA can reduce the total number of grafts. In this study, the mean number of grafts was significantly less in the free right ITA group than in the situ right ITA group ($P < .0001$). Furthermore, the mean number of distal anastomoses of the free right ITA was significantly higher than that of the in situ right ITA ($P < .0001$). The proximal anastomosis site of the free right ITA (other grafts or aorta) did not affect the patency rate at both of early and 1-year angiographic studies. Calafiore and colleagues[15] reported that the patency rate of the free right ITA proximally anastomosed to the aorta was inferior to that anastomosed to the left ITA. They suggested that the reason for this poor graft patency rate was because of a mismatch between the aorta and the conduit wall and a difference in the flow pattern. We did not observe an inferior patency rate of the free right ITA anastomosed to the aorta relative to that anastomosed to other grafts. We speculate that the routine use of intraoperative epiaortic echocardiography to detect a disease-free area of the aorta for proximal anastomosis may minimize the mismatch of the wall discrepancy.

There have been a few reports comparing the patency rates between the in situ right ITA and the free right ITA.[16,17] Recently, Glineur and associates[18] demonstrated that patency rates were not different between an in situ group and a Y-grafting group at 6-month postoperative angiography in a prospective randomized trial. Our 1-year follow-up study supports their findings. In this study, both early and 1-year angiographic studies were performed in 312 patients. Among those patients, 11 patients were newly found to have nonpatent right ITA grafts at 1-year angiography. The target coronary arteries had a low stenosis rate in 9 of these 11 patients. Competitive or reverse flow related to a low stenosis rate could be the potential cause of 1-year new nonpatency. It has been suggested that arterial grafts tend to fail when they are used for revascularization of target vessels with low-grade stenosis.[8] This tendency was observed in both the in situ and free right ITA grafts in our study.

A skeletonized ITA provides a longer length and better flexibility than a pedicled ITA. Skeletonization ensures that the right ITA reaches the posterolateral vessels through the transverse sinus as an in situ graft. Furthermore, multiple sequential grafting can be easily performed with a skeletonized free right ITA. The blood flow of a skeletonized ITA is reported to be greater than that of a pedicled ITA.[19] With the skeletonization technique, the use of bilateral ITAs might no longer be a risk factor for mediastinitis, because the collateral blood supply to the sternum can be preserved.[20,21]

In situ ITA grafts are sometimes at risk for injury in reoperations. Recently, Roselli and colleagues[22] reported an occurrence of ITA injury of 3% at reoperative cardiac surgery. They commented that the best way to prevent injury to a patent ITA graft is to position it properly at the original operation. Preventive strategies are not always effective, however, and intraoperative adverse events are difficult to eliminate. On the other hand, Endo and coworkers[12] reported that the right ITA was surrounded by loose connective tissue at reoperation and the patent ITA did not increase the risk of reoperation in their study. Our own study showed that the best patency of the right ITA could be obtained with in situ grafting to the LAD. Other configurations, however, such as in situ grafting to the lateral wall through the transverse sinus and free grafting to the lateral vessel with Y-composite graft, had only slightly inferior patency. These configurations may be much safer at reoperation than in situ right ITA graft to the LAD. The actual graft strategy should be made after considering the risk of injury at potential reoperations as well as graft patency outcomes.

This clinical study has the several limitations. It was a retrospective observational study and was not randomized. Also, we could not follow up all patients with right ITA grafts. Our findings may not be applicable in such groups as elderly patients and patients with renal insufficiency, who did not have undergo follow-up angiography.

In conclusion, patency rates of in situ and free right ITAs were identical at early and 1-year angiographic studies. In situ grafting to the LAD had the best patency among various configurations of right ITA graft; however, other configurations had also excellent patency. Grafting strategy of right ITA should be determined on the basis of conduit availability, target location, and other clinical factors.

