Improved Long-Term Prognosis of Elderly Women in the Era of Sirolimus-Eluting Stents

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Background: The angiographic characteristics and prognosis in elderly women in relation to the therapeutic impact of sirolimus-eluting stents (SES) need to be clarified.
Methods and Results: Quantitative coronary angiography analysis was performed in 1,374 patients with coronary artery disease: 670 patients were treated with a bare metal stent (BMS) and the remaining 704 were treated with SES. Patients were divided into 4 groups according to gender and age (<75 years M/F, ≥75 years M/F), and major adverse cardiovascular events (MACE) were compared among them. Women ≥75 years old tended to have 3-vessel disease with small vessel size and the incidence of MACE in this group was high in the BMS era. However, in the SES era, this prognosis improved by reducing all-cause death and target vessel revascularization.
Conclusions: Using SES has a therapeutic advantage for the high-risk population of elderly women with angiographically unsuitable lesions for percutaneous coronary intervention. (*Circ J* 2009; **73:** 1219–1227)

Key Words: Coronary artery disease; Elderly women; Sirolimus-eluting stent

Many pivotal trials have demonstrated that the sirolimus-eluting stent (SES) has significantly decreased the rate of restenosis and the need for recurrent intervention compared with bare metal stents (BMS)[1,2] In the real world, the SES is used for more complex lesions and favorable results have been achieved for percutaneous coronary intervention (PCI), especially a reduction in the need for revascularization[3–7]

Coronary artery disease (CAD) is now the main cause of death in women[8] The Women's Ischemia Syndrome Evaluation (WISE) Study demonstrated that women, especially older women, are particularly at risk of increased morbidity and mortality[9–11] Other studies evaluating the outcome of PCI have also reported higher rates of mortality and major complications in women compared with men[12–16] Therefore, it is possible that the poor outcome of PCI in elderly women is related to the development of severe atherosclerotic changes, probably because of clustering of coronary risk factors. However, there is a lack of data regarding the characteristics and prognosis in elderly women with CAD, and it remains unknown whether SES reduces the major adverse cardiovascular events (MACE) and improves the prognosis in this particular population.

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Methods

Patients

From April 2000 through December 2005, 2,597 patients with CAD underwent PCI at the National Cardiovascular Center, Suita, Japan (**Figure 1**). In Japan, SES became commercially available in August 2004, so in the present study, the BMS era was defined as between April 2000 and July 2004, and the SES era was between August 2004 and December 2005.

Of the total, 1,232 patients were treated in the BMS era and 1,365 patients were treated in the SES era. Patients with a history of coronary artery bypass graft surgery and patients with chronic total occlusion were excluded from the study because of the difficulty of quantitative coronary angiography (QCA) analysis. In addition, patients treated with balloon angioplasty, rotational atherectomy or directional coronary atherectomy alone were also excluded. In the SES era, we excluded patients treated with BMS that had been indicated because of planned surgery, intolerance of ticlopidine or the presence of large vessels >4.0 mm diameter. In the Osaka area, the Committee of Reimbursement for Health Insurance recommends that SES should not be used for patients with acute coronary syndrome, so patients treated with a BMS for acute coronary syndrome in the SES era were also excluded. Thus, the number of patients treated with a BMS in the SES era was 216 and that with SES was 704, and the percentage use of SES in the SES era was 52%. Finally, 670 patients were included in the BMS era and 704 in the SES era. We then subdivided these populations into 4 groups according to gender and age: men <75 years old, men ≥75 years old, women <75 years old, women ≥75 years old[17,18] The Ethical Review Board gave approval and the study was conducted according to the ethical principles of the Declaration of Helsinki and Good Clinical Practice guidelines. All subjects gave signed informed consent.

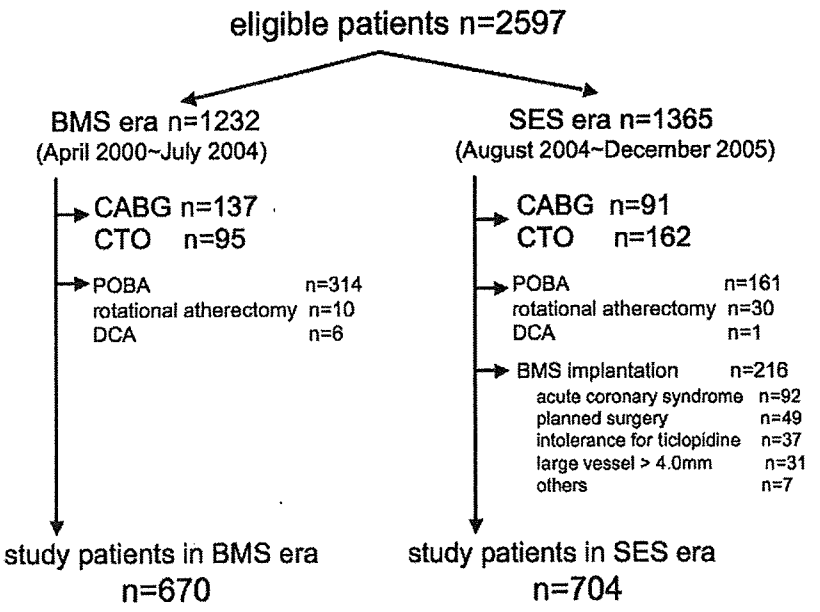

Figure 1. Flow chart of the present study. BMS, bare metal stent; SES, sirolimus-eluting stent; CABG, coronary artery bypass grafting; CTO, chronic total occlusion; POBA, plain old balloon angioplasty; DCA, directional coronary atherectomy.

Coronary Angiography and Quantitative Analysis

Selective coronary angiography was performed in multiple projections after administration of intracoronary nitroglycerin (0.125–0.25 mg). The angiographic characteristics of CAD were evaluated by computer-assisted quantitative analysis (CMS-QCA ver. 4.0, Medis, Leiden, The Netherlands), as reported previously[19] Briefly, we measured the diameter of the middle section in each major coronary segment (segments 1–3 of the right coronary artery, segments 6–8 of the left anterior descending artery, and segments 11 and 13 of the left circumflex artery) in order to calculate the average vessel diameter (AVD) for each patient. We defined segments with an irregular edge that narrowed to a diameter ≤1.5 mm as diseased lesions and calculated the average lesion length (ALL). In a previous study, lumen diameter <1.5 mm was related with sufficient sensitivity and specificity to fractional flow reserve <0.75, a level highly inducive to causing myocardial ischemia[20] The far distal portions of segments 8 and 13 that had a smooth and regular edge were not included in the ALL measurements. The QCA data were assessed by an experienced cardiologist (I.M.) who was unaware of the patients' status.

PCI Procedure

All procedural decisions, including device selection and adjunctive pharmacotherapy, were made at the discretion of the individual PCI operator. Intravenous heparin (5,000 IU) and intracoronary nitroglycerin (0.5 mg) were administered before PCI. After stent implantation, angiographic optimization was performed by high-pressure dilatation to achieve an acceptable angiographic result. Intravascular ultrasound was used according to the operator's decision. Procedural success was defined as residual stenosis <20% without major complications. All patients received 324 mg/day of aspirin for at least 24 h before the procedure. Dual antiplatelet therapy (aspirin 300 mg and ticlopidine 200 mg) was given to all patients treated with BMS for 2 weeks and in those treated with SES for at 3–12 months. For the assessment of restenosis, exercise test or stress scintigraphy was routinely performed at 6–8 months after PCI. If myocardial ischemia was noted in this initial non-invasive testing, follow-up coronary angiography was performed.

The following types of BMS were implanted: Multi-Link plus (Guidant, Santa Clara, CA, USA) 263 patients (39%); BX-Velocity (Cordis, Johnson & Johnson, Miami Lakes, FL, USA) 170 patients (25%); NIR (Medinol, Jerusalem, Israel; and Scimed, Boston Scientific, Maple Grove, MN, USA) 95 patients (14%); Multi-Link Penta (Guidant) 75 patients (10%); Duraflex (Avantec Vascular) 50 patients (7%); S670 (Medtronic, Shoreview, MN, USA) 17 patients (3%). In the SES era, Cypher (Cordis, Johnson & Johnson) was the only type of drug-eluting stent used.

Clinical Parameters and Follow-up

All the patients underwent assessment of coronary risk factors, angiography, and laboratory analyses including fasting glucose, hemoglobin A1c (HbA1c), total cholesterol (TC), triglycerides (TG), high-density lipoprotein-cholesterol-(HDL-C), low-density lipoprotein-cholesterol (LDL-C) and creatinine levels. Body mass index (BMI) was calculated as weight (kg)/height (m)^2.

Follow-up information was obtained at the outpatient's clinic or by a review of the medical records. Follow-up was completed for all patients (100%). The primary endpoint was defined as all-cause mortality, and the secondary endpoint was the occurrence of the MACE, which included all-cause death, non-fatal myocardial infarction (MI), heart failure (HF) and target lesion revascularization (TLR) related to PCI procedure and occurring in the follow-up period.

