

Original articles

Early neuropsychological dysfunction in elderly high-risk patients after on-pump and off-pump coronary bypass surgery

TOMOKO BABA¹, TOMOKO GOTO¹, KENGO MAEKAWA¹, ASUKA ITO¹, ATUSHI YOSHITAKE¹, and TAKAAKI KOSHII²

¹Department of Anesthesiology, Kumamoto Chuo Hospital, 1-5-1 Tainoshima, Kumamoto 862-0965, Japan

²Department of Cardiovascular Surgery, Kumamoto Chuo Hospital, Kumamoto, Japan

Abstract

Purpose. Advanced age is associated with systemic atherosclerosis and is a risk factor for neurological dysfunction after coronary artery bypass grafting (CABG). However, few studies have investigated early neurological dysfunction after off-pump CABG in elderly patients.

Methods. Data were collected prospectively on 218 patients (≥ 60 years) who underwent elective off-pump ($n = 89$) or on-pump CABG ($n = 129$). Four cognitive tests were performed preoperatively and 1 week postoperatively. Neuropsychological (NP) dysfunction was defined as a decrease in an individual's performance in more than two tests of at least 20% from baseline. We compared the incidence of NP dysfunction, stroke, graft patency grading, and systemic atherosclerosis between patients who underwent off-pump and on-pump CABG.

Results. Off-pump patients were more likely to have a history of cerebrovascular disease, peripheral vascular disease, smoking, multiple cerebral infarctions, and severe aortic atherosclerosis. None of the off-pump and three on-pump patients suffered intraoperative strokes ($P = 0.27$). The incidence of NP dysfunction was 11.2% in the off-pump group and 22.5% in the on-pump group, ($P = 0.02$). Multivariate analysis revealed that NP dysfunction was associated with cardiopulmonary bypass (CPB) and multiple cerebral infarctions. The off-pump group had fewer vessels grafted (2.4 vs 3.4; $P < 0.01$), and a higher rate of stenosis ($>50\%$) and occlusion of the grafted vessels (13.0% vs 7.4%; $P = 0.01$) than the on-pump group.

Conclusion. Off-pump CABG reduced postoperative NP dysfunction in elderly patients with severe systemic atherosclerosis compared to on-pump CABG.

Key words Off-pump CABG · Neuropsychological dysfunction · Atherosclerosis

Introduction

Neurological dysfunction is a devastating complication after coronary artery bypass grafting (CABG). On-pump CABG results in postoperative neuropsychological (NP) dysfunction in 20% to 80% of patients, and stroke occurs in 1% to 5% [1]. Recently, attention has been paid to delirium. Elderly patients generally have more extensive atherosclerosis in multiple vessels and an increased risk of neurological dysfunction [2,3]. We have demonstrated that the incidence of neurological dysfunction after on-pump CABG was increased in patients who had a higher total atherosclerotic score in the brain, carotid arteries, and ascending aorta [4]. Cardiopulmonary bypass (CPB) is a major cause of microemboli, hypoperfusion, and systemic inflammatory response. In addition, CPB involves surgical maneuvers on the ascending aorta, which may cause atheroembolism to the brain. Several studies have shown a reduced incidence of neurological dysfunction with off-pump CABG [5–8]. Cheng et al. [9] found no difference between off-pump and on-pump CABG in the incidence of stroke or early cognitive dysfunction in a metaanalysis of 37 randomized trials. Patients in these trials were relatively young. To date, few studies have investigated neurological dysfunction after off-pump CABG in elderly high-risk patients. This prospective study assessed the impact of CPB on early neurological outcomes in elderly patients with systemic atherosclerosis.

Patients, materials, and methods

Data were collected prospectively on 218 elderly Japanese patients who underwent elective off-pump ($n = 89$) or on-pump CABG ($n = 129$) performed by a single surgeon between January 2000 and December 2003. Elderly patients were defined as those aged 60 years or

Address correspondence to: T. Baba

Received: December 18, 2006 / Accepted: May 2, 2007

older. Demographic and preoperative parameters evaluated in the study included age, sex, years of education, history of hypertension with antihypertensive medication, diabetes mellitus (DM; insulin, oral hypoglycemic therapy, or diet), hyperlipidemia (total cholesterol ≥ 240 mg·dl⁻¹ or triglyceride ≥ 150 mg·dl⁻¹), renal insufficiency (creatinine ≥ 1.9 mg·dl⁻¹), and history of cerebrovascular disease (CVD) with stroke or transient ischemic attack. Postoperative myocardial infarction was defined as a maximal creatine phosphokinase muscle brain (MB) fraction level of more than 100 IU·l⁻¹ and postoperative atrial fibrillation was defined as those events occurring within 7 days of surgery. Informed consent was obtained from all participants and the study was approved by the medical ethics committees and the institutional review board.

Patient management

Our methods for patient evaluation have been published previously [10]. Briefly, all patients underwent preoperative magnetic resonance imaging and angiography (MRI; MRA) to assess cerebral ischemic changes (grade, 0–3), carotid artery stenosis (grade, 0–3), and cerebral arterial stenosis (grade, 0–3). The degree of atherosclerosis in the ascending aorta (grade, 0–3) was identified by intraoperative epiaortic ultrasonography.