## References


1. Loop FD, Lytle BW, Cosgrove DM, Stewart RW, Goormastic M, Williams GW, et al. Influence of the internal-mammary-artery graft on 10-year survival and other cardiac events. *N Engl J Med.* 1986;314:1-6.
2. Taggart DP, D'Amico R, Altman DG. Effect of arterial revascularization on survival: a systematic review of studies comparing bilateral and single internal mammary arteries. *Lancet.* 2001;358:870-5.
3. Cameron A, Davis KB, Green G, Schaff HV. Coronary bypass surgery with internal-thoracic-artery grafts—effects on survival over a 15-year period. *N Engl J Med.* 1996;334:216-9.
4. Buxton BF, Ruengsakulrach P, Fuller J, Rosalion A, Reid CM, Tatoulis J. The right internal thoracic artery graft—benefits of grafting the left coronary system and native vessels with a high grade stenosis. *Eur J Cardiothorac. Surg.* 2000;18:255-61.
5. Ascione R, Underwood MJ, Lloyd CT, Jeremy JY, Bryan AJ, Angelini GD. Clinical and angiographic outcome of different surgical strategies of bilateral internal mammary artery grafting. *Ann Thorac Surg.* 2001;72:959-65.
6. Fukui T, Takanashi S, Hosoda Y, Suehiro S. Early and midterm results of off-pump coronary artery bypass grafting. *Ann Thorac Surg.* 2007;83:115-9.
7. Fukui T, Takanashi S, Hosoda Y. Long segmental reconstruction of diffusely diseased left anterior descending coronary artery with left internal thoracic artery with or without endarterectomy. *Ann Thorac Surg.* 2005;80:2098-105.
8. Nakajima H, Kobayashi J, Tagusari O, Niwaya K, Funatsu T, Kawamura A, et al. Angiographic flow grading and graft arrangement of arterial conduits. *J Thorac Cardiovasc Surg.* 2006;132:1023-9.
9. Barner HB. Arterial grafting: techniques and conduits. *Ann Thorac Surg.* 1998; 66(5 Suppl):S25-8; discussion S25-8.
10. Pevni D, Uretzky G, Mohr A, Braunstein R, Kramer A, Paz Y, et al. Routine use of bilateral skeletonized internal thoracic artery grafting: long-term results. *Circulation.* 2008;118:705-12.
11. Chow MS, Sim E, Orszulak TA, Schaff HV. Patency of internal thoracic artery grafts: comparison of right versus left and importance of vessel grafted. *Circulation.* 1994;90(5 Pt 2):II129-32.
12. Endo M, Nishida H, Tomizawa Y, Kasanuki H. Benefit of bilateral over single internal mammary artery grafts for multiple coronary artery bypass grafting. *Circulation.* 2001;104:2164-70.
13. Puig LB, França Neto L, Rati M, Ramires JA, da Luz PL, Pileggi F, et al. A technique of anastomosis of the right internal mammary artery to the circumflex artery and its branches. *Ann Thorac Surg.* 1984;38:533-4.
14. Navia D, Vrancic M, Vaccarino G, Piccinini F, Raich H, Florit S, et al. Total arterial off-pump coronary revascularization using bilateral internal thoracic arteries in triple-vessel disease: surgical technique and clinical outcomes. *Ann Thorac Surg.* 2008;86:524-30.
15. Calafiore AM, Di Giammarco G, Luciani N, Maddestra N, Di Nardo E, Angelini R. Composite arterial conduits for a wider arterial myocardial revascularization. *Ann Thorac Surg.* 1994;58:185-90.
16. Calafiore AM, Contini M, Vitolla G, Di Mauro M, Mazzei V, Teodori G, et al. Bilateral internal thoracic artery grafting: long-term clinical and angiographic results of in situ versus Y grafts. *J Thorac Cardiovasc Surg.* 2000; 120:990-6.
17. Lev-Ran O, Pevni D, Matsa M, Paz Y, Kramer A, Mohr R. Arterial myocardial revascularization with in situ crossover right internal thoracic artery to left anterior descending artery. *Ann Thorac Surg.* 2001;72:798-803.
18. Glineur D, Hanet C, Poncelet A, D'hoore W, Funken JC, Rubay J, et al. Comparison of bilateral internal thoracic artery revascularization using in situ or Y graft configurations: a prospective randomized clinical, functional, and angiographic midterm evaluation. *Circulation.* 2008;118(14 Suppl): S216-21.
19. Gurevitch J, Kramer A, Locker C, Shapira I, Paz Y, Matsa M, et al. Technical aspects of double-skeletonized internal mammary artery grafting. *Ann Thorac Surg.* 2000;69:841-6.
20. Parish MA, Asai T, Grossi EA, Esposito R, Galloway AC, Colvin SB, et al. The effects of different techniques of internal mammary artery harvesting on sternal blood flow. *J Thorac Cardiovasc Surg.* 1992;104:1303-7.
21. Higami T, Maruo A, Yamashita T, Shida T, Ogawa K. Histologic and physiologic evaluation of skeletonized internal thoracic artery harvesting with an ultrasonic scalpel. *J Thorac Cardiovasc Surg.* 2000;120:1142-7.
22. Roselli EE, Pettersson GB, Blackstone EH, Brizzio ME, Houghtaling PL, Hauck R, et al. Adverse events during reoperative cardiac surgery: frequency, characterization, and rescue. *J Thorac Cardiovasc Surg.* 2008;135:316-23. 323.e1-6.

# Off-pump bilateral internal thoracic artery grafting in patients with left main disease

Toshihiro Fukui, MD, PhD,[a] Minoru Tabata, MD, MPH,[a] Susumu Manabe, MD, PhD,[a] Tomoki Shimokawa, MD, PhD,[a] Jun Shimizu, MD, PhD,[b] Satoshi Morita, MD, PhD,[c] and Shuichiro Takanashi, MD[a]

**Objective:** This study assessed the safety and efficacy of off-pump bilateral internal thoracic artery grafting in patients with left main disease.

**Methods:** We reviewed the records of 768 patients who underwent off-pump bilateral internal thoracic artery grafting between September 2004 and June 2009. Bilateral internal thoracic artery grafts were used for the left coronary system in all patients, of whom 268 had left main disease and 500 did not. We compared operative and postoperative variables and early and 1-year angiographic patency rates of the bilateral internal thoracic artery between the 2 groups.

