National Survey of Coronary Artery Bypass Grafting for Coronary Stenosis Caused by Kawasaki Disease in Japan

Etsuko Tsuda, MD; Soichiro Kitamura, MD; and The Cooperative Study Group of Japan

Background—We surveyed the national experience of coronary artery bypass grafting (CABG) for coronary sequelae of Kawasaki disease (kDa) in 2002.

Methods and Results—A questionnaire was returned from 323/552 (59%) institutions. Two hundred forty-four patients (188 male 56 female) since 1975 were identified. The mean number of grafts was 1.8 and the age at operation ranged from 1 to 44 years (median 11 years). The interval from the onset of kDa to operation ranged from 1 month to 42 years (median 8 years), whereas the follow-up period was from 7 days to 25 years (median 5 years). Prevalent myocardial infarction was found in 70 patients (28%). When the age at operation was older than 12 years, patency rates for internal thoracic artery grafts (ITA) at 1, 5, and 15 years were 95%, 91%, and 91%, respectively (n=156). When the age at operation was younger than 12 years, the corresponding values were significantly lower, with 1, 5, and 15 years being 93%, 73%, and 65%, respectively (n=146) (P<0.05). Reoperation was performed in 14 patients (6%). Death occurred in 15 patients (6%). None of the 14 late deaths were sudden. Six of 8 patients with a left ventricular ejection fraction (LVEF) <40% died.

Conclusion—The results of ITA in those aged 12 years or older were favorable. LVEF influenced prognosis. (Circulation, 2004;110[suppl II]:II-61–II-66.)

Key Words: Kawasaki disease ■ coronary artery disease ■ coronary artery bypass grafting

National surveys of Kawasaki disease (kDa) in Japan have been performed every 2 years since 1976. Recently, ≈6000 to 8000 kDa patients have been reported each year.1,2

In the recent study, coronary aneurysms were present in ≈6% at 1 month after the onset of kDa. The death rate caused by kDa and its cardiac sequelae was <0.1%.3 However, the incidence of coronary revascularization was not investigated. A national survey of catheter interventions after kDa was performed in 2000,4 whereas a previous multicenter cooperative study for coronary artery bypass grafting (CABG) after kDa in Japan was performed in 1991.5 After that survey, it was unknown how many patients underwent CABG for coronary arterial lesions caused by kDa. Knowledge about the results of CABG after kDa and its long-term outcome should help the management of future patients with severe coronary stenotic lesions caused by kDa.

Methods
The purpose of the study was to determine the prevalence and results of CABG for coronary stenosis caused by kDa in Japan. We surveyed all the institutions belonging to the Japanese Association for Thoracic and Cardiovascular Surgery by mail in February 2002. The contents of the questionnaire are listed here: sex; date of birth; date of operation; date of reoperation; history of kDa; date of the onset of kDa; medication of the acute phase of kDa; history of myocardial infarction; coronary arterial lesions at operation; used grafts; graft patency; date of angiography; left ventricular ejection fraction by left ventriculogram; catheter intervention; cardiac events (death, reoperation, myocardial infarction, angina, arrhythmia); date of the latest clinic attendance; medication after operation; and postoperative examination (treadmill test, radioisotope myocardial imaging).

Our questionnaires were returned from 323 of 552 (59%) institutions. We analyzed the prevalence of CABG, the graft patency, and the outcome of the patients who underwent CABG. Patency of the graft at postoperative angiograms was classified as patent, string sign, or occluded. For this study, a string sign was regarded as occluded. Graft patency rates were analyzed by the respective graft. Cardiac events after CABG were investigated for the group undergoing saphenous vein (SVG) and for the group undergoing arterial grafting without SVG.

Data Analysis
The mean values are shown as mean±1 SD. Graft patency rates and patient survival rates were analyzed by the Kaplan–Meier method and differences were assessed by the log–rank examination test. Scheffe S test was used for differences between groups after the Bartlett test was performed. Differences were considered statistically significant at P<0.05.