Patients were premedicated with morphine hydrochloride (5–10 mg) and scopolamine (0.3 mg) IM 30 min before transport to the operating room. Anesthesia was standardized for all patients: induction with diazepam (5 mg), fentanyl (10 μ g·kg⁻¹), and vecuronium bromide (12 mg) for muscle relaxation, followed by maintenance with fentanyl (total dose, including the induction dose, 30 μ g·kg⁻¹) and diazepam (total dose 0.5 mg·kg⁻¹). Depth of anesthesia was determined with the bispectral index (BIS) and aimed at a BIS between 40 and 60 during surgery. Isoflurane supplementation was used to achieve a BIS level below 60.

Surgical access to the heart was through a standard median sternotomy in all patients. On-pump CABG was performed under standard CPB and moderate hypothermia (30°C to 32°C), as described previously [4]. Mean perfusion pressures were maintained at a higher range (>70 mmHg) in patients with carotid stenosis and multiple cerebral infarctions. A single cross-clamp technique was used. Heparin was administered at 3 mg·kg⁻¹ in the on-pump and 1.5 mg·kg⁻¹ in the off-pump CABG group.

Off-pump CABG was performed with the Medtronic Octopus II or IV devices (Minneapolis, MN, USA) to stabilize the coronary vessels, and deep pericardial traction sutures were applied for cardiac displacement. Either a proximal vessel occluder or an intraluminal shunt was used, depending on the nature of the proxi-

mal obstructions. A humidified carbon dioxide blower (Medtronic DLP) was used to obtain a bloodless surgical field. Allocation to off-pump or on-pump CABG was based on the expertise of the surgeon. The absolute indications for off-pump CABG were patients with extremely atherosclerotic aorta, CVD, and severe obstructive arteriosclerosis. Other candidates included patients with malignancy or coagulopathy. The contraindications for off-pump CABG were cardiogenic shock, dangerous arrhythmias, and technical limitations such as intramyocardial vessels or large hearts. In 2 patients assigned to on-pump CABG, the procedure was converted to off-pump due to severe aortic atherosclerosis; 12 off-pump patients underwent conventional on-pump due to hemodynamic instability or to graft a deep intramyocardial coronary artery or a poor-quality vessel.

Neurologic assessment

NP dysfunction was measured by four tests administered to all patients preoperatively and 1 week postoperatively when they were free of the influence of sedative medication. Tests included the Hasegawa dementia scale (HDS), Kana pick-out test, the digit symbol substitution test, and the digit span test (forward and backward). The HDS (score 0 to 30, with 30 best) is a modification of the Mini-Mental State Examination. Scores less than 24 on the HDS are indicative of preoperative cognitive decline. The Kana pick-out test uses a story written with Kana (Japanese phonetic symbols) which is presented to the participants who are then asked to circle five vowel groups. These tests were performed preoperatively by one of three investigators (T.B., T.G., or A.Y.) and by the same investigator (T.B.), who were blinded to treatment allocation. NP dysfunction was defined as a decrease in an individual's performance in more than two tests of at least 20% from baseline. Stroke was defined as new neurologic deficits lasting more than 24 h, and these were evaluated by cranial computed tomography (CT) or MRI. After careful review of all available data, stroke was determined by staff neurologists. Operative mortality was defined as death within 30 days of surgery.

Graft patency grading

Graft angiography was performed prior to hospital discharge. Only patients with renal insufficiency or severe aortic atherosclerosis were excluded from postoperative angiography. The distal anastomosis of each graft was graded according to the scale of FitzGibbon et al. [11]: widely patent (FitzGibbon A), stenosis more than 50% (FitzGibbon B), occluded (FitzGibbon O).

Statistical analysis

Univariate comparisons of categorical preoperative, operative, and postoperative variables were performed between on-pump and off-pump CABG groups. Dichotomous variables were compared using the χ^2 test or Fisher's exact test. Comparisons between continuous variables were performed using Student's *t*-test for continuous variables. To assess the predictors of NP dysfunction, first univariate analyses were performed between patients with and without NP dysfunction. Stepwise logistic regression analysis was then performed, including factors associated with *P* values no greater than 0.20 in univariate analyses, and potential risk factors for NP dysfunction. These included history of CVD, peripheral vascular disease (PVD), carotid and cerebral artery stenosis, multiple cerebral infarctions, aortic atherosclerosis, CPB, and aortic manipulation. Odds ratios were calculated for each factor in the presence of the others in the final models. The C statistic and the Hosmer-Lemeshow goodness-of-fit statistic were calculated to assess the performance and calibration of the models. Values for results were expressed as means \pm SD. A significant difference was considered to exist for $P \leq 0.05$. All statistical analyses were completed using the SAS Institute statistics package (version 8.2; Cary, NC, USA).