**Results:** The perioperative mortality and incidence of postoperative complications were not significantly different between groups. In patients without left main disease, the left and right internal thoracic arteries were used for the left anterior descending artery in 87.4% and 12.2% of patients, respectively. In patients with left main disease, the left and right internal thoracic arteries were used for the left anterior descending artery in 70.5% and 29.1% of patients, respectively. In patients with left main disease, the patency rates for the left and right internal thoracic arteries at 1-year postoperative follow-up were 97.0% and 93.2%, respectively. In patients without left main disease, the patency rates for the left and right internal thoracic arteries at 1-year follow-up were 97.6% and 91.6%, respectively. The patency rates of the left and right internal thoracic arteries did not differ significantly in patients with or without left main disease ($P = .9803$ and $P = .7205$ in left and right internal thoracic arteries, respectively).

**Conclusions:** Off-pump bilateral internal thoracic artery grafting was safe and effective in patients with left main disease. The patency rates of both grafts were comparable to those of patients without left main disease. (J Thorac Cardiovasc Surg 2010;140:1040-5)

ACD

Coronary artery disease (CAD) with left main disease (LMD) has historically been considered to carry a higher operative risk in coronary artery bypass grafting (CABG) than CAD without LMD.[1,2] Recent advancement in operative techniques and perioperative management has enabled surgeons to perform CABG safely in patients with LMD. Generally, off-pump CABG is not preferred in patients with LMD because the displacement of the heart could cause torsion of LMD and acute hemodynamic deterioration.[3] Some investigators have reported the safety of off-pump CABG in patients with LMD in studies with a relatively small sample size.[4-7]

Bilateral internal thoracic artery (ITA) grafting for revascularization has better survival benefits than single ITA grafting,[8] and patency rates and survival benefits are satisfactory when bilateral ITA grafts are used for the left coronary system.[9] The combination of off-pump CABG with bilateral ITA grafting also yields favorable outcomes.[10] However, the rate of bilateral ITA use is still low.[11]

The aims of the present study are to assess the safety and efficacy of off-pump bilateral ITA grafting in patients with LMD and to assess early and 1-year angiographic results of bilateral ITA grafts in these patients.

## PATIENTS AND METHODS

### Patient Population

Between September 2004 and June 2009, 930 patients underwent isolated CABG at Sakakibara Heart Institute. Of those, 884 patients (95.1% of all isolated CABG cases) underwent isolated off-pump CABG and 768 patients (86.9% of all isolated off-pump CABG cases) underwent off-pump bilateral ITA grafting (Table 1). Table 2 shows the preoperative characteristics of these 768 patients, of whom 268 had LMD (LMD group) and 500 did not have LMD (non-LMD group). LMD was defined as the presence of 50% or greater stenosis in any angiographic view according to the Society of Thoracic Surgeons database.

### Operation

General anesthesia was induced with midazolam (0.2 mg/kg) and fentanyl (4 μg/kg). Neuromuscular block was achieved with vecuronium

From the Departments of Cardiovascular Surgery[a] and Anesthesiology,[b] Sakakibara Heart Institute, Tokyo, Japan; and Department of Biostatistics and Epidemiology,[c] Yokohama City University Medical Center, Yokohama, Japan.

Disclosures: None.

Received for publication Sept 17, 2009; revisions received Nov 2, 2009; accepted for publication Nov 27, 2009; available ahead of print March 2, 2010.

Address for reprints: Toshihiro Fukui, MD, PhD, Department of Cardiovascular Surgery, Sakakibara Heart Institute, 3-16-1 Asahi-cho, Fuchu City, Tokyo 183-0003, Japan (E-mail: tfukui-cvs@umin.ac.jp).

0022-5223/$36.00



doi:10.1016/j.jtcvs.2009.11.069

**Abbreviations and Acronyms**

CABG = coronary artery bypass grafting
CAD = coronary artery disease
ITA = internal thoracic artery
LAD = left anterior descending
LMD = left main disease

(0.1 mg/kg). After intubating the trachea, the lung was ventilated with 2% to 2.5% of sevoflurane with an air–oxygen mixture. Nicorandil and landiolol, a short-acting beta-one selective antagonist, were administered throughout the operation. Anticoagulation was achieved with heparin at 300 U/kg after all grafts were harvested for coronary revascularization. Phenylephrine was continuously administered during distal coronary anastomosis to maintain the mean blood pressure at more than 60 mm Hg without accelerating the heart rate. Beta-agonists were administered after the proximal anastomosis if necessary. There was no difference in anesthetic methods in patients with and without LMD.

Bilateral ITA grafts were routinely used in patients who required revascularization of both the left anterior descending (LAD) artery and left circumflex artery territories. Bilateral ITAs were used as in situ grafts in preference to free grafts. In general, the left ITA was used for revascularizing the LAD and the right ITA was used for revascularizing the circumflex artery territory or diagonal branch. However, in patients with unstable hemodynamics caused by critical LMD, the LAD was revascularized with the right ITA first and then the circumflex artery territory with the left ITA. When multiple grafting was necessary in the circumflex artery territory, multiple sequential grafting was applied with the free right ITA. The left ITA was used as an in situ graft in 760 patients (99.0%) and as a free graft in 8 patients (1.0%). The right ITA was used as an in situ graft in 582 patients (75.8%) and as a free graft in 186 patients (24.2%). When the free right ITA was anastomosed to the ascending aorta, an intraoperative epiaortic ultrasound was routinely used to detect a disease-free area of the aorta. When the free right ITA was anastomosed proximally to another graft (left ITA, radial artery, or saphenous vein graft), a Y-composite graft was created.