Results
Number of Operations
A total of 269 patients were reported by 54 institutions. The number of the reported patients by each institution were as follows: <5 patients were reported by 41 institutions, 5 to 9 patients were reported by 8 institutions, 10 to 19 patients were reported by 5 institutions, 20 to 49 patients were reported by 5 institutions.
reported by 2 institutions, 20 to 29 patients were reported by 1 institution, ≥ 30 patients were reported by 2 institutions. A history of kDa was uncertain in 25 patients (10%). Twenty patients among those 25 patients had undergone CABG when older than age 20 years. These patients were excluded from this study.

The remaining 244 patients who had undergone CABG since 1975 were included; 188 were male (77%) and 56 were female (23%). Four patients had undergone off-pump CABG. One patient underwent mitral valve replacement and 1 patient underwent mitral valvuloplasty. The number of operations per year since 1975 is shown in Figure 1.

Patient Population
The number of patients by age at operation is shown in Figure 2. The age at operation ranged from 1 to 44 years (median 11 years). The mean age at operation was 13.8 years. The age at onset of kDa was as follows: younger than 1 year, 76 (32%) patients; 1 year, 41 patients; 2 years, 35 patients; 3 years, 25 patients; 4 years, 20 patients; 5 years, 10 patients; 6 years, 10 patients; 7 years ≤ 17 patients; and unknown age, 10 patients. The onset of kDa was younger than 5 years in 197 patients (84%). The interval from the onset of kDa to operation ranged from 1 month to 42 years (median 8 years). The number of patients by interval from the onset of kDa to operation was as follows: younger than 5 years, 68 patients; 5 years to younger than 10 years, 62 patients; 10 years to younger than 15 years, 54 patients; 15 years to younger than 20 years, 33 patients; and 20 years or older, 17 patients.

Treatment in the Acute Phase of kDa
Acute phase treatment of kDa was as follows: aspirin for 63 (25%) patients; aspirin and intravenous immunoglobulin (IVIG) for 28 (12%) patients; IVIG for 11 (5%) patients; steroids and aspirin for 7 (3%) patients; steroids for 4 patients; steroids, IVIG, and aspirin for 2 patients; steroids and IVIG for 1 patient; and unrecorded treatment for 128 (53%) patients.

History of Myocardial Infarction
Myocardial infarction before CABG occurred in 70 patients (28%). A history of myocardial infarction ≥ 2 events was found in 15 patients (6%). The locations of myocardial infarction were as follows: posteroinferior in 41 (48%) patients; anteroseptal in 38 (48%) patients; lateral in 4 (5%) patients; and other in 3 (3%) patients.

Follow-Up
In the questionnaire, the day of the latest outpatient department (OPD) visit was provided for 236 patients and not given for 8. The age at the latest OPD visit ranged from 1 year to 50 years (median 20 years). In this study, the follow-up period means the interval from operation to the latest OPD attendance and ranged from 7 days to 25 years (median 5 years). The number of patients per follow-up period was as follows: < 1 year, 31 patients; 1 year to < 5 years, 79 patients; 5 years to < 10 years, 59 patients; 10 years to < 15 years, 40 patients; and > 15 years, 27 patients.

A postoperative angiogram was performed in 238 (98%) of the 244 patients. The interval from operation to the latest postoperative angiogram ranged from 6 days to 22.7 years (median 1.8 years). The number of patients by interval from operation to the latest postoperative angiogram was as follows: < 1 year, 87 patients; 1 year to < 5 years, 72 patients; 5 years to < 10 years, 40 patients; 10 years to < 15 years, 28 patients; and > 15 years, 11 patients.

