Original Article

Efficacy of Intraoperative Epiaortic Ultrasound Scanning for Preventing Stroke after Coronary Artery Bypass Surgery

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Purpose: The aim of this study was to clarify the efficacy of intraoperative epiaortic ultrasound scanning (EAS) for preventing cerebral emboli following coronary artery bypass grafting (CABG).
Patients and Methods: The intraoperative EAS was used to evaluate the ascending aorta in 909 consecutive CABG patients. When the scanning documented more than 3 mm of atheromatous thickness or plaque in the ascending aorta, we never manipulated it. Therefore 196 patients (21.6%) underwent off-pump CABG using composite grafts (85 cases, 9.4%) or in situ grafts (111 cases, 12.2%) with no aortic manipulation. The ascending aorta was confirmed to be free from significant atheromatous plaque by the EAS in 713 patients (78.4%). On-pump CABG was performed using aortic cannulation and total aortic clamping in 429 patients (47.2%). Off-pump CABG with aortocoronary bypass grafts was performed using side-bite aortic clamping in 165 cases (18.2%) or the other anastomotic devices in 63 cases (6.9%).
Results: There were five hospital deaths (0.6%) but no postoperative strokes. Postoperative coronary angiography revealed 98.8% (1,659/1,680) of the patency of the bypassed grafts.
Conclusions: It was suggested that the application of aortic clamping or cardiopulmonary bypass was not a risk factor of cerebral emboli when the ascending aorta was evaluated using the EAS. Furthermore, the application of aortic clamping with free grafts may provide eligible bypass graft patterns, leading to sufficient graft patency. (Ann Thorac Cardiovasc Surg 2009; 15: 98–104)

Key words: atherosclerosis, coronary artery bypass grafting, embolism, stroke, ultrasound

Introduction

Atherosclerosis of the ascending aorta has emerged as one of the most important risk factors for postoperative neurological complications following coronary artery bypass grafting (CABG) when the diseased aorta is manipulated by cannulation and clamping.[1–3] These maneuvers can be associated with intraoperative atheromatous embolization into the cerebral circulation, resulting in persistent cognitive deficit or postoperative stroke, a serious complication with a considerable mortality of up to 21%.[4]

The current trend is toward surgical treatment of coronary heart disease in older patients with a higher comorbidity. Moreover, the severity of ascending aortic atherosclerotic disease and the stroke rate are known to increase with age. Epiaortic ultrasound scanning (EAS)

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has been added to the armament of cardiac surgeons as a fast, noninvasive, and sensitive technique that provides information about the ascending aortic wall in its entire length and circumference.[5–7] Furthermore, epiaortic scanning is more accurate than palpation in identifying mobile atheroma in the ascending aortic lumen.[5,8]

We have evaluated the ascending aorta using intraoperative EAS to detect ascending aortic atherosclerosis in each patient undergoing CABG. The aim of this study was to clarify the efficacy of intraoperative epiaortic ultrasound for preventing cerebral emboli following CABG.

Patients and Methods

The study population consisted of 909 consecutive patients undergoing isolated primary CABG and intraoperative evaluation of the ascending aorta with EAS at Saitama Medical Center, Jichi Medical University, from August 2000 through December 2006. All patients who underwent any other associated procedures were not included in the present analysis. The decision of whether to perform off-pump CABG (OPCAB) or conventional on-pump CABG (CCAB) was based on the surgeon's individual choice. Both OPCAB and CCAB techniques were used according to the patient's comorbidities and the evaluation of the ascending aorta. We used OPCAB only when the patient was more than 70 years old or had comorbidity of chronic renal dysfunction. We preferred on-pump beating CABG when the patient had unstable hemodynamics resulting from acute coronary syndrome.

The final decision of whether to manipulate the ascending aorta was based on the evaluation of intraoperative EAS. Patients were divided into the following four groups. In 196 patients (21.6%), OPCAB (group 1) was performed using composite grafts (85 cases, 9.4%) or in situ grafts (111 cases, 12.2%) with no aortic manipulations. The ascending aorta was confirmed to be free from significant atheromatous plaque by EAS in 713 patients (78.4%). OPCAB with aortocoronary bypass grafts (group 2) was performed using side-bite aortic clamping in 165 cases (18.2%) or another anastomotic device in 63 cases (6.9%). On-pump beating CABG (group 3) was performed using aortic cannulation in 56 patients (6.1%). CCAB (group 4) was performed using aortic cannulation and total aortic clamping in 429 patients (47.2%).