HF was diagnosed if a patient showed signs of exertional dyspnea, orthopnea, rales in more than one-third of the lung fields, elevated jugular venous pressure or pulmonary congestion on chest X-ray related to cardiac dysfunction. MI was defined as 2 or more of the following: (1) typical chest pain >20 min duration not relieved by nitroglycerin; (2) serial ECG recordings showing changes from baseline in ST-T and/or Q-waves in 2 or more contiguous leads; (3) elevation of serum creatine kinase >2-fold of normal. TLR was defined as repeat PCI or coronary bypass surgery, performed because of restenosis or a new stenotic lesion in the target vessel. Definite and possible stent thrombosis were defined on the basis of the Academic Research Consortium

Table 1. Patient Characteristics in the BMS Era

	Men		Women	
	<75 years (n=406)	≥75 years (n=132)	<75 years (n=65)	≥75 years (n=67)
Age (years)	64±8‡	80±4	66±5	80±5†
BMI (kg/m²)	23.4±2.7	23.2±2.8	23.7±3.7	23.7±3.7
UAP, n (%)	248 (61)	86 (65)	47 (72)	52 (77)
Coronary risk factors				
Hypertension, n (%)	288 (71)‡	110 (83)	50 (77)	58 (87)
Hypercholesterolemia, n (%)	292 (72)	82 (62)	50 (77)	62 (93)#
Diabetes mellitus, n (%)	205 (51)	56 (42)	32 (49)	42 (63)#
Smoking, n (%)	182 (45)‡,¶	41 (31)	17 (26)	4 (6)#,†
Family history of CAD, n (%)	80 (20)	40 (31)	16 (24)	21 (31)
Serum creatinine ≥177 μmol/l, n (%)	26 (6)	29 (22)	9 (14)	8 (12)#
Peripheral vascular disease, n (%)	32 (8)‡	31 (24)	4 (6)	13 (19)†
Stroke, n (%)	62 (15)‡	41 (31)	14 (22)	10 (15)#
Previous MI, n (%)	145 (36)	51 (39)	23 (35)	33 (49)#,†
Previous HF, n (%)	53 (13)	20 (15)	8 (12)	11 (16)
No. of diseased vessels				
1	224 (55)‡	56 (42)	39 (60)	16 (24)#,†
2	140 (35)	59 (45)	21 (32)	27 (40)
3	42 (10)	17 (13)	5 (8)	23 (36)#,†
LVEF (%)	52±10	52±12	49±10	50±9
LVEF <40%, n (%)	81 (20)	21 (16)	12 (18)	11 (17)
Glycemic status				
Fasting glucose (mmol/L)	106±26	100±25	111±38	114±36#
HbA1c (%)	6.1±1.2	5.9±0.9	6.3±1.3	6.3±1.2#
Lipid profile				
Total cholesterol (mmol/L)	189±35¶	184±27	210±40	202±35#
Triglycerides (mmol/L)	135±79‡	109±57	123±67	107±40
HDL-cholesterol (mmol/L)	40±10¶	42±13	49±12	46±13#
LDL-cholesterol (mmol/L)	122±32	119±25	138±38	134±27#
Hb (g/dl)	14.3±1.7‡,¶	12.9±1.6	12.1±1.5	12.0±1.3#
Medical treatment				
Aspirin, n (%)	367 (90)	110 (83)	64 (99)	56 (84)†
β-blocker, n (%)	255 (63)	84 (64)	40 (52)	45 (67)
Calcium-channel blocker, n (%)	276 (68)	95 (72)	48 (74)	53 (79)
ACEI, n (%)	107 (26)	35 (27)	10 (15)	18 (26)
ARB, n (%)	52 (13)	25 (19)	14 (21)	14 (21)
Statin, n (%)	195 (48)	55 (42)	38 (59)	30 (45)
Average BMS diameter (mm)	3.2±0.3	3.1±0.3	3.0±0.3	2.9±0.3
Average BMS length (mm)	16.4±4.4	16.5±3.5	15.9±2.7	16.2±2.4
Complete revascularization in patients with multivessel disease, n (%)	264 (65)	84 (64)	33 (51)	35 (52)#,∫

#P<0.05 vs men ≥75 years, †P<0.05 vs women <75 years, ‡ vs men ≥75 years, ¶ vs women <75 years, ∫ vs men <75 years.
BMS, bare metal stent; BMI, body mass index; UAP, unstable angina pectoris; CAD, coronary artery disease; MI, myocardial infarction; HF, heart failure; LVEF, left ventricular ejection fraction; Hb, hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker.

stent thrombosis classification[21] Complete revascularization (CR) on QCA was defined as a residual stenosis <20% in the 3 major coronary arteries and their major branches (branch diameter >2 mm).

The clinical and angiographic characteristics and the incidence of MACE were compared among the 4 groups in the BMS and SES eras using the chi-square test (or Fisher's exact test) for categorical data, or analysis of variance (ANOVA) was performed for continuous data. For univariate analysis, the following clinical variables and risk factors were regarded as covariates: age, gender, glycemic status (fasting glucose and HbA1c level), lipid profiles (TC, TG, HDL-C, LDL-C), creatinine level, BMI and the use of cardiovascular medications. On the basis of the results of univariate analysis, multivariate logistic regression analysis was performed to investigate the independent predictors of small AVD (<3.0 mm) and long ALL (>20 mm). Event-free survival was estimated using the Kaplan-Meier method, and differences were assessed using the log-rank test. A P value <0.05 was considered to be statistically significant. All analyses were performed using Stat-View software, version 5.0 (SAS Institute Inc, Cary, NC, USA).

Results

Baseline Characteristics in the BMS Era

Table 1 shows the baseline characteristics of the 4 groups in the BMS era: 406 men <75 years old, 132 men ≥75 years old, 65 women <75 years old, and 67 women ≥75 years old. Compared with men ≥75 years old, women ≥75 years old had higher levels of fasting blood glucose, HbA1c, TC and LDL-C, lower levels of hemoglobin, and higher prevalence of smoking. A higher prevalence of peripheral vascular disease was seen in women ≥75 years old compared with women <75 years old. Furthermore, among the 4 groups, the prevalence of previous MI and 3-vessel disease was the highest in women ≥75 years old. There were no significant differences in the medical treatment of groups except for aspirin use.

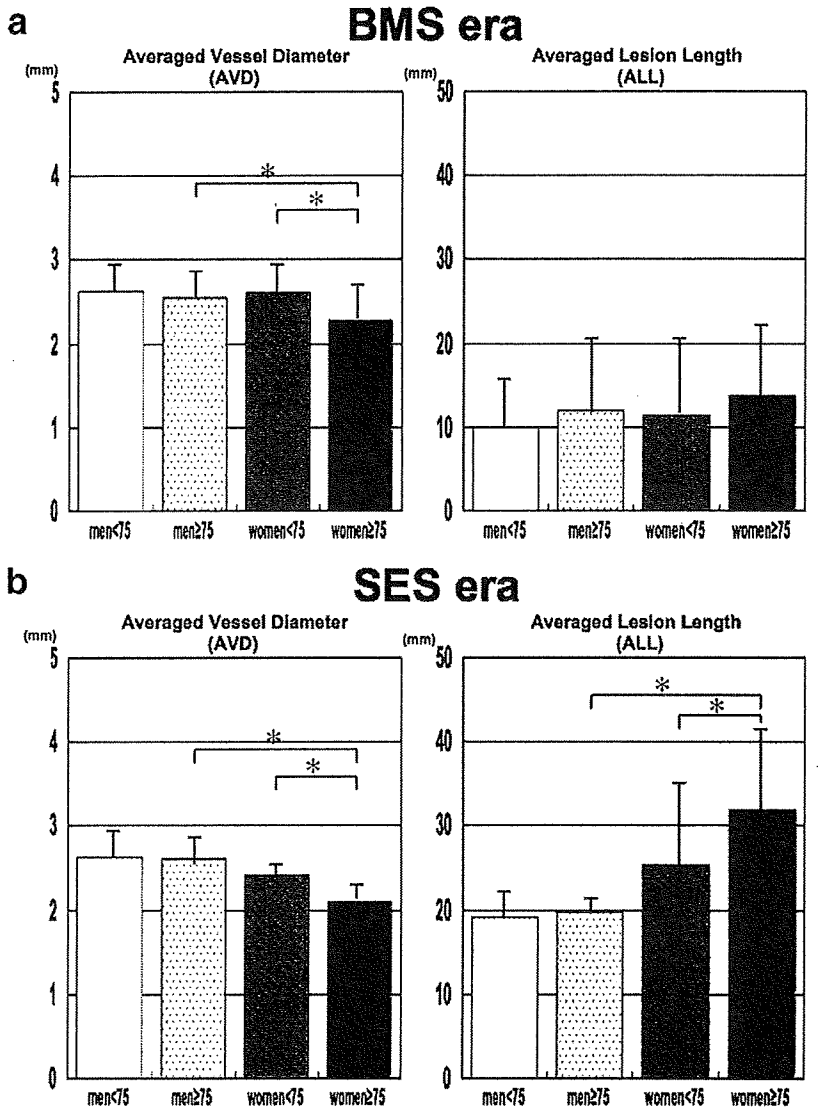

Figure 2. Comparison of quantitative coronary angiography results of AVD, ALL among the 4 groups in (**a**) bare metal stent (BMS) era and (**b**) sirolimus-eluting stent (SES) era. *P< 0.05.