CABG
Among the 244 patients undergoing CABG, the number of vessels grafted were: single graft, 102 (42%) patients; 2 grafts, 107 (44%) patients; 3 grafts, 30 (12%) patients; 4 grafts, 4 (1.6%) patients; and 1 patient (0.4%) received 5 grafts. A sequential graft in 4 patients and a Y graft in 1 patient were also performed. The mean number of grafts was 1.8 per patient. Grafts used were the internal thoracic artery (ITA) in 309 (70%) patients, SVG in 85 (20%) patients, the gastroepiploic artery (GEA) in 32 (7%) patients, radial artery in 8 (2%) patients, and other in 1 patient. The total number of grafts was 435. The number of grafts by year is shown in Figure 3. The target coronary arteries were the left anterior descending artery (LAD) in 232 (52%) patients, the right coronary artery (RCA) in 129 (30%) patients, the diagonal branch in 25 (6%) patients, the left circumflex (LCX; posterolateral artery, posterior descending
coronary artery) in 25 (6%) patients, and the obtuse marginalis (OM) in 24 (6%) patients.

The number of coronary artery lesions in the target vessels were as follows. In the LAD, localized stenosis, occlusion, and unrecorded there were 114, 80, and 38 lesions, respectively. In this study, segmental stenosis was regarded as occluded. In the RCA, for localized stenosis, occlusion, and unrecorded, there were 34, 73, and 22 lesions, respectively. In the diagonal branch, for localized stenosis, occlusion, and unrecorded, there were 17, 1, and 7 lesions, respectively. In the LCX, for localized stenosis, occlusion, and unrecorded, there were 14, 3, and 8 lesions, respectively. In the OM, for localized stenosis, occlusion, and unrecorded, there were 20, 2, and 2 lesions, respectively.

Treatment After CABG

Medicine after CABG was administered in 169 patients (69%), none was given in 31 patients (13%), and medication was unrecorded in 44 patients (18%). One hundred sixty-five patients (68%) received anticoagulants and 109 (45%) received antiplatelet agents. Antiplatelet agents plus warfarin were given to 50 patients (21%). Warfarin alone was administered to 6 patients (2%).

Treatment besides anticoagulants was given to 71 patients (30%). Medicines used were: nitrates, 37 (16%) patients; calcium antagonists, 26 (11%) patients; β-blockers, 14 patients (6%); antiarrhythmics, 5 (2%); angiotensin-converting enzyme inhibitor, 4 patients; diuretics, 3 patients; 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitor, 3 patients; digoxin, 2 patients; angiotensin I receptor blocker, 1 patient; and others, 2 patients.

Graft Patency

The patency of the respective grafts at the time of angiography was: ITA, 266 of 302 (88%); SVG, 50 of 79 (63%); GEA, 21 of 29 (72%); and radial, 7 of 7 (100%). A string sign was detected in 19 (6%) of the 338 arterial grafts.

Patency rates for ITA grafts at 1, 5, and 15 years were 95%, 91%, and 91%, respectively (n=156). When the age at operation was younger than 12 years, the corresponding values at 1, 5, and 15 years were 93%, 73%, and 65%, respectively (n=146). The patency rate for age at operation older than 12 years in ITA grafts was significantly higher than when the age at operation was younger than 12 years (P<0.001) (Figure 5).

When the age at operation was 12 years or older, patency rates of SVG at 1, 5, and 15 years were 97%, 85%, and 63%, respectively (n=37). When the age at operation was younger than 12 years, the corresponding values of SVG at 1, 5, and 15 years were 74%, 51%, and 47% (n=42). There was no significant difference between those 2 groups (Figure 6).

Cardiac Events

Fifteen deaths (6%) occurred among the 244 patients who had undergone CABG (Table 1). One operative death occurred in 1986. Nine of the 14 late deaths were sudden. The age at operation ranged from 15 months to 16 years (median 6 years). Two of the 9 patients had occluded grafts, and of the remaining 7 patients, 4 sudden deaths occurred within 1 year after operation. Three sudden-death patients had undergone SVGs, whereas the other patient had undergone CABG of the
left ITA to LAD at age 18 months in 1987. Three late sudden deaths occurred at 8 years, 12 years, and 15 years postoperatively. All 3 patients had undergone a graft to the LAD, using left ITA, SVG and left ITA, and SVG, respectively.

Two patients died after cardiac transplantation, which was performed because of intractable cardiac failure. One patient died of cardiac failure. There were 2 noncardiac deaths.