Evaluation of the ascending aorta

Palpation of the ascending aorta for identification of calcified areas was done with caution to avoid dislodgement of embolic materials. EAS was performed with a 7-MHz linear ultrasonic probe (PVF-745V, Toshiba, Tokyo). After the pericardium was opened, a plastic and sterile glove filled with saline solution as an acoustic medium was put on the ascending aorta to sustain an echo lucent window for optimal visualization of the anterior ascending aortic wall thickness. The probe was then manipulated gently to obtain longitudinal and transverse views from the aortic valve up to the brachiocephalic artery. Ascending aortic atherosclerotic disease was defined as normal/mild (aortic wall < 3 mm), moderate (aortic wall 3 to 5 mm), and severe (aortic wall thickness > 5 mm), and/or the presence of marked calcification, protruding or mobile intraluminal atheromatous portions, and ulcerated plaques) according to the classification reported by Wareing and colleagues.[9] In patients with the diseased ascending aorta, the decision of whether to avoid aortic manipulation was based on the location and characteristics of the atherosclerotic lesion. Side-bite clamping was believed safe in case of mild atherosclerotic lesions located in the posterior wall of the ascending aorta or at the level of the origin of the brachiocephalic trunk far enough from the site of the aortic clamping. Exophytic atherosclerotic lesions were considered an absolute contraindication to aortic manipulation. The severity of the atheromatous plaque in the ascending aorta according to the above criteria is summarized in Table 1.

Surgical procedures

OPCAB was carried out through a median sternotomy using a Medtronic tissue stabilizer system™ (Medtronic, Minneapolis, MN). Heparin (1.5 mg/kg) was administered intravenously after sternotomy to maintain an activated clotting time (ACT) of more than 300 seconds, and it was neutralized at the end of the procedure by using protamine sulfate (1.5 mg/kg). Blood in the operative field was collected by suction catheters and returned using a cell-saving device (Electa™ concept, Dideco, Mirandola Modena, Italy).

The ascending aorta was left untouched in 196 patients (21.6%) during OPCAB by means of composite grafts or in situ grafts. Both internal thoracic arteries were used as in situ grafts. But when the right internal thoracic artery was too short to reach the target coronary arteries, it was anastomosed to the left internal thoracic artery as a com-

Table 1. The frequency of atheromatous disease in the ascending aorta

	Group 1	Group 2	Group 3	Group 4	Overall
Normal/mild†	131 (66.8%)	166 (72.8%)	42 (75.0%)	365 (85.1%)	704 (77.4%)
Moderate	29 (14.8%)	50 (21.9%)	11 (19.6%)	64 (14.9%)	154 (16.9%)
Severe†	36 (18.4%)	12 (5.3%)	3 (5.4%)	0 (0%)	51 (5.6%)

†, a *p* value of less than 0.05 by statistical comparisons between the four groups; group 1, OPCAB with aortic no-touch; group 2, OPCAB with aortic manipulation; group 3, on-pump beating CABG; group 4, on-pump CCAB; CABG, coronary artery bypass grafting; CCAB, conventional coronary artery bypass grafting; OPCAB, off-pump coronary artery bypass.

posite graft. For complete revascularization, radial artery grafts were also implanted into the internal thoracic arteries as composite grafts. When the ascending aorta was considered to be safe for aortic manipulation on the basis of the EAS evaluation, side-bite clamping (165 cases, 18.2%) or Enclose II™ (Novare Surgical Systems Inc., Cupertino, CA) anastomotic devices (27 cases, 3.0%) were used. Passport proximal aortic connectors™ (Cardica, Redwood City, CA) were also used in 36 patients (4.0%) with severely diseased ascending aorta.

On-pump beating CABG was performed using a centrifugal pump kit and a membrane oxygenator coated with an antithromboembolic agent (Capiox™ Custom pack EBS™ CX-ESS, Terumo, Tokyo) to maintain a mean arterial pressure of more than 75 mmHg during the procedure. Heparin (1.5 mg/kg) was administered intravenously after sternotomy to maintain an ACT of more than 300 seconds, and it was neutralized at the end of the procedure by using protamine sulfate (1.5 mg/kg). Proximal anastomoses were sutured to the aorta using aortic side-bite clamping (25 cases, 2.8%) Enclose II™ anastomotic devices (1 case, 0.1%), and Passport proximal aortic connectors™ (11 cases, 1.2%) were also used in patients with severely diseased ascending aorta.