Table 2. Univariate and Multivariate Analyses of Data in the BMS Era

	Univariate analysis		Multivariate analysis	
	OR (95%CI)	P value	OR (95%CI)	P value
Predictors of small vessel diameter (AVD <3.0 mm)				
Fasting glucose	0.996 (0.993–0.999)	0.0025	0.996 (0.994–0.999)	0.0155
Total cholesterol	1.002 (0.998–1.006)	0.4309		
Triglycerides	0.997 (0.996–0.999)	0.0002	0.998 (0.996–0.999)	0.0016
HDL-cholesterol	1.003 (0.992–1.015)	0.5773		
LDL-cholesterol	1.004 (1.000–1.009)	0.0755		
HbA_{1c}	1.002 (0.949–1.058)	0.9369		
Creatinine >177 μmol/L	0.937 (0.500–1.756)	0.8399		
Hypertension	0.819 (0.577–1.164)	0.2661		
Women ≥75 years old	28.566 (3.965–205.803)	0.0009	26.523 (3.676–191.357)	0.0011
Predictors of long lesion length (ALL >20 mm)				
Fasting glucose	1.003 (1.001–1.006)	0.0124	1.003 (0.999–1.007)	0.0954
Total cholesterol	1.000 (0.997–1.004)	0.9786		
Triglycerides	1.001 (1.000–1.003)	0.0275	1.002 (1.000–1.004)	0.1088
HDL-cholesterol	0.987 (0.977–0.997)	0.0127	0.981 (0.966–0.996)	0.0135
LDL-cholesterol	0.999 (0.995–1.003)	0.5826		
HbA_{1c}	1.011 (0.970–1.054)	0.6035		
Creatinine >177 μmol/L	1.257 (0.743–2.125)	0.3938		
Hypertension	1.363 (1.013–1.834)	0.0409	1.080 (0.723–1.613)	0.7055
Women ≥75 years old	3.235 (2.144–4.881)	<0.0001	4.564 (2.533–8.223)	<0.0001

OR, odds ratio; CI, confidence interval; AVD, average vessel diameter; ALL, average lesion length. Other abbreviations see in Table 1.

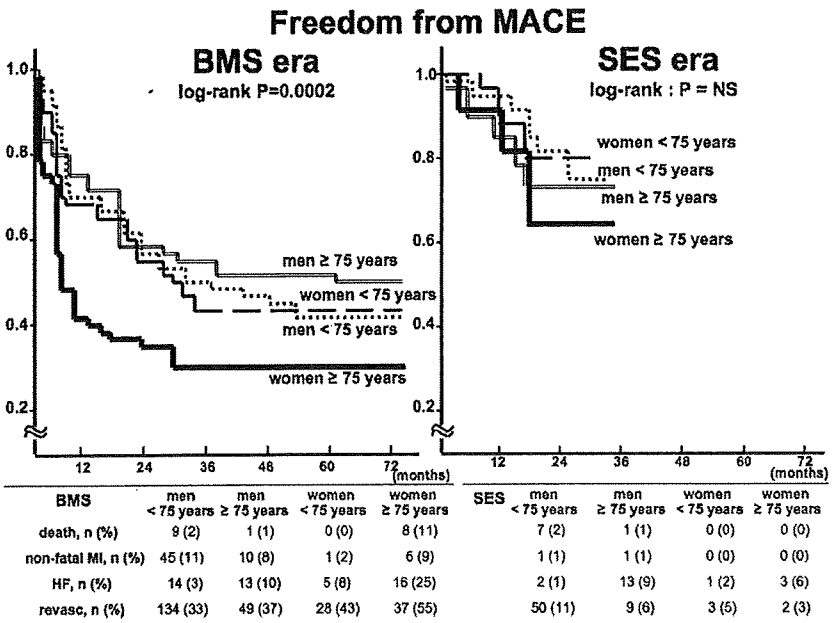

Figure 3. Kaplan-Meier curves of freedom from major adverse cardiovascular events (MACE) in bare metal stent (BMS, **Left**) and sirolimus-eluting stent (SES, **Right**) era. MACE includes death, non-fatal myocardial infarction (MI), heart failure (HF) and target lesion revascularization (revasc).

Table 3. Patient Characteristics in the SES Era

	Men		Women	
	<75 years old (n=450)	≥75 years old (n=145)	<75 years (n=57)	≥75 years (n=52)
Age (years)	63±8‡,¶	79±4	68±7	80±5†
BMI (kg/m²)	24.5±3.0	23.9±3.5	24.0±2.9	22.9±4.2
UAP, n (%)	54 (12)‡,¶	35 (24)	16 (28)	20 (39)#
Coronary risk factors				
Hypertension, n (%)	352 (78)	113 (78)	49 (85)	45 (88)
Hypercholesterolemia, n (%)	278 (62)¶	77 (53)	46 (79)	43 (82)#
Diabetes mellitus, n (%)	249 (55)	88 (61)	28 (48)	28 (55)
Smoking, n (%)	180 (40)¶	51 (35)	17 (30)	7 (14)#,†
Family history of CAD, n (%)	154 (34)‡	27 (19)	24 (41)	7 (14)†
Serum creatinine ≥177 μmol/L, n (%)	21 (5)	5 (3)	2 (3)	5 (10)#
Peripheral vascular disease, n (%)	38 (8)‡	29 (20)	7 (12)	3 (6)#
Stroke, n (%)	40 (9)‡	25 (17)	10 (17)	6 (12)
Previous MI, n (%)	222 (49)	73 (50)	29 (49)	24 (48)
Previous HF, n (%)	72 (16)	25 (17)	9 (15)	9 (18)
No. of diseased vessels				
1	215 (48)‡	52 (36)	19 (33)	11 (22)
2	158 (35)¶	46 (32)	24 (42)	21 (40)
3	70 (17)‡	47 (32)	14 (25)	20 (38)#
LVEF (%)	48±9	46±11	48±10	50±10
LVEF <40%, n (%)	81 (18)	38 (26)	13 (22)	9 (18)
Glycemic status				
Fasting glucose (mmol/L)	128±47	126±45	118±41	123±53
HbA1c (%)	6.6±4.4	6.1±1.0	6.1±1.0	6.3±1.2
Lipid profile				
Total cholesterol (mmol/L)	182±32‡,¶	173±26	202±49	184±30#,†
Triglycerides (mmol/L)	166±109	149±84	150±95	143±51
HDL-cholesterol (mmol/L)	41±10¶	40±11	51±14	40±15†
LDL-cholesterol (mmol/L)	110±28‡,¶	104±23	122±46	117±27#
Hb (g/dl)	13.8±1.8‡,¶	13.1±1.3	12.4±1.5	11.3±1.5#,†
Medical treatment				
Aspirin, n (%)	367 (90)	110 (83)	64 (99)	56 (84)†
β-blocker, n (%)	340 (76)	102 (70)	43 (74)	40 (78)
Calcium-channel blocker, n (%)	207 (46)	74 (51)	30 (52)	37 (73)#,†
ACEI, n (%)	121 (27)	38 (26)	9 (16)	11 (22)
ARB, n (%)	129 (29)	50 (35)	18 (31)	29 (55)#,†
Statin, n (%)	272 (60)‡,¶	72 (50)	46 (79)	26 (51)
Average SES diameter (mm)	2.9±0.3	2.9±0.3	2.9±0.3	2.8±0.3
Average SES length (mm)	21.6±4.3	21.0±3.9	25.9±3.2	30.8±3.6#
Complete revascularization in patients with multivessel disease, n (%)	351 (77)	109 (75)	38 (71)	34 (72)

#P<0.05 vs men ≥75 years, †P<0.05 vs women <75 years, ‡ vs men ≥75years, ¶ vs women <75 years.
SES, sirolimus-eluting stent. Other abbreviations see in Table 1.

