In Kaplan-Meier analysis, freedom from all-cause death at 1, 3, and 5 years were 95.4%, 89.7%, and 86.7% in the PCI, and 95.2%, 91.5%, and 87.5% in the CABG group, respectively (Figure 1A). There were no significant differences in the incidence of the all-cause death between the groups (p=0.19). Similarly, there were no differences in the incidence of composite cardiovascular event between the PCI and the CABG groups (p=0.89, Figure 1B).

Influence of preoperative glycemic control on outcomes after PCI and CABG

Diabetic profiles of the three groups are summarized in Table 2. Preoperative HbA1c level was similar between PCI and CABG in each group (p=0.15, p=0.67, and p=0.77, respectively). Baseline characteristics of the three groups are shown in supplemental files. Patients' characteristics in each group were generally similar to those of whole population.

Kaplan-Meier analysis: In the poor control group, freedom from all-cause death at 1, 3, and 5 years, were 93.9%, 87.1%, and 82.6% in the PCI, whereas 95.9%, 93.5%, and 91.2% in the CABG group, respectively (Figure 2A). The incidence of all-cause death was lower in the CABG group (p<0.01). The incidence of composite events in the CABG group tended to be lower than the PCI group (p=0.06, Figure 2B). In the good control group, however, freedom from all-cause death and the incidence of composite event were not different between the PCI and CABG groups (p>0.99 and p=0.32, Figure 2A and B). In the normal group, freedom from all-cause death and the incidence of composite event were not different between the groups (p>0.99 and p=0.96, Figure 3A and B).

Propensity-matched analysis: Propensity-matched all-cause mortality after PCI was higher than CABG in the poor control group (Hazard ratio [95%CI]: 2.56 [1.54-4.26], p<0.01) (Table 3). On the contrary, all-cause mortality was similar between PCI and CABG in the good control and the normal group (1.14 [0.75-1.72], p=0.55 and 0.93 [0.59-1.46], p=0.75, respectively).

Significant interaction p-value (0.04) indicates the survival benefit of CABG is prominent particularly in patients with poor glycemic control. Propensity-matched cardiovascular mortality after PCI was also higher than CABG in the poor control group (3.11 [1.66-5.83], $p<0.01$). However, the all-cause and cardiovascular mortalities were similar between PCI and CABG in the good control or nondiabetic groups.

The incidence of stroke after PCI was lower than CABG, regardless of the degree of glycemic control. Insignificant interaction p-value (0.99) indicates treatment modality (PCI or CABG) rather than the degree of glycemic control influences the postoperative stroke rate. The incidence of myocardial infarction after PCI was higher than CABG in the poor control group (3.29 [1.54-7.01], $p<0.01$), but similar in the good control or nondiabetic group. Insignificant p-value (0.50) indicates that treatment modality (PCI or CABG) rather than the degree of glycemic control influences the incidence of myocardial infarction. The incidence of composite cardiovascular event after PCI was higher than CABG in the poor control group (1.75 [1.18-2.59], $p<0.01$), but similar in the good control and normal groups.

DISCUSSION

Main findings

To our knowledge, this is the first multicenter registry that investigated the influence of the preoperative glycemic control using HbA1c level on long-term outcomes after PCI and CABG in patients with multivessel and/or left main disease. In patients with poor glycemic control, propensity-matched multivariate analysis showed that CABG reduced the all-cause and cardiovascular mortality compared with PCI. On the contrary, in patients with good glycemic control or nondiabetes, there were no significant differences in those endpoints between PCI and CABG. The incidence of myocardial infarction was lower after CABG than PCI; however, that of stroke was lower after PCI regardless of the degree of preoperative glycemic control. It is noteworthy that in patients with poor glycemic control, treatment with CABG was associated with better outcomes than PCI although the patients undergoing CABG included more high-risk patients and less postoperative medication than those of PCI. These results indicate that CABG may be a favorable revascularization strategy in diabetic patients suffering from poor preoperative glycemic control, and that preoperative strict glycemic control is recommended in diabetic patients undergoing PCI.

Diabetes and CABG outcomes

Depending on the severity of diabetes and its associated disorders and comorbidities, long-term survival is lower in diabetic as compared with nondiabetic patients [9]. Aggressive treatment to achieve glycemic control is associated with reduced mortality in patients with diabetes undergoing CABG [10]. Thus, long-term glycemic control may improve outcomes after CABG. HbA1c is not affected by short-term glycemic control, and therefore allows better assessment of glucose control over 3 to 4 months. Halkos and associates reported that poor glycemic control, as assessed by elevated HbA1c level, was strongly associated with adverse events after CABG both in-hospital and long-term follow-up [11]. They demonstrated that higher HbA1c (measured as continuous value) was associated with reduced long-term survival for each unit increase with hazard ratio of 1.15/unit. They also conclude that preoperative HbA1c level rather than diagnosis of diabetes is a better predictor for long-term survival after CABG.

Diabetes and PCI outcomes

Chronic hyperglycemia, as assessed by HbA1c level, is associated with an increased risk of cardiovascular disease in patients with diabetes [12]. Preprocedural high blood glucose level is associated with adverse outcomes after PCI for acute myocardial infarction [13]. However, the influence of preprocedurel elevated HbA1c level on long-term outcomes has been controversial. Mazeika and associates demonstrated that high HbA1c increased the angiographic restenosis in patients with diabetes [14]. However, several studies have reported that HbA1c level is not a predictor for cardiac events in patients with diabetes [15, 16]. That may be due to the difference in rates of drug-eluting stent use in each study. In addition, these results could partially explain the recent findings of randomized clinical trials that suggest a benefit of intensive glucose control (target 6.5%) in microvascular complications but not in macrovascular complications and death from any cause [17].

Optimal revascularization in patients with diabetes mellitus

Optimal revascularization strategy in patients with diabetes still has been controversial. Several observational studies reported the superiority of CABG in patients with diabetes mellitus with multivessel coronary artery disease [18, 19]. The present study also indicates CABG may be a better option in patients with multivessel or left main disease with uncontrolled diabetes. However, to conclude the superiority of CABG, there are several points to be addressed.