The operative technique of off-pump CABG has been described.[12] All arterial grafts were harvested in a skeletonized fashion using an ultrasonic scalpel (Harmonic Scalpel, Ethicon Endosurgery, Cincinnati, OH). We grafted all significantly diseased coronary vessels (at least a 50% diameter reduction) larger than 1 mm in diameter. Long segmental reconstruction was performed when the LAD was diffusely diseased or the septal and diagonal arteries were affected by severe atheromatous plaques. An arteriotomy was extended proximally and distally to the intact segment of the LAD. Endarterectomy was performed if the atheromatous plaque was circumferential or too hard to pass a needle through. The left ITA was anastomosed to the LAD with a long onlay patch technique using 7-0 and 8-0 polypropylene running sutures. The detailed technique and outcomes of long segmental reconstruction of the LAD have been described.[13]

## Angiography

Early postoperative angiography was performed in 615 patients (80.1%) after obtaining written informed consents. The median time to an early postoperative angiography was 10 days after surgery (range 1–20 days). If patients became symptomatic during a follow-up period, a diagnostic angiography was performed at that time. Unless patients became symptomatic within 1 year after surgery, a follow-up angiography was performed at 1 year after surgery. Follow-up postoperative angiography was performed in 381 patients (49.6%), and the median time was 12.2 months after surgery (range 2–21 months). Of these patients, 352 (45.8%) underwent both early and 1-year angiographic studies.

**TABLE 1. Distribution of patients undergoing isolated coronary artery bypass grafting**

| | Single ITA | Bilateral ITA | Total |
|---|---|---|---|
| On-pump CABG | 22 | 24 | 46 |
| Off-pump CABG | 116 | 768 | 884 |
| Total | 138 | 792 | 930 |

*CABG*, Coronary artery bypass grafting; *ITA*, internal thoracic artery.

Preoperative, intraoperative, postoperative, and angiographic variables were compared in patients with LMD and without LMD. The institutional review board approved this retrospective study and waived the need for written consents.

Nonelective operations included both emergency and urgent cases according to the definition of the Society of Thoracic Surgeons database. Operative death was defined as death occurring within 30 days after surgery. Low-output syndrome was defined as the postoperative need for any dose of adrenaline or more than 5 $\mu g/kg^{-1}/min^{-1}$ of dopamine or dobutamine. Perioperative myocardial infarction was defined as a positive result for new Q waves in an electrocardiogram or a peak creatine kinase MB level of greater than 10% of total creatine kinase. Respiratory failure was defined as requiring prolonged ventilation (>48 hours) or having pneumonia. A postoperative cerebrovascular accident was defined as having a new stroke or intracranial bleeding confirmed by computed tomography. In patients with preoperative stroke, postoperative stroke was defined as a worsening of the neurologic deficit with new radiologic findings.

Patent graft was defined as a graft without occlusion, significant stenosis (>90%), or string sign. String sign was defined as luminal narrowing throughout the entire conduit, including stenosis of 90% or greater.

Early and 1-year patency rates were calculated by dividing the number of patent grafts by the total number of grafts. If patients with early nonpatent grafts underwent a 1-year angiogram, those nonpatent grafts were also counted as 1-year nonpatent grafts.

## Statistical Analysis

All statistical analyses were performed using StatView 5.0 software (SAS Institute Inc, Cary, NC). Continuous variables are reported as the mean ± standard deviation if they are normally distributed. Otherwise, they are reported as a median. Continuous variables were compared by the Student *t* test, and discrete variables were compared by the chi-square test or Fisher's exact test. Actuarial event-free survival curves were estimated by the Kaplan–Meier method. The log-rank test was used to assess whether there was a difference in survival between subject groups.

# RESULTS

## Clinical Outcomes

Preoperative characteristics of both groups are shown in Table 2. Patients with LMD were older than those without LMD ($P$ = .0226). The rate of unstable angina ($P$ = .0010) and the mean Canadian Cardiovascular Society class ($P$ = .0079) were higher in patients with LMD than in those without LMD. The mean number of diseased vessels was larger in patients without LMD than in those with LMD ($P$ = .0117). Preoperative ejection fraction ($P$ = .0492) and creatinine levels ($P$ = .0318) were significantly better in patients with LMD than in those without LMD. More patients without LMD had a history of congestive heart failure ($P$ = .0359), prior myocardial infarction ($P$ = .0002), previous stroke ($P$ = .0326), and diabetes mellitus ($P$ = .0281) than those with LMD. More patients with