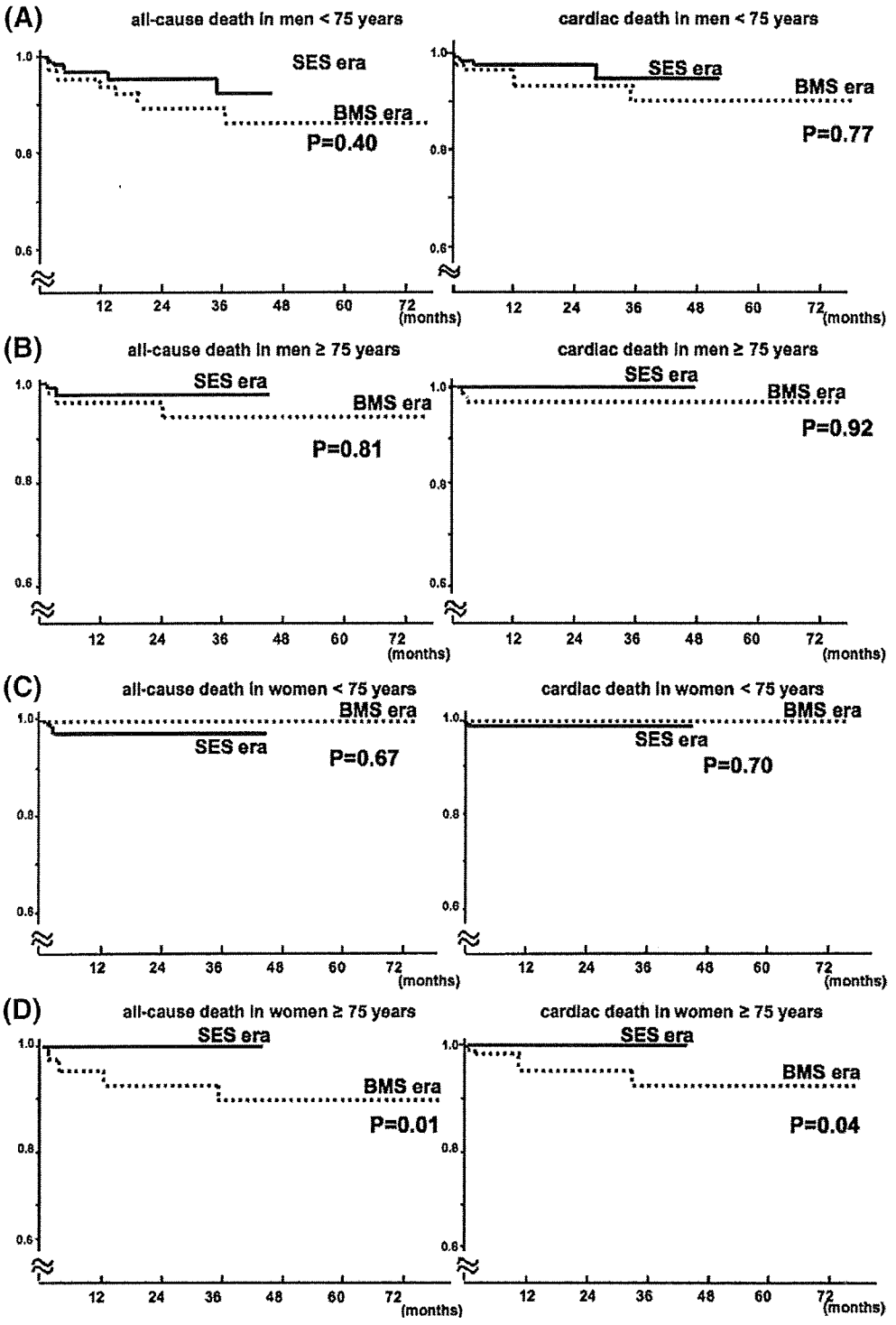

Figure 4. Kaplan-Meier curves of freedom from all-cause death and cardiac death in bare metal stent (BMS) era and sirolimus-eluting stent (SES) era. (**A**) men <75 years, (**B**) men ≥75 years, (**C**) women <75 years, (**D**) women ≥75 years.

QCA in the BMS Era

The results of QCA in the BMS era are summarized in **Figure 2a**. The AVD in women ≥75 years old was statistically significantly smaller than that in men ≥75 years old or <75 years old. ALL in women ≥75 years old was 13.8± 10.1 mm, which was not statistically significantly different from the other groups.

To investigate the independent predictors of small AVD (<3.0 mm) and long ALL (>20 mm), we performed univariate and multivariate logistic regression analysis (**Table 2**). Univariate analysis showed that hypercholesterolemia, TG, fasting blood glucose and women ≥75 years old were significant predictors for small AVD. By multivariate analysis, all of these variables were independent predictors of small

AVD. Regarding long ALL, TG, HDL-C, fasting blood glucose, hypertension and women ≥75 years old were significant predictors by univariate analysis. Multivariate analysis revealed that HDL-C and women ≥75 years old were strong independent predictors for long ALL.

MACE in the BMS Era

The event-free survival curve of the BMS era is shown in **Figure 3**. During the follow-up period of 75 months (median), women ≥75 years old had the highest incidence of cardiovascular events among the 4 groups. In particular, the incidence of TLR was high (55%), and the occurrence of death and HF was 11% and 25%, respectively, which were significantly higher in women ≥75 years old compared with other 3 groups. The prevalence of restenosis was 43% in elderly women with MACE.

Baseline Characteristics in the SES Era

Baseline characteristics of patients in the SES era are summarized in **Table 3**. The 4 groups consisted of 450 men <75 years old, 145 men ≥75 years old, 57 women <75 years old, and 52 women ≥75 years old. Overall, the patients' demographics were similar in the BMS era and the SES era, except for the prevalence of unstable angina pectoris and previous MI. When comparing elderly women in the BMS era and those in the SES era, their characteristics were similar except for the prevalence of unstable angina pectoris and peripheral vascular disease and the use of angiotensin-receptor blockers.

QCA in the SES Era

Figure 2b shows the results of QCA in the SES era. Although AVD was comparable between the 2 eras, ALL in the SES era (31.9±10.2 mm) was approximately 3-fold longer than that in the BMS era. In the SES era, smaller AVD and longer ALL were observed in women ≥75 years old, compared with women <75 years old and men ≥75 years old.

MACE in the SES Era

During the follow-up period of 34 months (median) in the SES era, there were no significant differences in MACE among the 4 groups (**Figure 3**). The incidence of TLR was low (3%) in women ≥75 years old.

As shown in **Figure 4**, the incidence of all-cause death and cardiac death in women ≥75 years old in the SES era was significantly lower than that of the BMS era. In detail, 9 patients died from: sepsis (n=1), cerebral bleeding (n=3), HF (n=3) and sudden death (n=2) in the BMS era, whereas no patients died in the SES era.

To clarify the role of CR, we compared the occurrence of MACE among the 4 groups, elderly women with and without CR in the BMS era (n=35 and 32, respectively) and those with and without CR in the SES era (n=34 and 18, respectively). As shown in **Figure 5**, there were no significant differences between patients with and without CR in the BMS era. In the SES era, patients with CR had a lower occurrence of MACE than patients without CR.

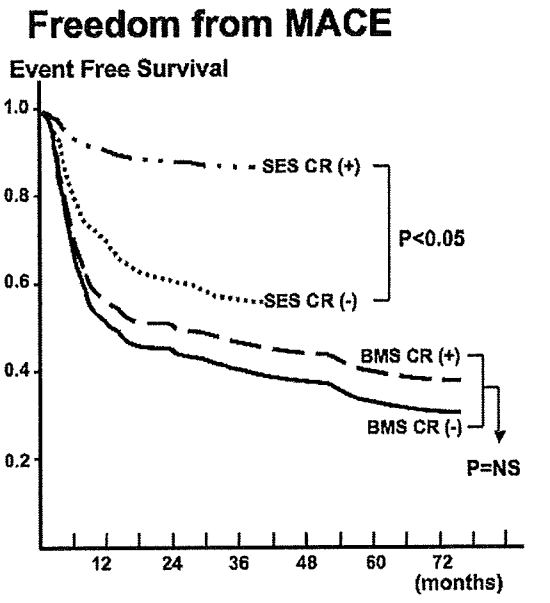

Figure 5. Kaplan-Meier curves of freedom from major adverse cardiovascular events (MACE) among women ≥75 years with and without complete revascularization (CR) in the bare metal stent (BMS) era (n=35 and 32, respectively) and those with and without CR in the sirolimus-eluting stent (SES) era (n=34 and 18, respectively).

Discussion

In the present study, elderly women (women ≥75 years old) who underwent PCI had angiographically smaller and longer coronary atherosclerotic lesions than men and women aged <75 years old. Although there was a high prevalence of MACE in this particular population in the BMS era, the use of SES in the current era reduced the occurrence of MACE, primarily by reducing all-cause death and TLR.