First, the present study was conducted in bare-metal stent era. Contemporary PCI procedures have already shifted from bare-metal to drug-eluting stenting with variable penetration rates. The striking efficacy of drug-eluting stents in preventing both clinical and angiographic restenosis has led to a rapid expansion of PCI use particularly for patients with complex multivessel disease [20]; however, improvement of survival has not yet been reported patients with diabetes with use of drug-eluting stents [21]. In the ARTS-2 study, survival rates at

3 years were not significantly different among the 3 groups of ARTS-2, ARTS-1 CABG, and ARTS-1PCI, initial advantage with sirolimus-eluting stent appeared to diminish at 3 years follow-up [22]. Furthermore, the pooled analysis of the pivotal randomized trials of the sirolimus-eluting stents suggested excessive mortality in diabetic patients treated with the sirolimus-eluting stents as compared with those treated with bare-metal stents [23]. Thus, CABG may also be a better option in patients with diabetes in drug-eluting stent era, as shown in the bare-metal stent.

Second, the present study included patients with left main disease. Most of the comparative studies between the outcomes of PCI and CABG excluded left main disease because it has generally been recommended to CABG. Recently, however, SYNTAX study demonstrated that PCI achieved equivalent survival and event-free outcomes to CABG in patients with low or intermediate SYNTAX score although CABG was better in patients with high SYNTAX score [24]. In addition, rate of patients with left main disease in CABG (28%) was far higher than that of PCI (4%) in the present study (Table 1). Furthermore, including left main disease would reflect the "real-world" patients undergoing coronary revascularization. Thus we consider that including left main disease in the present study did not weaken the conclusions.

Finally, the present study is an observational study. The discrepancy in outcomes between randomized controlled trials and registries comparing PCI with CABG is commonly ascribed to usual enrollment in the former of very selected low-risk patients with multi vessel coronary artery disease who are suitable for PCI, a feature that limits the ability to generalize conclusions to many high-risk patient categories in real-world clinical practice. On the other hand, observational study may expand the indications of PCI to more complex subsets of patients who were not indicated to CABG. In the present study, however, the CABG group included more complex patients than PCI such as left ventricular dysfunction and chronic kidney disease. Thus, we believe CABG can be a better option in treating preoperative poor glycemic control than PCI.

Study limitations

There are several important limitations of this study. First, we evaluated the preprocedural HbA1c level, but did not confirm the postoperative blood glucose management. Although we decided principles of the management in each institution, there might be any differences between the institutions. Furthermore, important medications, statins in particular, to prevent cardiovascular events are obviously underused. More optimal use of medications might have changed the long-term outcome of both PCI and CABG.

Conclusions

Poor preoperative glycemic control, as measured by an elevated HbA1c level, is associated with poor outcomes after PCI compared with CABG. CABG may be a favorable revascularization strategy in patients with multivessel coronary or left main disease, who suffer from poor preoperative glycemic control. Further study with drug-eluting stent is warranted.

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Disclosures

None

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FIGURE LEGENDS

Figure 1. Kaplan-Meier curves for each endpoint among all patients

A: All-cause death

B: Composite cardiovascular event

Figure 2. Kaplan-Meier curves for each endpoint among patients with preoperative poor glycemic control (diabetes with HbA1c ≥7%)

A: All-cause death

B: Composite cardiovascular event

Figure 3. Kaplan-Meier curves for each endpoint among patients with preoperative good glycemic control (diabetes with HbA1c <7%)