Reoperation
Fourteen of 244 patients underwent reoperation (6%) (Table 1). However, the reoperation rate was 20% for the 65 patients with >1 graft occlusion. The age at the first operation ranged from 2 to 16 years (median 9 years), and that at reoperation ranged from 6 to 29 years (median 14 years). The interval from the first operation to reoperation ranged from 20 days to 14 years (median 5 years). Thirteen patients underwent a repeat graft to a vessel previously grafted. Of the initial grafts, the SVG had been used in 4 patients, and the ITA was used in 10 patients. The LAD was involved in 13 and the RCA was involved in 1. The second grafts were patent in 10 patients.

Catheter Intervention for Anastomotic Stenosis
Catheter interventions for anastomotic stenosis were performed for 18 lesions in 17 patients (7%) (Table 1). Two patients had a catheter intervention because of cardiac events, one being syncope, and the other being angina of effort. The age at catheter intervention ranged from 4 to 30 years (median 13 years). The age at operation for these patients ranged from 2 to 27 years (median 11 years). The interval from operation to intervention ranged from 11 days to 15 years (median 6 months).

Percutaneous transluminal balloon angioplasty (PCBA) for 12 lesions of the arterial grafts was performed. The graft lesions were as follows: left ITA to LAD, 8: RITA to RCA, 3: and GEA to RCA, 1. PCBA was effective in 11 lesions (92%). Although PCBA was performed in 4 lesions involving the SVG to RCA, it was effective in only 1. Stent implantation for SVG to LAD stenosis was successful in 1 patient, whereas stent implantation for left ITA to LAD was performed in 1 other patient.

Intervention for Native Artery Lesions
Catheter interventions after CABG were performed in 5 lesions in 5 patients (2%). Four patients underwent catheter intervention for a vessel other than the grafted vessel. Three had percutaneous transluminal coronary rotational ablation and 1 had PCBA. One patient underwent percutaneous transluminal coronary rotational ablation for the same vessel that occluded its graft.

Other Cardiac Events
Other cardiac events after CABG occurred in 4 patients (Table 2). One patient underwent pacemaker implantation at operation. One patient with graft occlusion had an acute myocardial infarction 6 years after operation. Two patients had ventricular tachycardia.

Postoperative Clinical Status
Status of the 229 survivors was as follows: 205 were classified as New York Heart Association (NYHA) I and 8 were classified as NYHA II. Status was unrecorded in 16 patients. Four female patients had delivered children.

The left ventricular ejection fraction (LVEF) was recorded in 159 patients (64%) being: ≥50% in 138, <50% to ≥40%
in 13, and <40% in 8. The number of deaths in those groups was 2, 2, and 6, respectively (Table 2). There were significant differences between the groups (P<0.01). The patients with a LVEF <40% had a poor prognosis.

The results of treadmill tests were provided for 93 patients (38%). Ischemic changes in the electrocardiogram were detected in 18 patients (7%). Seventy-five patients (31%) had no such changes. Results of RI myocardial imaging were provided in 104 patients (43%). Myocardial damage or myocardial ischemia was detected in 46 patients (19%). Fifty-eight scans were normal (24%).

Discussion

Few CABG operations for coronary stenosis caused by kDa were performed in 1980,6 but by 1990 they had increased.7 In the past 5 years, according to the statistics of the Japanese Thoracic Surgery Association, the number of CABG after kDa as follows; 1996, 19; 1997, 19; 1998, 24; 1999, 29; and 2000, 27. CABG for kDa has been performed in ~30 patients per year recently. The prevalence based on annual attacks of kDa in Japan is ~0.5%. CABG was performed more often in males than in females, with a ratio of ~3:1. This ratio resembles that of the prevalence of giant aneurysms as a cardiac sequelae after kDa.2