ACD

**TABLE 2. Preoperative variables**

| | All | LMD group | Non-LMD group | *P* value |
|---|---|---|---|---|
| No. | 768 | 268 | 500 | |
| Age, y | 68.0 ± 9.5 | 69.1 ± 9.7 | 67.4 ± 9.3 | .0226 |
| Gender, female | 141 (18.4%) | 56 (20.9%) | 85 (17.0%) | .2182 |
| Body surface area ($m^2$) | 1.7 ± 0.2 | 1.7 ± 0.2 | 1.7 ± 0.2 | .6108 |
| Unstable angina | 239 (31.1%) | 104 (38.8%) | 135 (27.0%) | .0010 |
| CCS | 2.3 ± 0.9 | 2.4 ± 0.9 | 2.2 ± 0.9 | .0079 |
| Ejection fraction (%) | 56.1 ±11.8 | 57.3 ± 11.3 | 55.5 ± 12.0 | .0492 |
| Diseased vessels | 2.8 ± 0.4 | 2.8 ± 0.4 | 2.8 ± 0.4 | .0117 |
| Previous PCI | 222 (28.9%) | 74 (27.6%) | 148 (29.6%) | .6165 |
| Congestive heart failure | 103 (13.4%) | 26 (9.7%) | 77 (15.4%) | .0359 |
| Prior myocardial infarction | 363 (47.3%) | 102 (38.1%) | 261 (52.2%) | .0002 |
| Hypertension | 513 (66.8%) | 174 (64.9%) | 339 (67.8%) | .4679 |
| Diabetes mellitus | 361 (47.0%) | 111 (41.4%) | 250 (50.0%) | .0281 |
| Insulin | 79 (10.3%) | 13 (4.9%) | 66 (13.2%) | .0005 |
| Hyperlipidemia | 470 (61.2%) | 172 (64.2%) | 298 (59.6%) | .2446 |
| Smoking | 461 (60.0%) | 156 (58.2%) | 305 (61.0%) | .4995 |
| Previous stroke | 95 (12.4%) | 24 (9.0%) | 71 (14.2%) | .0326 |
| Peripheral vascular disease | 68 (8.9%) | 21 (7.8%) | 47 (9.4%) | .5525 |
| Creatinine (mg/dL) | 1.2 ± 1.3 | 1.0 ± 0.8 | 1.2 ± 1.6 | .0318 |
| COPD | 31 (4.0%) | 9 (3.4%) | 22 (4.4%) | .6122 |
| Nonelective | 93 (12.1%) | 54 (20.1%) | 39 (7.8%) | <.0001 |
| Preoperative IABP use | 46 (6.0%) | 29 (10.8%) | 17 (3.4%) | <.0001 |
| Redo | 6 (0.8%) | 2 (0.7%) | 4 (0.8%) | >.9999 |

*CCS*, Canadian Cardiovascular Society; *COPD*, chronic obstructive pulmonary disease; *IABP*, intraaortic balloon pump; *LMD*, left main disease; *PCI*, percutaneous coronary intervention.

ACD

LMD had emergency or urgent operations ($P < .0001$) and preoperative use of intraaortic balloon pump ($P < .0001$) than those without LMD.

Target coronary artery vessels of left and right ITA grafts are shown in Table 3. In patients with LMD, the right ITA was used as an in situ graft in 207 patients (77.2%) and as a free graft in 61 patients (22.8%). In patients without LMD, the right ITA was used as an in situ graft in 375 patients (75.0%) and as a free graft in 125 patients (25.0%). There was no statistical difference between the 2 groups in the in situ rate of right ITA ($P = .5472$).

In patients with LMD, left and right ITA grafts were used for the LAD in 189 patients (70.5%) and 78 patients (29.1%), respectively. In patients without LMD, left and right ITAs were used for the LAD in 437 patients (87.4%) and 61 patients (12.2%), respectively. The right ITA was used for the LAD more frequently in patients with LMD than in those without LMD ($P < .0001$). This tendency was also found when the target of the right ITA was compared between patients with unstable angina and patients with stable angina. The right ITA was more frequently used for the LAD in patients with unstable angina than in patients with stable angina (36.5% vs 24.4%, $P = .046$).

Operative and postoperative variables are listed in Table 4. Patients without LMD had a higher mean number of distal anastomoses per patient than those with LMD ($P = .0012$). The rate of long segmental reconstruction of the LAD was higher in patients without LMD than in those with LMD ($P < .0001$). Patients without LMD had significantly longer operation times than those with LMD ($P < .0001$). The transfusion rate was significantly higher in patients with LMD than in those without LMD ($P = .0393$). The operative mortality and incidence of postoperative complications were not significantly different between the 2 groups.

During the follow-up period, 1 patient died of heart failure, 2 patients had recurrent angina, 4 patients had congestive heart failure, and 1 patient had a stroke in the group with LMD. Freedom from death and other cardiac or cerebrovascular events was 96.5% ± 1.2% at 3 years. One patient died of heart failure, 3 patients had recurrent angina, and 9 patients had congestive heart failure in the group without LMD. Freedom from death and other cardiac or cerebrovascular events was 96.3% ± 0.9% at 3 years. There was no significant difference between the groups regarding event-free rate ($P = .8603$).

## Angiographic Outcomes

Early and 1-year postoperative angiograms were performed in 615 patients (80.1%) and 381 patients (49.6%), respectively. Table 5 lists the patency rates of the left and right ITAs at both early and 1-year angiographic studies.