A: All-cause death

B: Composite cardiovascular event

Figure 4. Kaplan-Meier curves for each endpoint among nondiabetic patients

A: All-cause death

B: Composite cardiovascular event

CV: cardiovascular

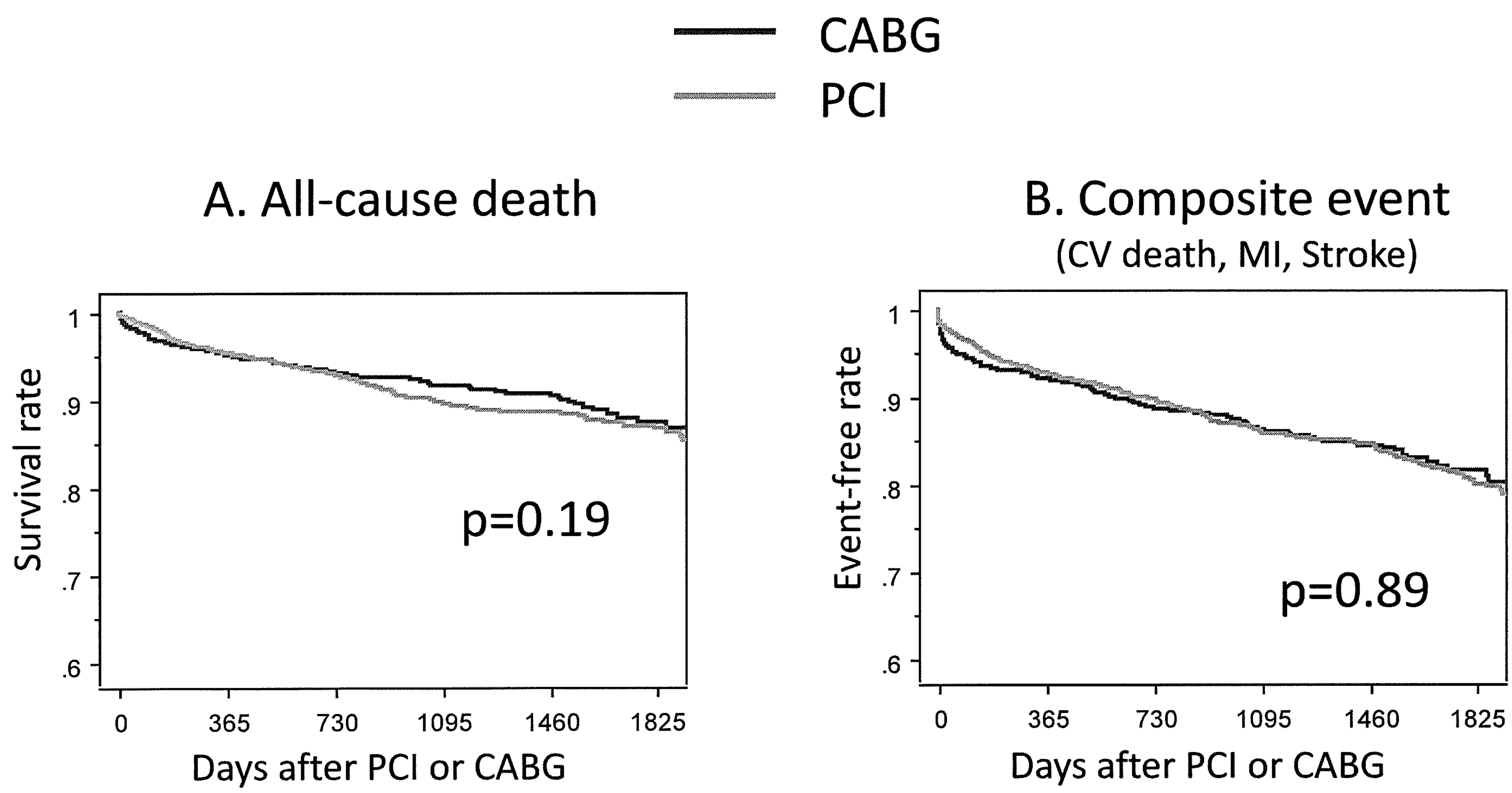
MI: myocardial infarction

Table 1. Baseline characteristics

	PCI (n=1975)	CABG (n=1175)	p value
Age	67.6 ± 9.9	66.9 ± 9.0	0.08
≥75 years	26%	21%	<0.01
Male gender	69%	72%	0.02
Body mass index	23.9 ± 3.4	23.5 ± 3.2	<0.01
≥25%	33%	30%	0.06
No. of diseased vessels	2.4 ± 0.5	2.6 ± 0.7	<0.01
Triple vessel disease	38%	70%	<0.01
Left main disease	4%	28%	<0.01
Proximal LAD disease	41%	61%	<0.01
Total occlusion	29%	57%	<0.01
Ejection fraction	61.3 ± 13.6	59.1 ± 14.8	<0.01
<40%	8%	12%	<0.01
Prior myocardial infarction	30%	37%	<0.01
Heart failure	16%	28%	<0.01
Atrial fibrillation	6%	6%	0.43
History of stroke	14%	22%	<0.01
Peripheral vascular disease	9%	22%	<0.01
Chronic pulmonary disease	2%	2%	0.18
Emergency procedure	4%	4%	0.5
Diabetes mellitus	57%	61%	0.02
Diabetes with any therapy	38%	45%	0.01
Diabetes with insulin therapy	12%	17%	<0.01
Hemoglobin A1c (%)	6.4 ± 1.5	6.4 ± 1.5	0.81
≥ 7.0%	28%	27%	0.56
Hypertension	72%	70%	0.33
Hyperlipidemia	52%	54%	0.56
Hemodialysis	4%	5%	0.17
Chronic kidney disease	40%	45%	<0.01
Malignancy	8%	6%	0.11
Hemoglobin	13.1 ± 2.0	12.7 ± 2.0	<0.01
< 12 mg/dl	25%	33%	<0.01
Current smoker	29%	25%	<0.01
Medication at discharge			
Statins	37%	18%	<0.01
Aspirin	86%	87%	0.02
Thienopyridines	74%	10%	<0.01
ACE inhibitor	27%	12%	<0.01
ARB	18%	8%	<0.01
β antagonist	25%	9%	<0.01
Calcium antagonist	60%	55%	<0.01
Nitrates	711%	48%	<0.01

LAD: left anterior descending artery
ACE: angiotensin converting enzyme
ARB: angiotensin receptor blockers

Figure 1A, 1B (All patients)