On-pump CCAB was performed by means of cardiopulmonary bypass with a roller pump (Stöckert 53, Munich, Germany), a membrane oxygenator (Capiox™ RX25, Terumo, Tokyo), and a 40 μm arterial blood filter (Autovent™, Pall Co., East Hills, NY). Moderate hypothermia (28ºC) and intermittent antegrade delivery of cold blood cardioplegia were used. Heparin (3.0 mg/kg) was administered intravenously after sternotomy to maintain an ACT of more than 400 seconds, and it was neutralized at the end of the procedure by using protamine sulfate (3.0 mg/kg). Blood from suction catheters was returned to the circuit of the cardiopulmonary bypass. Proximal anastomoses were sutured to the aorta during cross clamping, and aortic side clamping was never used during CCAB.

End-point

Stroke was defined as prolonged or any permanent deficit occurring during the in-hospital stay. In-hospital mortality included any cause of postoperative death during the in-hospital stay.

The estimated stroke risk score obtained from the American Heart Association (AHA) guidelines were calculated in all patients. Preoperative data were obtained relative to age, left ventricular ejection fraction less than 0.4, urgent surgery, emergency surgery, prior CABG, peripheral vascular disease (PVD), diabetes treated with medications, serum creatinine level more than 2.0 mg/dl, and renal failure on dialysis. The estimated risk of postoperative stroke was calculated in each patient using the formula published in the AHA 2004 guidelines by the Northern New England cardiovascular disease study group.[10] The predicted risk of stroke was obtained in each patient, and the mean value of the predicted risk was compared between groups according to surgical procedures. The mean value of the estimated risk was then compared to the incidence of postoperative stroke in each group.

Postoperative coronary angiography was performed in 548 patients (60.3%) during the in-hospital stay to examine the function of the bypassed grafts.

Statistics

Continuous variables were expressed as means ± standard deviations (SDs) and categorical variables as absolute numbers (percentages). Statistical analyses were performed using the Student's *t*-tests for continuous variables or Chi-square tests for categorical variables. The data analyses between the four groups were performed using the Kruskal-Wallis test and followed by the Mann-Whitney U test with Bonferroni correction as the post hoc test. A *p* value of less than 0.05 was considered significant.

Table 2. Clinical and operative patient data

	Group 1	Group 2	Group 3	Group 4
Number of patients	196	228	56	429
Mean age (y.o.)†	66.68	68.58	67.96	63.61
Age > 80 y.o.†	15 (7.7%)	20 (8.8%)	2 (3.6%)	2 (0.5%)
Age > 70 y.o.†	75 (38.3%)	112 (48.9%)	28 (50.0%)	115 (26.8%)
Male gender	164 (83.7%)	184 (80.7%)	47 (83.9%)	318 (74.1%)
Urgent	34 (17.4%)	34 (14.9%)	6 (10.7%)	59 (13.8%)
Emergent†	4 (2.0%)	20 (8.8%)	12 (21.4%)	0
Chronic renal failure (Cr >2.0)	25 (12.8%)	37 (16.2%)	10 (17.9%)	24 (5.6%)
Peripheral artery disease†	25 (12.8%)	17 (7.5%)	11 (19.6%)	11(2.6%)
Ejection fraction <0.4	27 (13.8%)	28 (12.3%)	10 (17.9%)	47 (10.9%)
Prior coronary bypass grafting	6 (3.1%)	1 (0.4%)	1 (1.8%)	4 (1.0%)
Number of grafted vessels†	2.44	3.13	2.88	3.28
Use of LITA	186 (94.9%)	210 (92.1%)	49 (87.5%)	414 (96.5%)
Use of RITA	135 (68.9%)	48 (21.1%)	23 (41.1%)	139 (32.4%)
Use of RGEA	80 (40.8%)	86 (37.7%)	20 (35.7%)	151 (35.2%)
Use of radial artery	35 (17.9%)	71 (31.1%)	10 (17.9%)	97 (22.6%)
Use of saphenous vein†	24 (12.2%)	175 (76.8%)	35 (62.5%)	286 (66.7%)
Partial clamping	0	165 (72.4%)	25 (44.6%)	0
Use of aortic connector	0	36 (15.8%)	11 (19.6%)	0
Use of Enclose II	0	27 (11.8%)	1 (1.8%)	0
Composite graft	85 (43.4%)	11 (4.8%)	13 (23.2%)	13 (3.0%)
Operative death	2 (1.0%)	1 (0.4%)	1 (1.8%)	1 (0.2%)

y.o., years old; †, a p value of less than 0.05 by statistical comparisons between the four groups; group 1, OPCAB with aortic no-touch; group 2, OPCAB with aortic manipulation; group 3, on-pump beating CABG; group 4, on-pump CCAB; CABG, coronary artery bypass grafting; CCAB, conventional coronary artery bypass grafting; Cr, serum creatinine; OPCAB, off-pump coronary artery bypass; LITA, left internal thoracic artery; RGEA, right gastroepiploic artery; RITA, right internal thoracic artery.