Although the largest number of patients at the onset of kDa were younger than 0 years, the age at operation and the interval from the onset of kDa to operation varied. Deciding the optimal time for CABG is difficult and depends on the characteristics of the coronary arterial lesions caused by kDa. The degree of progression of coronary stenotic lesions after kDa varies, and the rate differs from patient to patient. Stenotic lesions caused by intimal thickening progress only slowly in most patients.8–10 Many patients likely to benefit from CABG are asymptomatic but are at risk for acute myocardial infarction, which most often complicates giant aneurysms without stenosis. Correct indications and timing of CABG surgery after kDa greatly contribute to the patency of the grafts.11

ITA grafts have been common since the middle 1980s.11 These grafts allow for somatic growth in children and have prolonged good patency.12 Although the patency rates of SVG were lower than that for ITA grafts, some patients have maintained prolonged patency of a SVG.13 ITA grafts are more likely to be patent if the age at operation is 12 years or older, according to this study, presumably because at this age the diameters of the vessels are appropriate for anastomosis. However, CABG may be successful at age 2 years or older in skilled surgical hands.6,8 Although the application of CABG for kDa may be limited in children, it can be as safely performed for older children and young adults as it is in older adults.

There are 2 main reasons for graft occlusion. One is competition from native coronary flow, and the other is scar formation at the anastomatic site, especially in young children.15 For anastomatic stenosis of ITA grafts, PCBA is useful.16 When needed, it should be performed early after CABG. The procedure decreases the number of reoperations. A string sign was detected in 6% of the arterial grafts. Three patients also had a string sign in angiograms performed after reoperation to the same native arteries. The main reason for this phenomenon may be competition of flow between the graft and native coronary artery. Furthermore, intimal thickening of the native coronary arterial wall may be one cause of graft occlusion. This problem must be resolved to improve the patency rates of the grafts.

The 2 major causes of death for patients with coronary arterial lesions caused by kDa are sudden death and cardiac failure.2–9 Sudden deaths were more common in the present study, and ITA grafts appeared to be better at preventing sudden death. The prognosis is poor for patients with a decreased LVEF. Cardiac failure is caused by myocardial damage caused by myocardial infarction, and severe myocardial damage often results in fatal arrhythmias.17 The extent of myocardial damage greatly influences the prognosis. To prevent the damage, the timing of coronary revascularization needs to be optimal.

Anticoagulant therapy after CABG was given to 68% of the patients. Its purpose is to prevent thrombus formation in the aneurysm and sudden death caused by acute myocardial infarction. The exact indications for long-term anticoagulation require clarification. Other medication may be required for the treatment of cardiac failure, myocardial protection, and arrhythmias. This study shows that decreased LVEF adversely influences the prognosis. Such data will have to be investigated and guidelines for medication should be developed in the future.

The postoperative condition of patients surviving CABG is good. However, most of the patients who have undergone CABG have multiple vessel disease caused by kDa. Progression of disease in nongrafted native coronary arteries and the patency of the grafts in the long-term require life-long follow-up. Furthermore, it is important to prevent further myocardial infarction and decrease in LVEF. Good coronary revascularization prevents death and improves the quality of life for many years.15 Combined use of catheter interventions and surgery for native coronary artery and post-CABG lesions are needed for coronary revascularization in the long-term.

Our study is limited because the indication for CABG, the follow-up period, and the timing of the angiographic studies after CABG are not standard, and the study is retrospective and based on multi-institution data by the limited questionnaires. Furthermore, because of improvement of surgical technique for CABG over 25 years, it was difficult to discuss the patency of the grafts and the prognosis of the patients as a whole without considering the change of the time.

Conclusion

Two hundred forty-four patients (188 male 56 female) encountered since 1975 were reviewed by questionnaire. The mean number of the grafts was 1.8. Patency rates of ITA graft in those aged 12 years or older were favorable. LVEF influenced the prognosis.