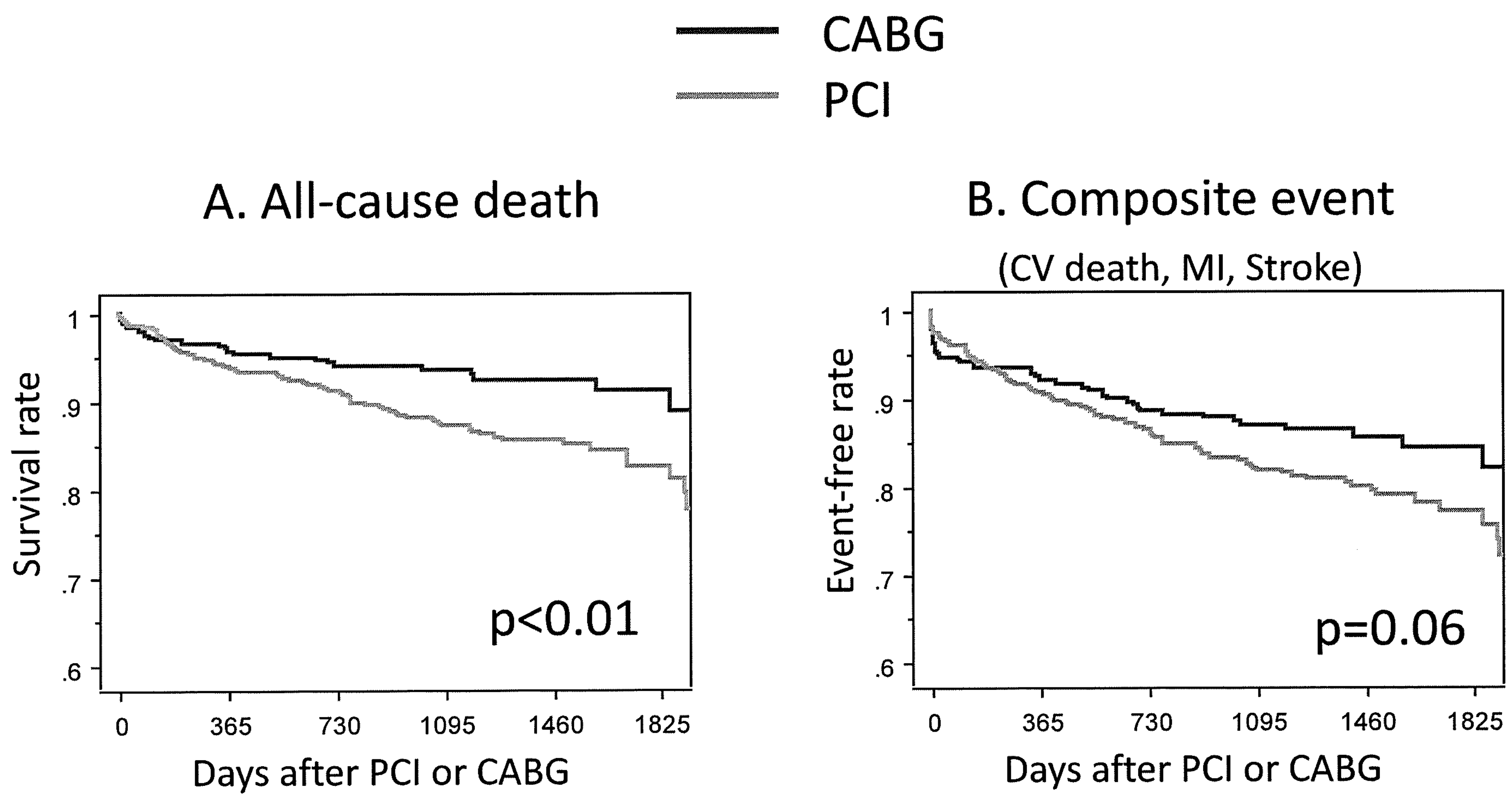
No. at Risk

	0	1yr	2yrs	3yrs	4yrs	5yrs
PCI	1975	1842	1739	1299	705	249
CABG	1175	1089	1031	721	379	135

No. at Risk

	0	1yr	2yrs	3yrs	4yrs	5yrs
PCI	1975	1778	1684	1205	651	226
CABG	1174	1043	967	670	349	125

Figure 2A, 2B (Poor control group)