Results

Emergent cases and comorbidity of peripheral artery disease were less often in the CCAG patients compared with the remaining three groups, as shown in Table 2. The incidence of use of saphenous vein grafts was lower in OPCAB (with aortic no-touch) patients compared with the remaining three groups. The CCAB group consisted of younger patients who were unlikely to have comorbidity and operative risk factors.

As shown in Table 1, the frequencies of normal aortic wall, moderate atherosclerotic disease, and severe disease were 77.4%, 16.9%, and 5.6%, respectively. Approximately 30% of patients undergoing OPCAB had moderate or severe atheromatous disease in the ascending aorta. The incidence of the atheromatous disease in OPCAB patients was almost double in CCAB patients.

The overall postoperative stroke rate after OPCAB with aortic no-touch, OPCAB with aortic manipulation, CCAB, and on-pump beating CABG was 0%, though the AHA estimated stroke risk scores of OPCAB with aortic no-touch, OPCAB with aortic manipulation, on-pump beating CABG, and CCAB patients were 1.20%, 1.15%, 1.31%, and 1.07%, respectively. Even if OPCAB and on-pump beating CABG patients were quite likely to have high risks for postoperative stroke, there were no complications of stroke or any neurological deficit following any CABG procedures.

There were five in-hospital deaths (0.6%). The causes of these deaths were intestinal necrosis (1), pneumonia (1), mediastinitis (1), perioperative coronary spasm (1), and Stevens-Johnson syndrome (1).

The postoperative coronary angiography was performed in 548 patients and revealed that the overall patency rate of the bypassed grafts was 98.8% (1,659/1,680). As shown in Table 3, there was no significant difference in the patency of the bypassed grafts between the four groups.

Comments

The reported incidence of postoperative stroke following isolated coronary artery bypass surgery ranges from 1.4% to 3.8%.[1,11] The database of the Society of Thoracic Surgeons showed that postoperative stroke occurred in 1.65% and postoperative transient ischemic attack in 0.74% of

Table 3. Graft patency

	Group 1	Group 2	Group 3	Group 4
Number of patients	196	228	56	429
CAG undergone	121	138	15	274
Bypassed grafts	312	424	40	904
Patent grafts	307 (98.4%)	419 (98.8%)	39 (97.5%)	894 (98.9%)
Patency of LITA	124/126	130/131	15/15	262/264
RITA	93/93	40/40	6/6	102/103
RGEA	44/45	60/61	1/1	116/117
RA	27/28	55/56	4/4	72/73
SVG	19/20	124/126	13/14	332/337

group 1, OPCAB with aortic no-touch; group 2, OPCAB with aortic manipulation; group 3, on-pump beating CABG; group 4, on-pump CCAB; CABG, coronary artery bypass grafting; CAG, postoperative coronary angiography; CCAB, conventional coronary artery bypass grafting; OPCAB, off-pump coronary artery bypass; LITA, left internal thoracic artery; RA, radial artery; RGEA, right gastroepiploic artery; RITA, right internal thoracic artery; SVG, saphenous vein graft.

patients.[12] According to recent data, postoperative stroke following cardiac surgery is associated with 19% of in-hospital mortality, and only 25.8% of patients return to a normal level of activity.[13]

van der Linden and colleagues[14] could not show a reduction in the prevalence of postoperative strokes with minor modifications in surgical technique in a series of 921 consecutive patients undergoing cardiac surgery. The prevalence of strokes in their series was 1.8% in patients without atherosclerotic disease of the ascending aorta and 8.7% in patients with the disease despite minor surgical modifications. This may advocate a more aggressive change of the operative technique in the presence of severe ascending aortic atherosclerotic disease. In the group of patients who underwent the beating heart and aortic no-touch concept, the stroke rate was near 0%, and we regard this strategy as a very promising method for patients with extensive ascending aortic disease.[15] A lower frequency of postoperative stroke after off-pump CABG has been reported.[16–18] Patel and colleagues[19] have also described a near 0% stroke rate using beating heart total arterial revascularization without aortic manipulation.