In patients with LMD, the patency rates of the ITA grafts were 98.6% (left ITA) and 98.6% (right ITA) at early

**TABLE 3. Targets of left and right internal thoracic artery grafts**

| | Left internal thoracic artery | Right internal thoracic artery | No. |
|---|---|---|---|
| LMD group (n = 268) | LAD | Diagonal branch | 89 (33.2%) |
| | LAD | Circumflex artery | 95 (35.4%) |
| | LAD | Inflow of other graft | 5 (1.9%) |
| | Diagonal branch | LAD | 8 (3.0%) |
| | Diagonal branch | Circumflex artery | 1 (0.3%) |
| | Circumflex artery | LAD | 66 (24.6%) |
| | Inflow of other graft | LAD | 4 (1.4%) |
| Non-LMD group (n = 500) | LAD | Diagonal branch | 202 (40.4%) |
| | LAD | Circumflex artery | 211 (42.2%) |
| | LAD | Inflow of other graft | 24 (4.8%) |
| | Diagonal branch | LAD | 5 (1%) |
| | Diagonal branch | Circumflex artery | 1 (0.2%) |
| | Circumflex artery | LAD | 49 (9.8%) |
| | Circumflex artery | Diagonal branch | 1 (0.2%) |
| | Inflow of other graft | LAD | 7 (1.4%) |

*LAD*, Left anterior descending artery; *LMD*, left main disease.



angiography and 97.0% (left ITA) and 93.2% (right ITA) at 1-year angiography. There were no significant differences in early ($P > .9999$) and 1-year ($P = .2547$) patency rates between the left and the right ITAs.

In patients without LMD, the patency rates of the ITA grafts were 99.0% (left ITA) and 99.3% (right ITA) at early angiography and 97.6% (left ITA) and 91.6% (right ITA) at 1-year angiography. Although there was no significant difference in the early patency rate ($P > .9999$) between the left and the right ITAs, there was a significant difference in the 1-year patency rate ($P = .0056$).

When patency rates of the left ITA were compared in patients with and without LMD, there were no significant differences in early ($P = .6999$) or 1-year ($P = .9803$) patency rates between the 2 groups. When the patency rates of the right ITA were compared in patients with and without LMD, there were no significant differences in early ($P = .4264$) or 1-year ($P = .7205$) patency rates between the 2 groups.

## DISCUSSION

The present study demonstrates the safety and efficacy of off-pump bilateral ITA grafting in patients with LMD. Furthermore, this study showed good early and 1-year patency rates of bilateral ITA grafts in this patient group.

The current gold standard of care for LMD is CABG. The American College of Cardiology/American Heart Association guidelines recognize only CABG as having a class IA indication for treatment of LMD.[14,15] The evolution of surgical techniques and perioperative management has improved surgical outcomes. Percutaneous coronary intervention procedures recently have been performed for LMD and reported to have comparable results with

**TABLE 4. Operative and postoperative data**

| | All | LMD group | Non-LMD group | *P* value |
|---|---|---|---|---|
| Anastomoses/patient | 4.2 ± 1.2 | 4.0 ± 1.2 | 4.3 ± 1.1 | .0012 |
| Long segment reconstruction of LAD | 309 (40.2%) | 77 (28.7%) | 232 (46.4%) | <.0001 |
| Operation time (min) | 279.5 ± 56.9 | 268.2 ± 56.8 | 285.5 ± 56.1 | <.0001 |
| Transfusion | 268 (34.9%) | 107 (39.9%) | 161 (32.2%) | .0393 |
| Intubation (h) | 9.6 ± 14.8 | 10.0 ± 10.2 | 9.5 ± 16.8 | .6485 |
| Intensive care unit stay (d) | 1.9 ± 7.8 | 2.6 ± 13.0 | 1.5 ± 1.8 | .0598 |
| Operative death (within 30 d) | 7 (0.9%) | 2 (0.7%) | 5 (1.0%) | >.9999 |
| Reexploration because of bleeding | 6 (0.8%) | 1 (0.4%) | 5 (1.0%) | .6706 |
| Low output syndrome | 10 (1.3%) | 6 (2.2%) | 4 (0.8%) | .1055 |
| Perioperative myocardial infarction | 11 (1.4%) | 4 (1.5%) | 7 (1.4%) | >.9999 |
| Severe ventricular arrhythmia | 6 (0.8%) | 0 | 6 (1.2%) | .0969 |
| Atrial fibrillation | 191 (24.9%) | 66 (24.6%) | 125 (25.0%) | .9789 |
| Required hemodialysis | 13 (1.7%) | 7 (2.6%) | 6 (1.2%) | .2492 |
| Stroke | 10 (1.3%) | 3 (1.1%) | 7 (1.4%) | >.9999 |
| Mediastinitis | 10 (1.3%) | 3 (1.1%) | 7 (1.4%) | >.9999 |

*ITA*, Internal thoracic artery; *LAD*, left anterior descending artery; *LMD*, left main disease.

ACD

**TABLE 5. Cumulative angiographic patency rates of left and right internal thoracic artery grafts**

| | Early (n = 615) | 1 y (n = 381) |
|---|---|---|
| Total | 98.9% (1217/1230) | 94.8% (722/762) |
| LMD group | 98.6% (424/430) | 95.1% (251/264) |
| Left internal thoracic artery | 98.6% (212/215) | 97.0% (128/132) |
| Right internal thoracic artery | 98.6% (212/215) | 93.2% (123/132) |
| Non-LMD group | 99.1% (793/800) | 94.6% (471/498) |
| Left internal thoracic artery | 99.0% (396/400) | 97.6% (243/249) |
| Right internal thoracic artery | 99.3% (397/400) | 91.6% (228/249) |

*LMD*, Left main disease.