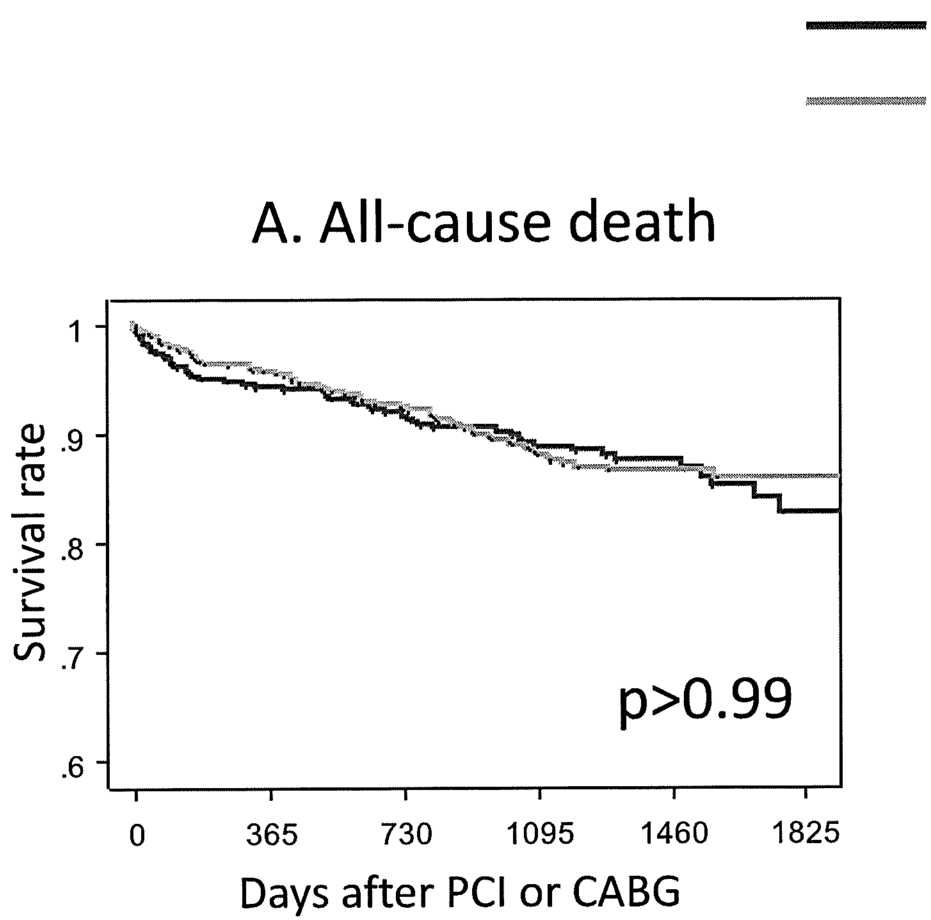
A. No. at Risk

	0	1yr	2yrs	3yrs	4yrs	5yrs
PCI	562	514	481	349	186	60
CABG	323	299	286	193	110	43

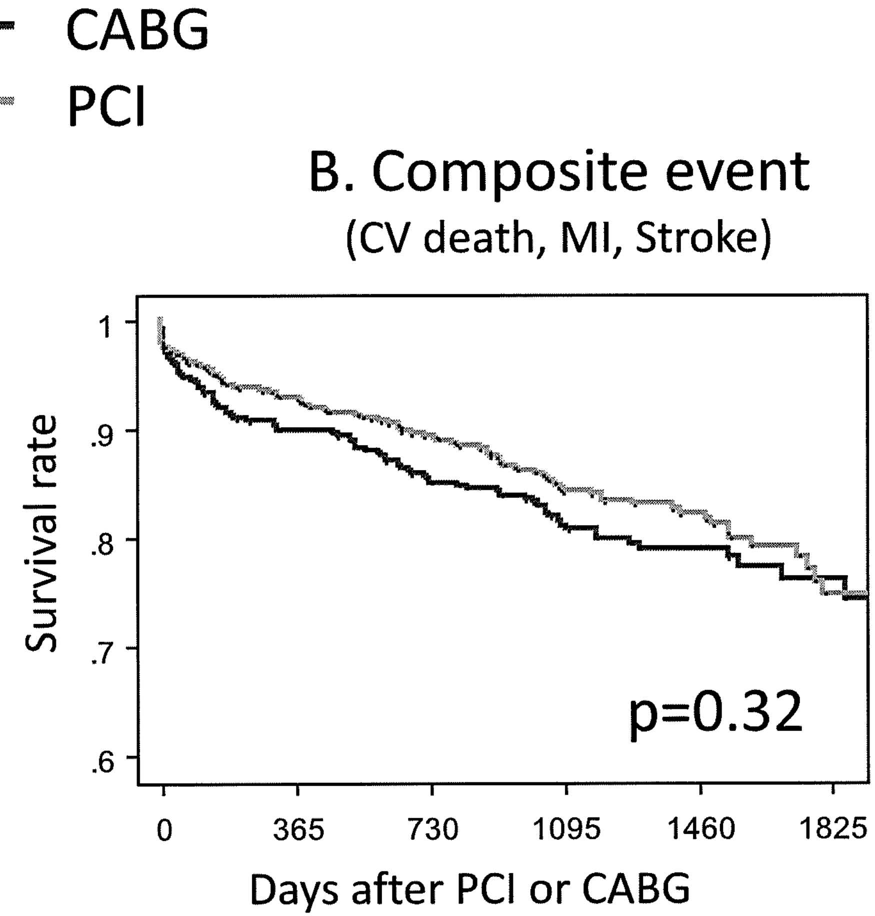
B. No. at Risk

	0	1yr	2yrs	3yrs	4yrs	5yrs
PCI	562	491	446	315	166	53
CABG	323	286	266	180	102	40

Figure 3A, 3B (Good control group)

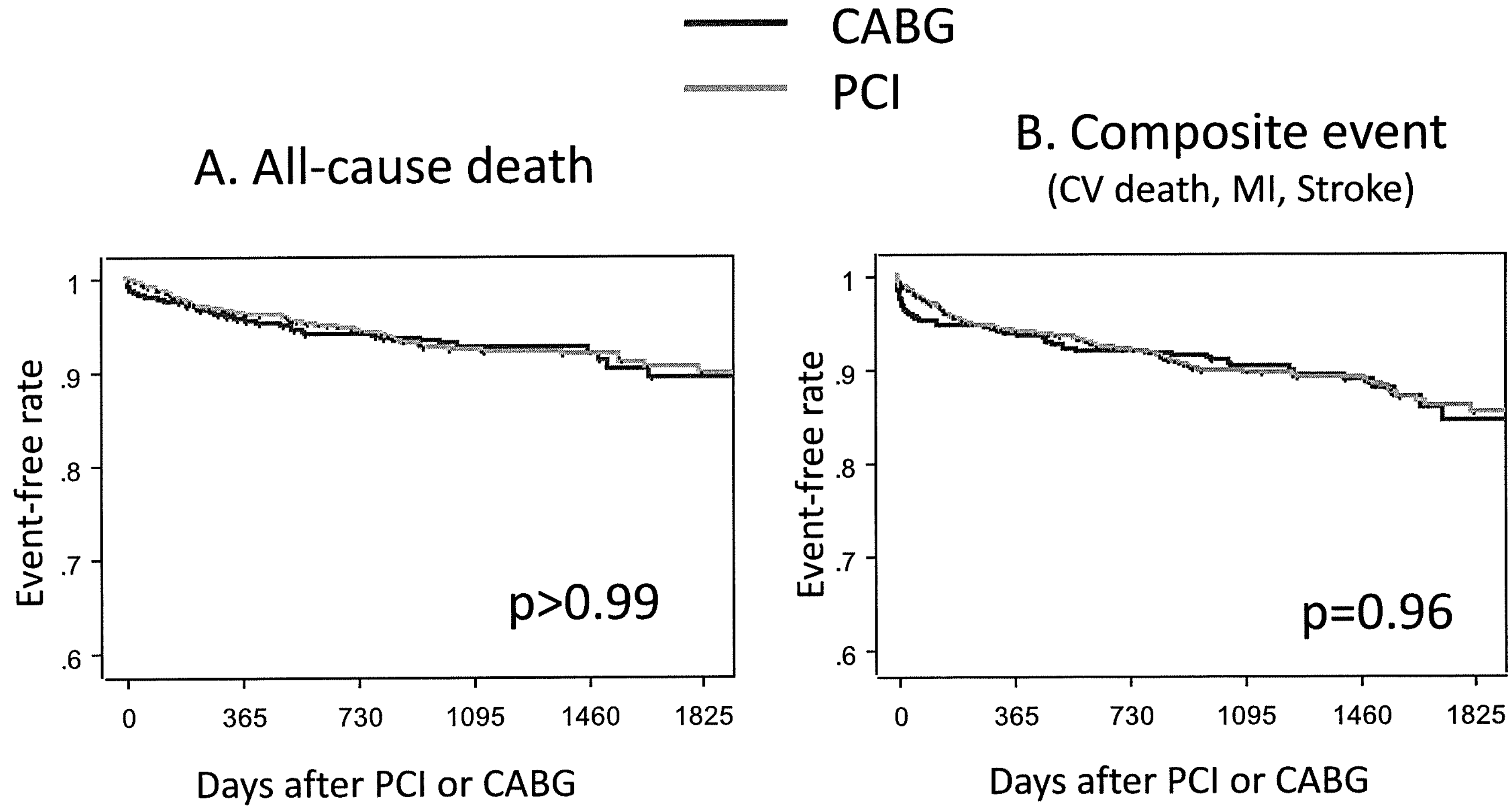


No. at Risk	0	1yr	2yrs	3yrs	4yrs	5yrs
PCI	555	518	486	357	190	67
CABG	399	366	344	247	138	50



No. at Risk	0	1yr	2yrs	3yrs	4yrs	5yrs
PCI	555	502	462	329	174	59
CABG	398	346	316	222	126	47

Figure 4A, 4B (Normal group)



No. at Risk

	0	1yr	2yrs	3yrs	4yrs	5yrs
PCI	858	812	805	595	331	125
CABG	453	426	403	283	133	39

No. at Risk

	0	1yr	2yrs	3yrs	4yrs	5yrs
PCI	858	787	742	571	313	117
CABG	453	413	387	238	124	41

Impact of Proximal Anastomosis Procedures on Stroke in Off-Pump Coronary Artery Bypass Grafting