Morphological Characteristics of CAD in Elderly Women

Sharaf et al using severity scores to describe the advanced and diffuse atherosclerotic changes in 323 women with CAD[22] This score assesses the severity of a diseased lesion by its percentage diameter stenosis; however, that method can underestimate the severity of stenosis, particularly in patients with diffuse coronary narrowing, because it is difficult to identify a normal reference segment on angiography. Therefore, we used QCA to assess the whole coronary tree in a large population (n=1,374). As reported previously, QCA is more accurate, objective and reproducible than manual caliper measurements[19,23,24] The parameters we used (ie, AVD and ALL) enabled us to evaluate in detail the absolute values for the entire coronary tree, and our QCA analysis revealed that severe atherosclerotic changes had developed in women ≥75 years old (**Figures 2,4**). In addition, the morphological characteristics of CAD were more severe in the SES era than in the BMS era, because the ALL was >30 mm on average. We previously reported that morphological changes such as small vessels and diffuse narrowing developed in patients with diabetes mellitus or impaired glucose tolerance[19] As shown in **Table 1**, women ≥75 years old had higher fasting glucose and HbA_{1c} levels than similar aged men. Additionally, glucose metabolism, represented by the fasting glucose level, was a significant determinant for small vessels and diffuse coronary narrowing (**Table 2**). Therefore, elderly women (≥75 years old) may have a high prevalence of abnormal glucose tolerance than other patients and this metabolic abnormality seems to be an important factor in the development of severe coronary atherosclerotic changes (**Table 2**).

Improved Prognosis of Elderly Women With CAD in the SES Era

In the BMS population of the present study there was a high incidence of MACE in women ≥75 years old. Small vessel size and long lesion length were associated with development of restenosis in the BMS era[25,26] and we found a strikingly high rate of TLR in women ≥75 years old in the present study. Because of the higher risk of developing restenosis, the benefit of CR on long-term prognosis might be traded off, as shown in **Figure 5**. The incidence of death and HF in women ≥75 years old were also higher than in other groups.

Many recent studies have demonstrated that SES strongly inhibit neointimal hyperplasia and reduce the need for TLR[1,2] SES can be used in complex lesions that seemed unsuitable for PCI in the BMS era[3–7] Considering the greater efficacy of SES and their increased use in lesions that were unsuitable for PCI in women ≥75 years old (eg, ALL >30 mm on average), it can be proposed that the improved clinical outcomes, including all-cause and cardiac death, might be related to a reduction in ischemic events, which has resulted from the low restenosis rates associated with the use of SES. In addition, the reduction in ischemic events may prevent HF and arrhythmias.

Study Limitations

There are some biases and differences in patient selection for this retrospective study; for example, the difference between the BMS and SES eras for lesion length in elderly women may reflect a change in the indication for PCI. However, the general policy and procedure of PCI performed at our institution did not change from 1 era to the next. Moreover, the increased usage of angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers and statins should be taken into consideration as modifiers of the results. Although the prevalence of unstable angina differed between the BMS and SES era, an unstable clinical presentation did not exert a significant impact on outcome as reported in previous studies[27–29]

Conclusions

Elderly women with CAD have particular characteristics of coronary atherosclerosis, such as small vessels and diffuse coronary narrowing, which could be related to abnormal glucose tolerance and/or dyslipidemia. In the BMS era, this particular patient group had the worst long-term prognosis compared with men or women <75 years old. However, in the SES era, this difference in prognosis has been alleviated, mainly because of a reduction in all-cause death and TLR.

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CURRENT TOPICS REVIEW ARTICLE

Current status of coronary artery bypass grafting

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Abstract The number of cases of coronary artery bypass grafting (CABG) reached more than 21 000 in Japan in 2002, and the operative mortality decreased to less than 1%, including emergency operations. The annual number of CABGs in Japan declined 17% after 2003 to 18 000 cases in 2005 owing to unrestricted percutaneous coronary intervention (PCI) with drug-eluting stents. However, CABG is the best treatment for multivessel coronary artery disease based on the comparative data of PCI versus CABG. There have been two trends in CABG during the last decade. One is the widespread use of off-pump (OP) CABG, and the other is multiple coronary artery revascularization. In 2004 and 2005, approximately 60% of all isolated CABG procedures in Japan were performed without cardiopulmonary bypass. In a study of long-term outcomes comparing PCI with drug-eluting stents versus CABG with only arterial grafts, the latter was carried out in 52% of total cases and in 66% of OPCAB cases. OPCAB with multiple arterial grafts has become the standard CABG in Japan.

Key words Coronary artery bypass · Percutaneous coronary intervention

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Introduction

Coronary artery bypass grafting (CABG) performed with cardiopulmonary bypass (CPB) has become an established treatment for patients with coronary artery disease. The number of CABGs reached 21 000 cases in 2002, and the mortality associated with elective CABG became less than 1% according to the database of the Japanese Association for Thoracic Surgery. However, the annual number of CABGs declined 17% after 2003 to 18 000 cases in 2005 owing to the unrestricted percutaneous coronary intervention (PCI) with introduction of the drug-eluting stent (DES) in Japan. During the last decade, two major revolutions in CABG have been seen. One is the development of CABG without CPB, and the other is CABG with multiple arterial grafts. These new trends are much more advanced in Japan than in either North America or Europe. Here, I review the current status and future of CABG.

Comparison of CABG and PCI

CABG versus POBA (Primary Old Balloon Angioplasty)

Since the 1980s, multiple randomized controlled trials (RCTs) on PCI versus CABG have been conducted.[1–4] The Emory Angioplasty Surgery Trial (EAST) showed an 8-year mortality of 17.3% in the CABG group compared with 21.7% mortality in the PCI group.[1] The relative mortality difference of 4.3% between PCI and CABG for patients with multivessel disease was not significant because of the small numbers of patients enrolled.[2] The largest RCT of CABG versus PCI was the Bypass Angio-

plasty Revascularization Investigation (BARI) trial from 1988 to 1991.[3] The 7-year mortality rate was significantly better in the CABG group (16.6%) than in the PCI group (19.1%), although the 2.5% difference occurred in the 7.3% of patients with multivessel disease who were most suitable for either PCI or CABG.[4] In many RCTs, including the BARI study, CABG was most favorable in diabetic patients.[5] Repeated revascularization was significantly higher in the PCI patients than in those who underwent CABG because of restenosis. A meta-analysis of nine RCTs studying CABG versus PCI in patients with multivessel disease revealed that survival was equivalent at 1 and 3 years, but the initial CABG group had significantly better 5- and 8-year survivals than the initial PCI group.[6]

CABG versus bare metal stents

Several RCTs of CABG versus PCI with bare metal stents (BMS) have been reported. The Arterial Revascularization Therapies Study (ARTS) was a highly PCI-friendly trial regarding enrollment.[7] Only 5% of the patients enrolled were very low risk: no previous PCI, no congestive heart failure, no recent myocardial infarction, no cerebrovascular disease, young age (mean 61 years), and good left ventricular (LV) function (mean LV ejection fraction 0.61). The 1-year mortality rates and major adverse cardiac and cerebral events rate were the same.[8] By 1 year, however, repeat revascularization was required more frequently in PCI patients (16.8%) than in CABG patients (3.5%). The 5-year mortality and major adverse cardiac and cerebral events rates were 7.1% and 13.5%, respectively, in the CABG group and 8.0% and 18.0% in the PCI group. At 5 years the repeat revascularization rate was 8.8% for the CABG patients and 30% for the PCI patients. There was a study bias in that one member of the board of this study was a vice president of Cordis, a division of Johnson & Johnson Company.[9]

The study called Coronary Angioplasty with Stenting versus Coronary Bypass Surgery in Multivessel Disease (ERACT II) revealed that the 30-day mortality was 0.9% in the stent group and 5.6% in the CABG group.[10] This high mortality of CABG was attributed to a relative delay of therapy in unstable patients. Because of this high early mortality in the CABG group, the 5-year mortality was better in the stent group (7.2%) than in the CABG group (11.6%). The 5-year major adverse cardiac and cerebral events rate was better in the CABG group (23.6%) than in the stent group (34.7%). The problems with CABG in the ERACT II study were a small surgical volume (<100 cases a year) in participating centers and low use of the left internal thoracic artery (LITA) (89% among patients who, on average, were 62 years of age).[11] The quality of surgical therapy in this study might have been poor.

The SoS trial in Europe and Canada demonstrated that repeated revascularization was significantly higher in the stent group than in the CABG group (21% vs. 6%: hazard ratio 3.85, $P < 0.0001$) at the 2-year median follow-up.[12] Although the incidence of death or Q-wave myocardial infarction was not different between the PCI and CABG groups, the cumulative deaths at a 2-year median follow-up were significantly higher in the stent group than in the CABG group (8 vs. 22 deaths: hazard ratio 2.91, $P < 0.01$). There was no further follow-up because the SoS study was funded by stent manufacturers.[9]

In addition to the RCTs, a large observational study from New York cardiac procedure registries from 1997 to 2000 analyzed 59 000 patients with multiple-vessel disease who underwent PCI with BMS or CABG.[13] At the 3-year follow-up, repeat revascularization was seven times higher in the PCI group (35.1% of PCIs vs. 4.9% of CABGs). In the case of three-vessel disease with a proximal left anterior descending artery (LAD) lesion, the hazard ratio for CABG regarding 3-year adjusted mortality compared to that of PCI was 0.64 in all patients, 0.69 in diabetic patients, and 0.68 in patients with poor LV ejection fraction (LVEF) <0.40. In patients with two-vessel disease with a proximal LAD lesion, the hazard ratio of mortality was 0.75 in all patients, 0.71 in diabetic patients, and 0.64 in patients with poor LVEF <0.40. In 2000, according to the New York cardiac registries, PCI with BMS seemed not to be appropriate for multivessel coronary artery disease.