Acknowledgments

We greatly appreciate all the surgeons who participated in this survey. We thank Professor Peter Olley and Dr Setsuko Olley for their kind English language consultation.
The Department of Surgery or Department of Cardiovascular Surgery were involved in the following 54 participating institutions in 2002: Nara Medical University School of Medicine (Shigeki Taniguchi, MD); Tokyo Women’s Medical University (Masahiro Endo, MD); Osaka University Graduate School of Medicine (Hikaru Matsuda, MD); Kinki University School of Medicine (Takehiro Inoue (MD); Nippon Medical School (Hitoshi Yamaguchi, MD); Kurume University (Nobuhiko Hashida, MD); Kitazato University Hospital (Kunioyoshi Okahashi, MD); Fukushima University School of Medicine (Tadashi Tashiro, MD); Sakakibara Heart Institute (Takao Ida, MD); Yamato Seiwa Hospital (Akihiro Nabuchi, MD); Toranomon Hospital (Naruse Yoshihiro, MD); Keio University School of Medicine (Hitoshi Kobayashi, MD); Hiroshima City Hospital (Osamu Oba, MD); Kobe City General Hospital (Michihiro Nasu, MD); Kanagawa Cardiovascular and Respiratory Center, (Hirokazu Kajiwara, MD); Shin-tokyo Hospital (Hitoshi Hirose, MD); Omiya Medical Center, Jichi Medical College (Atsushi Yamaguchi, MD); Funabashi Municipal Medical Center (Yoshinari Takahara, MD); Oita University Hospital (Tetsuo Hadama, MD); Tenri Hospital (Takaaki Sugita, MD); Sendai National Hospital (Masahiro Obuchi, MD); Toyama Medical and Pharmaceutical University (Kazuaki Fukahara, MD); Nagasaki University Graduate School of Biomedical Sciences (Kiyoyuki Eishi, MD); Omura Municipal Hospital (Tatsuya Imada, MD); Ryukyu University Hospital (Kageharu Koja, MD); Tsukiyama General Hospital (Chiaki Waki, MD); Ehime University School of Medicine (Kanji Kawachi, MD); Saijoiku Yamaguchi General Hospital (Tatsuo Oda, MD); Hyogo College of Medicine (Yuji Miyamoto, MD); Mutsu Red Cross Hospital (Mitsuhiko Matsumoto, MD); Nagano Children’s Hospital (Yorikazu Harada, MD); Shizuoka Red Cross Hospital (Shigei Higashi, MD); Hamamatsu Medical Center (Hiroshi Hata, MD); Tosei Hospital (Toshihiko Ichihara, MD); Yamada Red Cross Hospital (Yoshiko Katayama, MD); Osaka Medical College (Yoshishide Sawada, MD); Koshigaya Hospital Dokkyo University of Medicine (Nobuaki Kaki, MD); Saitama Medical School (Syuei Kyo, MD); University of Yamashita Faculty of Medicine (Masahiko Matsumoto, MD); Mitsui Memorial Hospital (Takeshi Miyairi, MD); Mito Saishikei General Hospital (Setsuo Katoaka, MD); Kikuna Memorial Hospital (Noboru Murata, MD); Toyohashi Higashi Hospital (Masaaki Hashimoto, MD); Sapporo National Hospital (Koji Ishi, MD); Hiroaki University School of Medicine (Ikuo Fukuda, MD); Gunma Graduate School of Medicine (Yasu Morishita, MD); Gunma Prefectural Cardiovascular Center (Tatsuo Kaneko, MD); Keio University School of Medicine (Honkei Shin, MD); Nagoya City University Graduate School of Medical Science (Akira Mishima, MD); Jyuntendo Hospital (Atsushi Amano, MD); Jichi Medical College (Morito Kato, MD); Tachikawa General Hospital (Shigetaka Harutani, MD); Kushi General Hospital (Makoto Takahira, MD); National Cardiovascular Center (Junjiro Kobayashi, MD, and Katsutoshi Yagihara, MD).

References
National Survey of Coronary Artery Bypass Grafting for Coronary Stenosis Caused by Kawasaki Disease in Japan
Etsuko Tsuda, Soichiro Kitamura and The Cooperative Study Group of Japan

Circulation. 2004;110:II-61-II-66
doi: 10.1161/01.CIR.0000138194.61225.10
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2004 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/110/11_suppl_1/II-61

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/