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ABSTRACT ***Background:*** **There are many options for proximal anastomosis during off-pump coronary artery bypass grafting (CABG), but the efficacies of these procedures have not been well clarified. Therefore, we examined the clinical impact of our strategy to modify the proximal anastomosis procedure for aortic atherosclerosis.** ***Methods:*** **We retrospectively reviewed 535 consecutive patients undergoing off-pump CABG between 2004 and 2007. The patients were divided into three groups depending upon the type of proximal anastomosis procedure: 241 patients with normal or mild atherosclerosis underwent partial clamping (clamp group), 81 patients with moderate atherosclerosis underwent the procedure with Heartstring (Guidant Corporation, Santa Clara, CA, USA), 28 patients underwent with Enclose II (Novare Surgical Systems, Inc., Cupertino, CA, USA) (device group), and 185 patients underwent the procedure without clamping, including six with severe atherosclerosis (no-touch group).** ***Results:*** **There were seven in-hospital mortalities (1.3%) and five strokes (0.9%). There was no difference in the mortality rate (clamp, 1.2%; device, 1.8%; no-touch, 1.1%; $p = 0.42$) or stroke rate (clamp, 0.8%; device, 2.8%; no-touch, 0.5%; $p = 0.09$) among the three groups. Graft patency was similar regardless of the method (clamp, 94.7%; Heartstring, 96.7%; Enclosed II, 96.0%; $p = 0.80$).** ***Conclusions:*** **Our strategy to modify the proximal anastomosis procedure resulted in a low stroke rate. Aortic clamping could be performed safely in patients with normal or mild atherosclerotic aorta. In patients with moderate atherosclerosis, the result of an anastomotic device may need a further investigation.** doi: 10.1111/j.1540-8191.2009.00911.x *(J Card Surg 2009;24:644-649)*

Stroke after coronary artery bypass grafting (CABG) is a devastating complication. It occurs for various reasons, but the liberation of atheromatous debris from a diseased ascending aorta is the most significant mechanism.[1,2] Therefore, a careful assessment of the ascending aorta and a judicious selection of operative procedure are essential for stroke prevention. Epiaortic ultrasonographic scanning is a widely established method to detect atherosclerotic changes in the aorta.[2-5] We have modified the aortic anastomosis procedure using epiaortic ultrasonographic scanning. There are many options for proximal anastomosis during off-pump CABG, but the efficacies of these procedures have not been well clarified. The objective of this study was to retrospectively review our experience and investigate the impact of this procedural modification on clinical outcome.

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MATERIALS AND METHODS

We retrospectively analyzed 535 consecutive patients, from a single institution, who underwent off-pump CABG between September 2004 and June 2007. Patients who underwent any associated procedures were excluded from the analysis. During this period, all isolated CABGs were scheduled to be performed off-pump. Six patients who were converted to an on-pump CABG were excluded from the study. We routinely performed coronary angiograms before discharge for patients who underwent off-pump CABG, regardless of the patient's symptoms. Patients who died, refused angiographic evaluation, were older than 75 years old, or had renal dysfunction (serum creatinine >1.2 mg/dL) were excluded from the angiographic study. Postoperative angiographic study was performed in 432 patients (80.7%). Our Institutional Ethics Committee waived the need for patient consent and provided approval before publication of the data.

Epiaortic ultrasonography

Epiaortic ultrasonographic scanning was conducted when the revascularization strategy included proximal

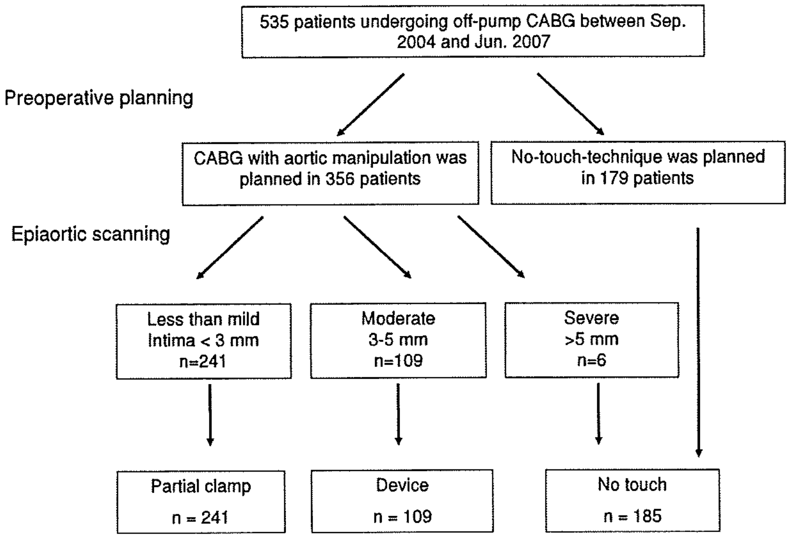

Figure 1. *Schematic of our strategy to modify the proximal anastomosis procedure using epiaortic ultrasonography.*

anastomosis to the aorta. There were 179 patients who did not receive aortic scanning, because aortic no-touch technique had been planned preoperatively. The scanning was performed with a 7.5-MHz linear ultrasonic probe (Sonos 7500; Philips Medical Systems, Andover, MA, USA), coated with ultrasonic gel as an acoustic medium, and packed in a sterile plastic sleeve. Ascending aortic atherosclerotic disease was defined as normal/mild (intimal thickness <3 mm), moderate (intimal thickness 3 mm to 5 mm), and severe (intimal thickness >5 mm; or the presence of marked calcification, protruding mobile intraluminal atheromatous portions, and ulcerated plaques).

Strategy of proximal anastomosis

The proximal anastomosis procedure was modified according to the results of epiaortic scanning (Fig. 1). Aortic scanning was performed on 356 patients who were to receive proximal anastomosis to the aorta. Partial clamping was performed in 241 patients who had normal or mild aortic atherosclerosis. A less invasive anastomotic device was selected for 109 patients who had moderate aortic atherosclerosis. Heartstring (Guidant Corporation, Santa Clara, CA, USA) was selected for 81 patients and Enclose II (Novare Surgical Systems, Inc., Cupertino, CA, USA) was selected for 28 patients. The selection of the two anastomotic devices depended on the preference of each surgeon. In six patients who had severe aortic atherosclerosis, the operative procedure was modified to an aortic no-touch technique.