CABG versus drug-eluting stents

Coating stents with an antiproliferation drug inhibits intimal hyperplasia after PCI.[14] Commercially available sirolimus (CYPHER; Cordis Corporation, FL, USA) and paclitaxel (TAXUS; Boston Scientific, MA, USA) stents have been widely used. A meta-analysis of 11 RCTs of drug-eluting stents (DESs) versus BMSs demonstrated that the major adverse cardiac events rate of death, myocardial infarction, or target-vessel revascularization was 7.8% with DESs and 16.4% with BMSs; and the restenosis rate was 8.9% with DESs and 29.3% with BMSs. However, not a single trial demonstrated a mortality benefit of the DES or a benefit with regard to myocardial infarction. Sudden acute thrombosis has become a major concern with DESs.[15–17] The antiproliferative agent of DESs may inhibit the intimal function that induces the anticoagulation process and prohibits

the coagulation process. Even after the agent is completely released, the polymer may remain and cause allergic inflammation, leading to restenosis or thrombotic occlusion. A small but significantly increased risk of death or myocardial infarction was reported recently (0.5%–1.0% per year) in patients who have a DES due to stent thrombosis.[18] Anecdotally, thrombotic occlusion has been reported to occur immediately after cessation of antiplatelet therapy.[19] The U.S. Food and Drug Administration (FDA) stated in December 2006 that use of a DES should be limited to patients who have clinical and coronary anatomical features similar to those of the patients treated in the pivotal trials conducted by the manufacturers for FDA approval. Many cardiologists recommend permanent antiplatelet therapy, including clopidogrel (Plavix; Sanofi Aventis, NJ, USA) or GP IIb/IIIa receptor blocker, after PCI with DES in patients for whom the quality of life or a bleeding event would be worse than with CABG.

Few RCTs of CABG versus PCI with DES have been reported.[20] CABG with bilateral ITA to the left coronary system versus PCI with DES in patients with multivessel disease demonstrated better long-term survival and angina- and intervention-free rates.[21] Because the results of PCI with DESs were not better than those of PCI with BMSs, CABG should be the first option, at least for multivessel disease. PCI can be used to treat proximal lesions, but patients are susceptible to disease progression. As the anastomoses are in the distal portion of the coronary branches with CABG, it could protect against sudden coronary occlusion and myocardial infarction.

CABG without CPB

In 1967, Kolessov grafted the LITA to the LAD through a left thoracotomy under beating-heart conditions.[22] Myocardial revascularization with cardioplegic arrest became the standard CABG procedure with the development of the CPB technique and myocardial preservation methods for cardiac arrest during the early 1980s. The Cleveland Clinic study demonstrated significantly better long-term survival and graft patency with LITA-to-LAD grafting than with saphenous vein grafting, described in 1986 by Loop and associates.[23] LAD proved to be the most important coronary artery, and grafting it with LITA guaranteed 10-year survival and graft patency of more than 90%. Similar results were reported by Kitamura et al. in Japan.[24] On the other hand, the restenosis rate of PCI to a LAD lesion with BMS has been reported to be 20%–30%.

During the late 1990s, a new technique of myocardial revascularization without CPB and with a minimal skin incision was developed by Subramanian[25] and Calafiore et al.[26] A small left thoracotomy in the fourth intercostal space to graft the LITA to the LAD without CPB was called minimally invasive direct coronary artery bypass (MIDCAB), or the left anterior small thoracotomy (LAST) operation. This revival of beating-heart coronary artery surgery was related to the significant cerebral morbidity associated with CPB among high-risk patients. The MIDCAB approach was indicated for patients with single-vessel disease with LAD lesions or those with multivessel disease who had severe co-morbidity, which is not suitable for CPB use. MIDCAB was introduced to Japan during the late 1990s, but its use had almost disappeared there before 1999 because the initial clinical results were disappointing. Cardiac surgeons were not accustomed to the left thoracotomy approach for harvesting the LITA or to an anastomosis under beating-heart conditions (before the introduction of robotic surgical system and a suction-type stabilizer).

The systemic inflammatory reaction initiated by CPB results in an immunological reaction and damage to various organs. Neurological, renal, and gastrointestinal function was impaired by microemboli due to mechanical damage to the blood and aortic wall.

The pioneering efforts by Benetti et al.[27] and Buffolo et al.[28] in South America proved the feasibility of OPCAB through a median sternotomy during the 1990s. Initially, OPCAB was applied to the LAD, diagonal, and main right coronary arteries with minimal hemodynamic alterations during a full median sternotomy. A suction-type mechanical stabilizer and deep pericardial stitches invented by Lima, in addition to an apical suction device, allowed exposure of all coronary branches.[27,30] Trendelenburg positioning by the operating table and other techniques resulted in exposure of the lateral and inferior coronary artery branches.

According to the database of the Japanese Association for Thoracic Surgery, the percentage of OPCAB operations among the total CABG cases was 35% in 2001, 46% in 2002, 55% in 2003, and 60% in 2004. The frequency of OPCAB reached a plateau in 2005 and 2006 according to the database of the Japanese Association of Coronary Artery Surgery. Thus, OPCAB has become the standard method for CABG in Japan, whereas the incidence of OPCAB cases among all CABGs in North America was only 20% and in Germany 5%. As some groups in the United States are performing 90% or more of the CABGs without CPB, the incidence of OPCAB in standard hospitals might be less than 10%.

The indications for OPCAB are the high-risk factors of CPB: cerebrovascular disease, chronic renal failure,

chronic obstructive pulmonary disease (COPD), atheromatous or calcified ascending aorta, old age, and cancer. In contrast, the indications for conventional CABG are unstable hemodynamic status, shock, lethal arrhythmia, percutaneous cardiopulmonary support (PCPS), and discontinuation of OPCAB. Anatomical and physiological contraindications are thought to be intramuscular, diffusely calcified, or extremely small LAD, enlarged left ventricle with poor contractility [LVEF 30%, LV end-diastolic volume index (LVEDVI) >100 ml/m^2], significant mitral regurgitation, and acute myocardial infarction with ventricular tachyarrhythmia. Many retrospective studies have been published comparing clinical outcomes after OPCAB with conventional CABG.[31–33] In moderate-risk and high-risk patients, the operating time, intubation time, length of intensive care unit (ICU) stay, length of hospital stay, perioperative myocardial infarction, amount of bleeding and transfusion, inflammatory reaction, stroke, neurocognitive dysfunction, atrial fibrillation, and inotrope requirements were in favor of OPCAB. For OPCAB, the number of cases of bypass grafting was reported be less than that of standard CABG because of technical difficulty.[34] Graft patency and long-term outcomes in OPCAB cases compared with conventional CABG are still controversial. The meta-analysis of previous RCTs by Cheng and associates[35] showed no significant differences in the 30-day mortality, myocardial infarction, stroke, renal dysfunction, intra-aortic balloon pump (IABP) support, wound infection, rethoracotomy for bleeding, or reintervention for mixed-risk patient population. However, OPCAB significantly decreased atrial fibrillation [odds ratio (OR) 0.58, transfusion (OR 0.43), inotrope requirements (OR 0.48), respiratory infection (OR 0.41), ventilation time (–2.4 h), ICU stay (–0.3 day), and hospital stay (–1.0 day]. Results of graft patency and neurocognitive function were inconclusive. In-hospital and 1-year medical costs were generally higher for standard CABG.

A meta-analysis of 42 nonrandomized trials of high-risk patients by Puskas and associates[36] demonstrated a significant reduction in mortality after OPCAB versus conventional CABG in various high-risk patient subsets (OR 0.58). Mortality was reduced in patient subgroups with high-risk factors of Euroscore >5 (OR 0.39), LV dysfunction (OR 0.55), atheromatous aorta (OR 0.54), and multiple risk factors (OR 0.60). In contrast, increased age, left main coronary artery disease, diabetes mellitus, renal dysfunction, and COPD were not related to the operative mortality irrespective of CPB.