CABG;[16] however, long-term results have not been reported. A meta-analysis of LMD also supports the superiority of CABG over percutaneous coronary intervention in revascularization of LMD; the study showed that repeated revascularization was less frequent after CABG than after percutaneous coronary intervention.[17] Generally, off-pump CABG is not preferred in patients with LMD because displacement of the heart could induce hemodynamic deterioration.[3] On the other hand, several studies have shown the safety and feasibility of off-pump CABG in patients with LMD.[4-7] Dewey and colleagues[6] reported that the use of cardiopulmonary bypass is an independent risk factor for death in patients with LMD, with an odds ratio of 7.3 (95% confidence interval, 1.3–138.4). Thomas and colleagues[7] reported that off-pump CABG was safely performed in patients with and without LMD. They speculated that the favorable outcomes after off-pump CABG were achieved because of the improved myocardial preservation, reduced reperfusion injury, and absence of the hypothermic insult. Even in those series, bilateral ITA grafting was infrequently performed.

Several institutions have reported that bilateral ITA grafting results in better survival and greater freedom from reintervention than single ITA grafting.[18,19] However, the American College of Cardiology/American Heart Association guidelines still do not recommend the use of bilateral ITA grafting because there are insufficient data for detailed analysis.[14] Bilateral ITA grafting has not become a routine strategy, even in elective patients, for multiple reasons, including increased operative difficulty, increased operating times, and risk of wound complications.[14] There are only a few reports regarding myocardial revascularization with bilateral ITA grafting in patients with LMD.[20] We have routinely used bilateral ITA grafts for CABG when feasible even in high-risk patients with LMD. There are various grafting strategies with bilateral ITA grafts. Although our first choice is the left ITA for the LAD, we use the right ITA for the LAD more frequently in those with LMD than in those without LMD. Patients with unstable hemodynamics cannot tolerate torsion of the left main trunk because of the circumflex position without LAD grafting. In those patients, we graft the LAD with the right ITA and then graft the circumflex territory with the left ITA. The left ITA to the LAD would suffer from increased physical tension when the heart is pulled toward the right during the anastomosis of the circumflex territory. However, in patients with stable hemodynamics, revascularization of the LAD was performed with the left ITA as usual.

The present study used intraaortic balloon counterpulsation in a higher proportion of patients with LMD than in patients without LMD. Suzuki and colleagues[21] demonstrated that using an intraaortic balloon pump during off-pump CABG was effective in high-risk patients. They comment that the effects of intraaortic balloon pump support, such as the reduction of ventricular afterload, improvement of diastolic coronary perfusion, and enhancement of subendocardial perfusion, are beneficial to the displaced heart in maintaining hemodynamic stability during off-pump CABG. These benefits may have influenced the favorable results after off-pump CABG in our study. In the present study, all intraaortic balloon pumps were placed preoperatively. We believe that insertion of an intraaortic balloon pump should not be delayed in hemodynamically unstable patients with LMD.

We have demonstrated that clinical and angiographic outcomes are not significantly different in patients with and without LMD at early and 1-year follow-ups. The 1-year patency rate of the right ITA graft was relatively low in patients without LMD. However, there was no significant difference in the patency rates of the right ITA grafts in patients with or without LMD.

We used the ITA as a skeletonized graft. A skeletonized ITA provides a longer length and better flexibility than a pedicled ITA. Skeletonization ensures that the right ITA reaches the posterolateral vessels through the transverse sinus as an in situ graft. Furthermore, multiple sequential grafting can be performed easily with a skeletonized free right ITA. With the skeletonization technique, using bilateral ITAs may no longer be a risk factor for mediastinitis because the collateral blood supply to the sternum is preserved.[22] In the present study, the overall mediastinitis rate of 1.3% is not particularly high; however, the best practice in the literature is approximately 0.3%.[23] At Sakakibara Heart Insitute, the mediastinitis rate in patients undergoing non-bilateral ITA grafting was 0% (0/116). However, there was no difference regarding the mediastinitis rate between patients with bilateral ITA and patients with non-bilateral ITA ($P = .3756$).

### Study Limitations

Our study has the following limitations. It is a retrospective observational study, not a randomized controlled trial. We did not compare off-pump CABG with bilateral ITAs with other types of CABG (single ITA grafting or conventional on-pump CABG) in patients with LMD; however, at least we showed that our routine off-pump CABG with bilateral ITAs is safe and effective in patients with LMD. In addition, we did not follow up all patients with bilateral ITA grafts. Our findings may not be applicable to patient groups who did not have a follow-up angiogram, namely, the elderly and patients with renal insufficiency.

## CONCLUSIONS

Off-pump bilateral ITA grafting in patients with LMD can be performed safely with acceptable early and 1-year patency rates.