Operative technique

Heparin (3.0 mg/kg) was administered intravenously after sternotomy to maintain an activated clotting time of more than 400 seconds, and it was neutralized at the end of the procedure with protamine sulfate (3.0 mg/kg). After hemostasis was achieved, patients who underwent CABG with a saphenous vein graft received a continuous heparin infusion to maintain an activated clotting time of 160 to 180 seconds until warfarin control was achieved. Aspirin was given to all patients.

Diagnosis of brain infarction

Stroke was suspected from any new global or focal neurological deficit and was confirmed by computed tomography or magnetic resonance imaging (MRI). It was diagnosed definitively by an attending neurologist. Reversible cerebral ischemic events were not considered as stroke. Stroke etiologies were identified and divided into thromboembolism and hypoperfusion. Thromboembolism was further divided into embolic, lacunar, and thrombotic.

Statistical analysis

Continuous variables are reported as mean ± standard deviation (SD). The chi-square test was used to analyze between group differences in the categorical variables. The Kruskal-Wallis test was used to analyze differences in continuous variables. Statistical significance was accepted at $p < 0.05$ and was performed with SPSS statistical software (SPSS version 11.0; SPSS Japan, Tokyo, Japan).

RESULTS

There were significant differences in age, gender, history of stroke, ischemic MRI findings, carotid artery stenosis, three-vessel disease, number of distal anastomoses, anticoagulant use, and new-onset atrial fibrillation (Table 1). Patients in the device group were older, more likely to have a history of stroke, show ischemia on MRI, and have carotid artery stenosis. Moreover, these patients were more likely to have a new-onset of atrial fibrillation and anticoagulant therapy. Those patients in the no-touch group had a lower prevalence of three-vessel disease and a lower number of distal anastomoses.

TABLE 1
Patient Characteristics

Characteristics	Clamp n = 241	Device n = 109	No-Touch n = 185	p Value
Preoperative				
Age (years)	68.1 ± 9.1	70.9 ± 8.4	68.4 ± 8.8	0.01
Male	73.0% (176)	83.5% (91)	90.3% (167)	≤0.01
Coronary risk factor				
Hypertension	75.5% (182)	75.2% (82)	71.9% (133)	0.67
Diabetes	42.7% (103)	38.5% (42)	38.4% (71)	0.60
Insulin dependent	10.0% (24)	8.3% (9)	9.2% (17)	0.14
Hyperlipidemia	63.9% (154)	57.8% (63)	54.6% (101)	0.88
History of stroke	9.1% (22)	20.2% (22)	10.8% (20)	0.01
Ischemic finding in MRI	49.5% (106)	56.9% (62)	43.8% (81)	0.05
Carotid artery stenosis	7.1% (17)	16.5% (18)	8.1% (15)	0.01
Three-vessel disease	80.9% (195)	79.8% (87)	40.0% (74)	≤0.01
Operative				
Emergent surgery	12.4% (30)	13.8% (15)	13.5% (25)	0.92
Results of aortic scanning	Normal or mild	Moderate	Severe 6 unknown 179	
No. of distal anastomosis	4.4 ± 1.2	4.2 ± 1.2	3.6 ± 1.3	≤0.01
Postoperative				
Anticoagulant use	84.2% (203)	92.7% (101)	29.7% (55)	≤0.01
New onset of atrial fibrillation	28.2% (68)	44.0% (48)	31.4% (58)	0.01

Parentheses represent the actual number of patients in each group.
MRI = magnetic resonance imaging.

There were seven in-hospital mortalities (1.3%), and five strokes (0.9%) (Table 2). The stoke rate in patients who received aortic scanning was 1.1% (four of 356). There was no difference in the mortality rate among the three groups. Patients in the device group had a slightly higher stroke rate than those who underwent clamp or no-touch procedures but the difference was not statistically significant. All strokes occurred postoperatively and the profile of each stroke patient is shown in Table 3. Patients who developed postoperative atrial fibrillation were more likely to have a stroke than those who did not, but there was no difference in the stroke rate for patients that did or did not undergo aortic manipulation (Table 4).

The operative procedures were compared among patients with three-vessel disease to determine whether the proximal anastomosis method affected the choice of a graft (Table 5). The number of distal anastomoses was similar among the three groups. The operative procedures were similar between those in the clamp and the device groups. Composite grafting and use of the gastroepiploic artery were more frequently chosen for the no-touch procedures, whereas the saphenous vein was chosen less frequently. Graft patency was similar regardless of the method (Table 6).

DISCUSSION

Our strategy to modify the proximal anastomosis procedure following epiaortic ultrasonographic scanning resulted in a low stroke rate. Aortic clamping could be performed safely in patients with a normal or mild atherosclerotic aorta. In patients with moderate atherosclerosis, the use of less invasive devices may need a further investigation. Each proximal anastomosis procedure resulted in a similar patency rate.

In conventional on-pump CABG, stroke occurs at a rate of 0.8% to 5.2%.[6] The presence of atherosclerosis in the ascending aorta, a leading risk factor for stroke, is associated with a fourfold increase in stroke.[1,2] Transcranial Doppler ultrasonography has shown that surgical manipulation of the ascending aorta with atherosclerosis may liberate atheromatous debris and cause brain embolism.[7] Therefore, the detection of atherosclerosis in the ascending aorta and a procedural modification to minimize aortic manipulation are essential to reduce the risk of stroke after CABG. Epiaortic ultrasonographic scanning is a widely established method to detect atherosclerosis in the aorta.[2-4] A low stroke rate (2.3%) has been achieved using epiaortic scanning with on-pump CABG followed by a procedural modification.[5]

TABLE 2
Clinical Results

	Overall n = 535	Clamp n = 241	Device n = 109	No-Touch n = 185	p Value
In-hospital mortality	1.3% (7)	1.2% (3)	1.8% (2)	1.1% (2)	0.42
Stroke	0.9% (5)	0.8% (1)	2.8% (3)	0.5% (1)	0.09

Parentheses represent the actual number of patients in each group.