A recent meta-analysis of graft patency by Takagi et al. demonstrated a 27% increase in overall graft occlusion with OPCAB, especially a 28% increase in venous graft occlusion.[37] This result may be related to the hypercoagulability status after OPCAB. Previous reports showed improved venous graft patency with early administration of antiplatelet drugs and no change in LITA grafts irrespective of anticoagulation or an antiplatelet regimen.[38]

Arterial grafts in CABG

The superiority of the ITA graft over a saphenous vein graft (SVG) has been widely accepted since angiographic studies during the 1980s.[23] The clinical importance of LITA-to-LAD grafts was emphasized by a long-term follow-up study compared with SVGs over 20 years.[39] SVGs developed intimal hyperplasia and graft atherosclerosis, which caused late graft occlusion, so various arterial grafts have been adopted over the last 30 years. The right ITA,[40–42] right gastroepiploic artery (GEA),[43,44] radial artery (RA),[45,46] and inferior epigastric artery[47,48] have been used in addition to LITA as in situ grafts, free grafts, or composite grafts. Total arterial OPCAB might be the ideal CABG. According to the database of the Japanese Society of Coronary Surgery in 2004, LITA grafts comprised 38% of all grafts; other arterial grafts were GEA grafts (9%), RA grafts (15%), and SVGs (24%). Thus, arterial grafts account for 76% of all grafts in Japan nowadays, which is significantly higher than in Western countries. Arterial CABGs were performed in 52% of cases according to the database of the Japanese Association for Thoracic Surgery in 2005. Among the OPCAB cases, 66% of CABGs were performed with only arterial grafts in Japan. Although there is no statistical study, it is possible that among the OPCAB cases more than 80% of the grafts were arterial. We believe that total arterial OPCAB should be considered one of the ideal CABGs.[49,50]

There is strong evidence that LITA should be used for revascularization of the LAD artery.[23,24,51–56] Even in patients >80 years of age and in emergent situations, LITA was recommended for LAD revascularization to achieve a better outcome.[57] Crossover RITA-to-LAD was reported to be as good as LITA-to-LAD, although the graft patency of RITA-to-RCA territory was poor.[58,59] There are several comparative studies that showed improved outcomes for patients who had bilateral ITA grafts regarding long-term survival and the cardiac event rate.[60–62] Not a few studies have shown an increase in the risk of deep wound infection by bilateral ITA harvesting, especially in diabetic patients.[63,64] The technique of skeletonizing ITAs with an ultrasonic scalpel may decrease the number of sternal wound complications in diabetic patients.[65,66] Based on our personal experience, bilateral ITA use should be avoided in patients over 80 years of

age, those with insulin-dependent diabetes (IDDM), and those with COPD on medication. Crossover bypass of RITA to LAD should be also avoided when aortic valve stenosis or an aortic aneurysm is present because of a possible future median resternotomy.

The ITA grafts are viable with active biological potency, which has active dilatation and thinning (string phenomenon) of no flow patency.[67] Despite the potential biological superiority of ITA to SVG, which can release nitric oxide from the endothelium to protect against atherosclerosis,[68] flow competition was high when a composite arterial graft was attached to the side of LITA if LAD stenosis was moderate.[69–71] Therefore, we usually use LITA as an individual graft to the LAD when the LAD has only 75% stenosis. As elderly Japanese women have small, fragile ITAs, it might be better to avoid a sequential bypass with ITA and attachment of free graft to ITA.

The RA grafts were revived during the late 1980s when they were found still to be patent in patients who had undergone CABG 13–18 years earlier.[45] The graft, however, is prone to spasm by manipulation because of its thick muscular wall. The technique of harvesting RAs and the use of calcium channel blockers improved early and late graft patency. Acar and associates reported that the 5-year graft patency rate for RA was 84% and that of LITA was 90%.[45] Recently, SVGs have been replaced by RA grafts. Many studies have shown better outcomes with RA grafts than with SVGs,[72–74] although some reported similar long-term graft patency.[75–77] RA grafts frequently showed a flow competitive phenomenon with mildly stenotic native coronary arteries when they were used as composite grafts compared with aorta-to-coronary conduits.[69–71,78] The long-term patency of these competitive RA grafts was poor according to our angiographic analysis.[71] The long-term patency of RA grafts should be better than that of SVGs when good forward flow is present. However, the SVG still has a role as a graft to moderately stenotic RCA territory because of the poor early graft patency of RITA-to-RCA grafts and high incidence of flow competition of composite RA grafts to RCA branches.[58,59,69,70,78]

Use of in situ GEA for CABGs was first reported in 1987, with early graft patency ranging from 90% to 100%.[43,44] The long-term graft patency at 10 years was not better than that for SVGs.[79] GEA is prone to flow competition compared with LITA because GEA is the third branch of the abdominal aorta and has 10–15 mmHg lower pressure at the end compared to the end of LITA.[80–82] Although skeletonized and composite use of GEA has been reported for larger internal diameters and flow, the effect of avoiding flow competition has not been proved.[83–85]

Innovative techniques

Totally endoscopic CABG (TECAB) has been tried in several institutions using a robotic surgical system (da Vinci system; Intuitive Surgical, Sunnyvale, CA, USA).[86,87] The major obstacle to TECAB is the technical difficulty of constructing accurate distal anastomoses. Efforts to put together a distal sutureless automatic anastomosis device are underway. Several automatic anastomosis devices for anastomosis of an SVG to the ascending aorta have been invented. However, most devices were not put on the market because of poor intermediate graft patency and cumbersome handling.[88]

Hybrid therapy for coronary revascularization has been designed. Single-vessel mini-thoracotomy (MIDCAB), followed by angiographic confirmation of the LITA-to-LAD graft and PCI for circumflex and RCA branches has been performed in the hybrid operating room in some centers.[89] Multivessel mini-thoracotomy, which is a LITA-to-LAD bypass combined with a composite RA-to-marginal branch graft, followed by associated PCI with DES in the catheterization laboratory has been tried in a few institutions.

Awake OPCAB has been tried in Turkey in patients who had contraindications to general anesthesia.[90,91] In Japan, awake OPCAB under thoracic epidural anesthesia was attempted by Kanazawa University. These techniques must await further evaluation.

Conclusion

Percutaneous coronary intervention with a drug-eluting stent has dramatically changed the treatment of multivessel coronary artery disease. Appropriate patient education and improvement of surgical techniques with less invasiveness is mandatory for better clinical management of ischemic heart disease. In addition, cardiac surgeons must present these innovations to the public in Japan. CABG is still the best treatment for multivessel disease and left main coronary artery disease.

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右内胸動脈と橈骨動脈の I-composite graft を使用した OPCAB

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はじめに

心拍動下冠状動脈バイパス術（OPCAB）の手術成績向上のための重要な因子として，グラフト選択があげられる．左内胸動脈（LITA）と大伏在静脈（SVG）のみの時代と異なり，選択肢が増加した結果，バイパス手術に対する各施設の考え方が明瞭に分かれ，かつ顕著に示されるところであると思われる．

OPCAB における多枝バイパス例で頻用される composite graft も，その使用状況はやはり千差万別である．われわれの施設では，主として回旋枝領域に対して右内胸動脈（RITA）と橈骨動脈（RA）の I-composite graft を多用している．本稿では，RITA と RA の I-composite graft を使用した OPCAB の手術成績を報告し，グラフト選択に対するわれわれの考え方を述べることとする．

Ⅰ．対象および方法

1. 対　象

2002 年 1 月～2006 年 8 月までに施行した OPCAB 例 164 例のうち，RITA を RA で延長する I-composite graft を使用した 37 例（22.6%）を対象とした．患者背景を表 1 に示す．年齢は 50～85（平均 67.4±7.5）歳，男性 32 例（86.5%）であった．左主幹部（LMT）病変を 19 例（51.4%）に認めた．糖尿病合併例は 18 例（48.6%）で，うち insulin 投与例は 4 例（10.8%）であった．再手術は 2 例（5.4%）で，緊急手術例はなかった．透析例もなかったが，多発性嚢胞腎のため将来的に透析導入が予想される腎機能低下例を 1 例認めた．

表 1．患者背景（$n=37$）

年　齢	67.4±7.5（50～85）歳
性別（男/女）	32/5 例
LMT 病変	19 例（51.4%）
糖尿病	18 例（48.6%）
[insulin 使用]	[4 例（10.8%）]
高血圧	29 例（78.4%）
高脂血症	23 例（62.2%）
術前 IABP	1 例（ 2.7%）
再手術	2 例（ 5.4%）
緊急手術	0 例（ 0.0%）
透析例	0 例（ 0.0%）

IABP：大動脈内バルーンパンピング

2. 手術方法

グラフトはいずれも full skeletonization で剝離し，採取した．Harmonic Scalpel（Ethicon Endosurgery 社，Cincinnati）を用いて，内胸動脈は Higami らの方法[1]，胃大網動脈（GEA）は