Motallebzadeh and colleagues[20] examined embolic signals of the middle cerebral artery intraoperatively using bilateral transcranial Doppler ultrasonography. The randomized study demonstrated that the embolic signals were more prevalent during on-pump conventional CABG compared with OPCAB. Emboli during on-pump CABG can arise from a variety of sources, for example, from aortic cannulation and through the application and removal of aortic clamps releasing debris from atherosclerotic plaques. Traditionally, most neurological complications after on-pump conventional CABG have been attributed to the use of cardiopulmonary bypass and manipulation of the ascending aorta.

Although ascending aortic atherosclerosis has been considered to be an independent predictor of stroke in previous studies, the diseased ascending aorta was not associated with postoperative neurological events in our study, possibly demonstrating a preventive effect of the EAS and surgical modifications used. Modifications using OPCAB and aortic no-touch techniques seem to play a very promising role in the management of ascending aortic atherosclerosis. In our series, the routine use of intraoperative EAS in CABG patients can lead the surgeons' decisions toward modifications of operative techniques in the presence of ascending aortic atherosclerosis. The use of EAS aiming to minimize the risk of intraoperative embolism can also provide optimal planning of operative strategy.

Computed tomography identifies the most severely involved aortas, but underestimates mild or moderate involvement. In our preliminary data, the frequency of diseased ascending aorta detected by computed tomography as a preoperative evaluation in CABG patients was approximately 12%, whereas intraoperative EAS detected moderate or severe atheromatous aortic disease in 22.6% of the same series of patients. Hangler and colleagues[5] have demonstrated that moderate atherosclerotic disease was detected in 47.5% of CABG patients and severe disease in 9.6% when the ascending aorta was evaluated by intraoperative EAS. Trehan and colleagues[6] have also demonstrated that 28.5% of CABG patients had moderate or severe atherosclerosis in the ascending aorta. Transesophageal echocardiography is useful for aortic arch examination, but examination of the ascending aorta may be limited by the intervening trachea. Intraoperative palpation underestimates the high-risk aorta. The highest-risk aortic pattern is a protruding or mobile aortic plaque, which may be missed by intraoperative palpation. Intraoperative assessment with EAS is superior to these methods and modalities.

Hirose and colleagues[21] have demonstrated that a side clamp applied for aortocoronary bypass in OPCAB did not increase the risk of postoperative stroke. Aortocoronary bypass is often required in addition to an in situ bypass for the optimal grafting plan of multivessel CABG. In situ OPCAB is theoretically free from postoperative stroke because it does not require aortic manipulation or cardiopulmonary bypass. However, aortocoronary bypass using free grafts is very often beneficial for multivessel revascularization because of the limited availability of in situ grafts and/or a sufficient graft flow of aortocoronary bypass grafts. In an aortocoronary bypass, side clamping the ascending aorta for proximal anastomosis is necessary. If the EAS detects the presence of atherosclerosis in the posterior wall of the ascending aorta and not in the anterior wall, the side clamp can be safely applied onto the ascending aorta. When the use of aortocoronary free grafts is considered beneficial on the basis of the coronary artery anatomy, the EAS can play an important role in safe manipulations of the ascending aorta. If the EAS examination detects the presence of atherosclerosis in the entire wall of the ascending aorta, OPCAB with in situ and/or composite grafts should be performed, avoiding any manipulations of the ascending aorta.

A few postoperative strokes were reported in a larger series of OPCAB with no aortic manipulation.[18,22] The risk of postoperative stroke does not seem to completely vanish, even after a carefully planned and performed operation. The timing of embolic strokes after surgery has a bimodal distribution. Almost 50% of strokes occur after uneventful recovery from anesthesia, from the second postoperative day onward. Hirose and colleagues[21] have reported that the new onset of postoperative atrial fibrillation was also found to be a risk factor of postoperative stroke. Motallebzadeh and colleagues[20] have suggested that embolisms from the left atrium and ventricle, as well as extracranial and intracranial vascular disease, might be causes of such late strokes.

We conclude that the application of aortic clamping or cardiopulmonary bypass is not a risk factor of cerebral emboli when the ascending aorta is evaluated using the EAS. Furthermore, the application of aortic clamping with free grafts may provide eligible bypass graft patterns and lead to sufficient graft patency.

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