TABLE 3
Profile of Stroke Patients

No.	Group	Age/Sex	Cause of Stroke	Timing of Onset	CT/MRI Findings	Carotid Lesion	Stroke History	AF	Anticoagulant	Coronary Risk Factor
1.	Clamp	68/male	Embolic	5	Left corona radiata	Not screened	No	Yes	Yes	HT, HLP DM (insulin)
	Stroke occurred just after cessation of postoperative atrial fibrillation. The INR value at the time of stroke onset was 2.51									
2.	Device (Heartstring)	81/male	Embolic	2	Multiple	Not screened	No	Yes	No	DM, smoking
	Stroke occurred just after cessation of postoperative atrial fibrillation. The INR value at the time of stroke onset was 1.62									
3.	Device (Heartstring)	76/female	Hypoperfusion	1	Right corona radiata	No	Yes	Yes	No	HT, DM, HD
	Stroke occurred after recovery from hypovolemic shock during postoperative hemodialysis									
4.	Device (Heartstring)	88/female	Embolic	1	Bilateral cerebellum	Unilateral	Yes	Yes	Yes	HT
	She had symptomatic severe unilateral carotid artery occlusion. Stroke occurred after the recovery from anesthesia									
5.	No-Touch	80/male	Thrombotic	6	Multiple	No	No	No	No	HT, HLP
	Stroke occurred after weight loss due to polyuria. He had an almost normal ascending aorta									

CT = computed tomography; MRI = magnetic resonance imaging; INR = international normalized ratio; AF = atrial fibrillation; HT = hypertension; HLP = hyperlipidemia; DM = diabetes mellitus; HD = chronic hemodialysis.

Although the efficacy of off-pump CABG to reduce stroke remains controversial,[8-10] it has been effective for reducing stroke in patients with aortic atherosclerosis.[11,12] Off-pump CABG does not require aortic manipulation, except when performing a proximal anastomosis to the aorta, and there are a wide variety of proximal anastomosis procedures that minimize aortic manipulation. The strategy for managing aortic atherosclerosis in off-pump CABG is drawing interest, but has not yet been established.

There is no consensus as to whether avoiding aortic manipulation actually reduces stroke even in patients undergoing off-pump CABG. According to Calafiore et al., the use of side-clamping during off-pump CABG results in a similar stroke rate as patients undergoing conventional on-pump CABG.[13] However, epiaortic ultrasonography can aid in the selection of good candidates for aortic clamping and reduce their stroke risk. We found a low stroke rate (0.8%) in patients of the clamp group who had a normal or mild atherosclerotic aorta. These results suggest that aortic clamping is safe in patients with normal or mild atherosclerotic aorta.

TABLE 4
Predictors of Stroke

Characteristics	Stroke Rate (%) With Characteristics	Stroke Rate (%) Without Characteristics	p Value
Age >70 years	1.47	0.38	0.37
History of stroke	3.13	0.64	0.11
Carotid artery stenosis	2.00	0.48	0.29
Ischemic finding in MRI	0.82	0.51	1.00
Aortic manipulation	1.14	0.54	0.66
Postoperative atrial fibrillation	2.27	0.28	0.04

MRI = magnetic resonance imaging.

The efficacy of using a less invasive device to reduce stroke, especially in patients with atherosclerotic aorta, has not been determined. One small study (n = 19) found a relatively high stroke rate (5.2%) following the use of the Heartstring device in patients with a diseased aorta.[14] In patients with a moderately atherosclerotic aorta, we used Heartstring and Enclose II and the stroke rate (2.8%) was slightly higher than in patients who underwent clamps or no-touch procedures. Due to differences in patient background, it may be simplistic to compare stroke rates among these groups. However, our study is too small to determine the efficacy of anastomotic devices for patients with an atherosclerotic aorta, further investigation is considered necessary.

The aortic no-touch technique is an effective method to reduce stroke.[13,15,16] Our study also confirmed a low stroke incidence (0.5%) in no-touch group including six patients with a severe atherosclerotic aorta. However, use of the aortic no-touch technique may limit the revascularization strategy. In most studies, the number of distal anastomoses is lower in those undergoing an aortic no-touch procedure (Lev-Ran et al.; 2.30 vs. 2.54, $p = 0.003$,[16] Bolontin et al.; 2.27 vs. 3.11, $p < 0.001$).[16,17] The in-flow source was limited to only three in situ grafts. Revascularization for the lateral wall usually requires composite grafting, whereas revascularization for the right coronary artery usually requires the use of the gastroepiploic artery. The consequence of this special strategy has not been completely clarified, but Gaudino et al. suggested that using the radial artery as a composite graft is more vulnerable to the detrimental effect of flow competition.[18] We usually performed the no-touch technique only in patients whose target right coronary artery is severely stenosed and suitable for grafting with gastroepiploic artery. And currently, the no-touch technique is our first-choice treatment only for patients with severe atherosclerosis.

TABLE 5
Impact of the Proximal Anastomosis Procedure on Graft Choice

Characteristics	Clamp n = 195	Device n = 87	No-Touch n = 74	p Value
Number of distal anastomosis	4.6 ± 1.1	4.5 ± 1.1	4.5 ± 1.0	0.40
Frequency of use of composite graft	52.8% (103)	60.0% (52)	85.1% (63)	≤0.01
Frequency of use of each graft				
LITA	100% (195)	97.7% (85)	98.6% (73)	0.13
RITA	90.8% (177)	95.4% (83)	93.2% (69)	0.38
RA	60.5% (118)	48.3% (42)	55.4% (41)	0.16
SV	93.3% (182)	94.3% (82)	14.9% (11)	≤0.01
GEA	9.2% (18)	3.4% (3)	60.8% (45)	≤0.01

Parentheses represent the actual number of patients in each group. The number of distal anastomoses represents the mean ± standard deviation.
LITA = left internal thoracic artery; RITA = right internal thoracic artery; RA = radial artery; SV = saphenous vein; GEA = gastroepiploic artery.

TABLE 6
Angiographic Patency

	Clamp	Heartstring	Enclose II	p Value
Saphenous vein	94.5% (156/165)	96.4% (53/55)	94.7% (18/19)	0.87
Radial artery	95.0% (57/60)	100% (5/5)	100% (6/6)	0.75

Parentheses represent the actual number of patients with patent grafts/the total number of patients studied.

Study limitation

The limitations of the study include those inherent to all retrospective, nonrandomized studies. The number of study patients was relatively small, which did not allow us to make strong conclusions regarding the effect of an off-pump procedure on a rare complication such as stroke. Graft patency was only assessed in the immediate postoperative period. Therefore we can not determine the effects of this strategy on long-term graft patency or the recurrence of angina symptom based on our study design.

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