キーワード：OPCAB，内胸動脈，橈骨動脈，グラフト選択

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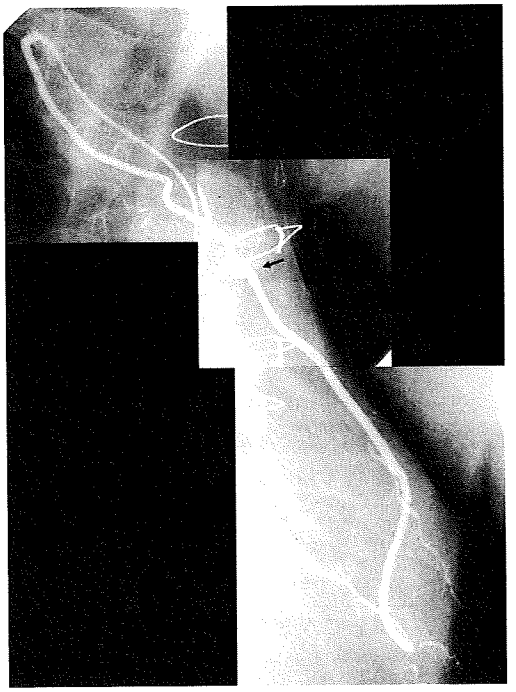

図 1. RITA-RA の I-composite graft による対角枝と後側壁枝への sequential bypass

矢印は RITA と RA の端々吻合を示す．RITA は全長剝離することなく，上行大動脈のレベルで RA に乗り換えている．側々吻合を parallel に行っているが，グラフト長にゆとりがあるためその走行に無理がない．

Asai らの方法[2]に準じて行った．RITA の剝離は中枢側の半分程度までにとどめた．RA は前腕の長軸切開で全長にわたって剝離し，papaverine hydrochloride を浸透させたガーゼで包み，20 分間ほど自己血圧で拡張させた．Heparin 静脈注射後，各グラフトを切断，*in situ* グラフトの内腔には papaverine hydrochloride を注入した．まず，8-0 Prolene（Ethicon 社，Somerville）を用いて，離断した RITA と RA を端々吻合し，I-composite graft を作成した．RITA，RA とも十分に cut back をして密にならない運針を行い，巾着効果による狭窄をつくらない結紮をするよう心がけた．

左側心膜を吊り上げて，まず LITA を左前下行枝（LAD）に吻合した．次にハートポジショナーで心臓を脱転し，右冠状動脈（RCA）領域，左回旋枝（LCX）領域の順に吻合した（図 1）．

表 2. 手術成績（$n=37$）

吻合総数	113 枝
平均バイパス枝数	3.1±0.7（2～5）枝
RITA-RA 吻合数	48 枝
RITA-RA グラフト開存率	97.90%
周術期心筋梗塞	2 例（ 5.4%）
IABP 使用例	5 例（13.5%）
人工呼吸管理＞24 時間	1 例（ 2.7%）
同種血輸血回避率	86.5%（32 例）
術後脳梗塞	0 例（ 0.0%）
縦隔洞炎	0 例（ 0.0%）
再開創止血	0 例（ 0.0%）
手術死亡	0 例（ 0.0%）
入院死亡	0 例（ 0.0%）
術後 CK 値	1,003±633 IU/*l*
術後 CK-MB 値	26.6±64.3 IU/*l*
術後 GOT 値	58±47 IU/*l*

いずれも 2 分間の ischemic preconditioning を行った後，外シャント[3]を挿入しつつ，スタビライザー使用下に吻合した．

Ⅱ．結　　果（表 2）

手術死亡，入院死亡は認めなかった．周術期心筋梗塞を 2 例（5.4%）に認めた．1 例は再手術例（SVG-LAD，LCX の 2 枝バイパス術後 18 年目）で，初回グラフトのびまん性の狭窄病変により手術適応になったが，今回術後造影で SVG（-LCX）の完全閉塞を認め，この領域の問題と考えられた．もう 1 例は術翌日発症と考えられる梗塞で，シンチグラムにより回旋枝領域のうちバイパスを行わなかった領域の梗塞であった．いずれも経過をとおして血行動態の悪化はなく，また術後グラフト造影ですべてのグラフトの良好な開存を確認した．大動脈内バルーンパンピング（IABP）は 5 例（13.5%）で使用したが，いずれも 2 病日までに離脱した．24 時間を超える術後人工呼吸管理を 1 例（2.7%）に要した．同種血輸血回避率は 86.5%（32 例）であった．術後脳梗塞，縦隔洞炎あるいは前腕創合併症は認めなかった．

術後の CK，CK-MB，GOT の最大値（IU/*l*）はそれぞれ平均で 1,003±633，26.6±64.3，58±47 であった．バイパス枝数は 2～5（平均 3.1±0.7）本，RITA-RA グラフトの遠位側吻合数は 48（平均 1.3）枝であった．LITA は 37 本 38 枝（1 例のみ対角枝に sequential bypass を施行），

GEA は 26 本 27 枝に吻合した．腎機能低下や大動脈の性状不良を理由に術後グラフト造影を行わなかったものが 3 例あり，これらは負荷 Tl 心筋シンチグラムで虚血のないことを確認した．残り 34 例のグラフト造影では，RITA と RA の吻合部狭窄や string sign を認めなかった．RITA-RA グラフト 1 枝が閉塞しており，近接期の開存率は 97.9%であった．

Ⅲ．考　　察

Off-pump であるか否かにかかわらず，冠状動脈バイパス術（CABG）の基本は LITA-LAD であると考える．われわれも単独でこの吻合を行うことを標準術式としている．以前から LITA-LAD の良好な長期開存性が報告されていた[4]が，最近の報告でも[5]LITA-LAD の 10 年開存率は 85%で，特に LAD の径が 2 mm 以上であった場合には 100%であったという．RITA-LAD というグラフトデザインは基本的に選択していない．最近は full sleletonization により剝離するため，確かに RITA のグラフト長が得られるようになったが，かなり末梢部分で LAD に吻合されるという事情にかわりはない．また，LAD へのグラフトが胸骨の下を横断している症例の再手術のリスクはきわめて高いものとなる．なるべく上行大動脈の頭側を走行するように工夫をする[13]が，その場合はさらにグラフト長に制限が加わることになる．LITA の太い部分を最重要枝である LAD に吻合することを基本にすべきである．

OPCAB における aorta no touch に関して，われわれは厳格に順守している．脳梗塞[6]や大動脈解離[7]の危険が高くなる以上，side biting clamp は極力行わず，各種開発されている中枢側吻合用デバイスも使用していない．Symmetry Bypass Connector（St. Jude Medical 社，Saint Paul）にせよ，PAS-Port Aortic Connector System（Cardica 社，Redwood City）にせよ，グラフト閉塞率が高く，高率に心事故を発生させることが報告されている[8,9]．また，Heartstring Proximal Seal System（Guidant 社，Indianapolis）や Enclose Ⅱ（Novare Surgical Systems 社，Cupertino）といった手縫いで行うためのデバイスは，その良好な初期成績が報告されている[10,11]が，脳梗塞発生の懸念[12]は払拭できないと考える．AC バイパスが必要であると判断した場合，われわれは躊躇なく on-pump による手術を選択する．上行大動脈上エコーによる入念な評価が重要であることは論をまたないが，on-pump とすることで脱血による血圧コントロールが容易になる．十分に血圧を下げて side biting clamp を行うことで，リスクを軽減させうるものと考えている．たとえば，左室駆出率＜20%といった低左心機能例に対する多枝バイパス術では，近接期にできるだけ流量の多いグラフトのほうが有利であると考え，on-pump beating bypass を選択し，AC バイパスを含めることが多くなっている．

以前より当科では，RCA 領域には GEA を基本グラフトとしているため，残りの回旋枝領域に対するグラフト選択が議論の対象になることが多い．直接 *in situ* RITA が届く場合はよいが，AC バイパスをできるだけ行わない方針のため往々にしてグラフト長が不足する．そこで RITA と RA の I-composite graft を使用するようになった．

この I-composite graft に対するわれわれのイメージは，両側の内胸動脈（ITA）を基本にしつつ不足する長さを RA で補塡するというものではなく，むしろ RA の中枢側吻合を RITA におくというものである[14]．つまり術野で無理なく composite graft を作成することができる程度（だいたい中枢側半分くらい）しか RITA を剝離しない．RITA を全長剝離する場合に比べ，RITA の太い部分で RA に乗り換えることになり，端々吻合部の口径差がほとんどなく，この吻合部が弱点になることは少ないと思われる．また RITA の末梢で吻合するよりも高血流量のグラフトが期待できると考える[15]．Sajja ら[15]は 18 例の検討で，RITA と RA の I-composite graft の free flow は 98.06±16.93 m*l*/分であり，LITA の 55.80±8.99 m*l*/分より良好であったと報告している．

RITA を部分的に胸壁に残すことで，術後の創傷治癒に有利であるという効果もある[15,16]．ITA を full skeletonization で剝離することで縦隔洞炎の危険を減少させ[17]，さらに RITA の全長剝離を回避することにより，より安全になると思われる．

吻合操作上の利点を述べる．RITA-RA のグ