## References


1. Baur HR, Peterson TA, Amar O, Gannon PG, Gobel FL. Predictors of perioperative myocardial infarction in coronary artery operation. *Ann Thorac Surg*. 1981; 31:36-44.
2. Chaitman BR, Rogers WJ, Davis K, Tyras DH, Berger R, Bourassa MG, et al. Operative risk factors in patients with left main coronary-artery disease. *N Engl J Med*. 1980;303:953-7.
3. Watters MP, Ascione R, Ryder IG, Ciulli F, Pitsis AA, Angelini GD. Haemodynamic changes during beating heart coronary surgery with the 'Bristol Technique'. *Eur J Cardiothorac Surg*. 2001;19:34-40.
4. Yeatman M, Caputo M, Ascione R, Ciulli F, Angelini GD. Off-pump coronary artery bypass surgery for critical left main stem disease: safety, efficacy and outcome. *Eur J Cardiothorac Surg*. 2001;19:239-44.
5. Mannam G, Sajja LR, Dandu SB, Pathuri SN, Saikiran KV, Sompalli S. Off-pump coronary revascularization for left main coronary artery stenosis. *Asian Cardiovasc Thorac Ann*. 2008;16:473-8.
6. Dewey TM, Magee MJ, Edgerton JR, Mathison M, Tennison D, Mack MJ. Off-pump bypass grafting is safe in patients with left main coronary disease. *Ann Thorac Surg*. 2001;72:788-91.
7. Thomas GN, Martinez EC, Woitek F, Emmert MY, Sakaguchi H, Muecke S, et al. Off-pump coronary bypass grafting is safe and efficient in patients with left main disease and higher EuroScore. *Eur J Cardiothorac Surg*. 2009;36:616-20.
8. Taggart DP, D'Amico R, Altman DG. Effect of arterial revascularization on survival: a systematic review of studies comparing bilateral and single internal mammary arteries. *Lancet*. 2001;358:870-5.
9. Cameron A, Davis KB, Green G, Schaff HV. Coronary bypass surgery with internal-thoracic-artery grafts—effects on survival over a 15-year period. *N Engl J Med*. 1996;334:216-9.
10. Kim KB, Cho KR, Chang WI, Lim C, Ham BM, Kim YL. Bilateral skeletonized internal thoracic artery graftings in off-pump coronary artery bypass: early result of Y versus in situ grafts. *Ann Thorac Surg*. 2002;74:S1371-6.
11. Tabata M, Grab JD, Khalpey Z, Edwards FH, O'Brien SM, Cohn LH, et al. Prevalence and variability of internal mammary artery graft use in contemporary multivessel coronary artery bypass graft surgery: analysis of the Society of Thoracic Surgeons National Cardiac Database. *Circulation*. 2009;120:935-40.
12. Fukui T, Takanashi S, Hosoda Y, Suehiro S. Early and midterm results of off-pump coronary artery bypass grafting. *Ann Thorac Surg*. 2007;83:115-9.
13. Fukui T, Takanashi S, Hosoda Y. Long segmental reconstruction of diffusely diseased left anterior descending coronary artery with left internal thoracic artery with or without endarterectomy. *Ann Thorac Surg*. 2005;80:2098-105.
14. Eagle KA, Guyton RA, Davidoff R, Edwards FH, Ewy GA, Gardner TJ, et al., American College of Cardiology; American Heart Association. ACC/AHA 2004 guideline update for coronary artery bypass graft surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1999 Guidelines for Coronary Artery Bypass Graft Surgery). *Circulation*. 2004;110:e340-437.
15. Smith CR. Surgery, not percutaneous revascularization, is the preferred strategy for patients with significant left main coronary stenosis. *Circulation*. 2009;119:1013-20.
16. Teirstein PS. Percutaneous revascularization is the preferred strategy for patients with significant left main coronary stenosis. *Circulation*. 2009;119:1021-33.
17. Takagi H, Kawai N, Umemoto T. Stenting versus coronary artery bypass grafting for unprotected left main coronary artery disease: a meta-analysis of comparative studies. *J Thorac Cardiovasc Surg*. 2009;137:e54-7.
18. Lytle BW, Blackstone EH, Loop FD, Houghtaling PL, Arnold JH, Akhrass R, et al. Two internal thoracic artery grafts are better than one. *J Thorac Cardiovasc Surg*. 1999;117:855-72.
19. Endo M, Nishida H, Tomizawa Y, Kasanuki H. Benefit of bilateral over single internal mammary artery grafts for multiple coronary artery bypass grafting. *Circulation*. 2001;104:2164-70.
20. Paolini G, Zuccari M, Di Credico G, Gallorini C, Stefano PL, Castiglioni A, et al. Myocardial revascularization with bilateral internal thoracic artery in patients with left main disease: an incremental risk? *Eur J Cardiothorac Surg*. 1994;8:576-9.
21. Suzuki T, Okabe M, Handa M, Yasuda F, Miyake Y. Usefulness of preoperative intraaortic balloon pump therapy during off-pump coronary artery bypass grafting in high-risk patients. *Ann Thorac Surg*. 2004;77:2056-9.
22. Higami T, Maruo A, Yamashita T, Shida T, Ogawa K. Histologic and physiologic evaluation of skeletonized internal thoracic artery harvesting with an ultrasonic scalpel. *J Thorac Cardiovasc Surg*. 2000;120:1142-7.
23. Rosmarakis ES, Prapas SN, Rellos K, Michalopoulos A, Samonis G, Falagas ME. Nosocomial infections after off-pump coronary artery bypass surgery: frequency, characteristics, and risk factors. *Interact Cardiovasc Thorac Surg*. 2007;6:759-67.