Results

Preoperative characteristics of both groups are shown in Table 1. Patient age, years of education, and the prevalence of preoperative cognitive decline were similar in the two study groups. In addition, differences in ejection fraction, incidence of unstable angina, and extent of coronary artery disease were not statistically significant. The off-pump group was more likely to have a higher rate of history of CVD, PVD, smoking, multiple cerebral infarctions, and aortic atherosclerosis than the on-pump group. EuroSCORE values were also higher in the off-pump patients.

There were 24 patients with severe aortic atherosclerosis. Among these patients, 7 were on-pump, who underwent surgery with modified cannulation and clamping ($n = 5$), or aortic no-touch technique ($n = 2$). The remaining 17 off-pump patients had no aortic manipulation. A side-clamp ($n = 3$) or a mechanical aortic connector system (St Jude, St Paul, MN, USA) ($n = 10$) was used to construct proximal anastomoses in 13 of these off-pump patients.

Perioperative data and cardiac complications are shown in Table 2. The off-pump group had shorter procedure and ventilation times. The CPB duration was 138 ± 40 min and the duration of aortic cross-clamping

was 90 ± 36 min in the on-pump group. The mean number of grafts per patient was significantly lower in the off-pump group than the on-pump group. There were 6 perioperative myocardial infarctions in the off-pump group, compared with none for the on-pump group ($P < 0.01$).

Of the 218 patients, 210 (96.3%) had coronary angiography of 626 grafted coronary arteries prior to hospital discharge. The angiographic gradings of distal anastomoses were better in the on-pump than the off-pump group (92.6% FitzGibbon A, 4.8% FitzGibbon B, and 2.6% FitzGibbon O; vs 87.0%, 11.1%, and 1.9%, respectively; $P = 0.01$). This difference was especially noted in the posteroinferior wall of the left ventricle for the circumflex artery distribution (93.2% FitzGibbon A, 3.4% FitzGibbon B, and 3.4% FitzGibbon O; vs 82.5%, 13.4%, and 4.1%, respectively; $P < 0.01$).

Neurologic outcomes and the results of NP tests are listed in Table 3. Among the 218 patients enrolled, there was 1 hospital death from acute aortic dissection, in the off-pump group. Three patients in the on-pump group had intraoperative strokes. One of these patients a 79-year old man with aortic arch atheroma (10.2 mm), developed left-sided hemiplegia, and a CT scan revealed bilateral multiple infarctions. The other 2 patients developed left upper monoparesis and left-sided hemiparesis; CT showed a single small infarction in the right cerebral hemisphere in both patients. No strokes were identified in any off-pump patient ($P = 0.27$).

The two groups had similar baseline scores for the four NP tests, and more patients in the on-pump group lost 20% or more of their NP function than in the off-pump group. NP dysfunction occurred in 29 (22.5%) patients of the on-pump group and 10 (11.2%) of the off-pump group ($P = 0.024$). Table 4 shows the risk factors for NP dysfunction identified by univariate analysis. Multiple cerebral infarctions and use of CPB were significantly associated with NP dysfunction. Stepwise logistic regression analysis identified multiple cerebral infarctions (odds ratio, 2.242; 95% confidence interval, 1.37 to 3.69; $P = 0.001$) and use of CPB (odds ratio, 2.907; 95% confidence interval, 1.33 to 6.91; $P = 0.011$) as independent predictors of NP dysfunction (C = 0.69 Hosmer-Lemeshow goodness of fit; $P = 0.68$).

Discussion

Although off-pump patients were more likely to have history of a CVD, PVD, smoking, multiple cerebral infarctions, and severe aortic atherosclerosis than on-pump patients, off-pump CABG reduced postoperative early NP dysfunction in elderly patients. The off-pump CABG group had fewer vessels grafted, and higher rates of stenosis and occlusion of the grafted vessels and

Table 1. Characteristics of patients in the two groups^a

	Off-pump (<i>n</i> = 89)	On-pump (<i>n</i> = 129)	<i>P</i> value
Age (years) ^b	71.9 ± 5.8	70.8 ± 5.3	0.135
Sex (male/female)	68/21	84/45	0.075
Education (years) ^b	10.9 ± 3.0	10.2 ± 2.6	0.051
Hypertension	72 (80.9)	98 (76.0)	0.388
Diabetes mellitus	39 (43.8)	50 (38.8)	0.455
Hyperlipidemia	48 (53.9)	66 (51.2)	0.687
Renal insufficiency (Cr ≥ 1.9 mg·dl ⁻¹)	10 (11.2)	15 (11.6)	0.929
Hemodialysis	5 (5.6)	8 (6.2)	>0.999
Peripheral vascular disease	22 (24.7)	11 (8.5)	0.001
Abdominal aortic aneurysm	8 (9.0)	7 (5.4)	0.307
Cerebrovascular disease	22 (24.7)	13 (10.1)	0.004
Smoking	62 (69.7)	71 (55.0)	0.030
Unstable angina	18 (20.2)	29 (22.5)	0.691
Left main trunk disease	34 (38.2)	59 (45.7)	0.269
Triple-vessel disease	47 (52.8)	84 (65.1)	0.068
Ejection fraction (%)			
>60	64 (71.9)	95 (73.6)	0.960
40–60	19 (21.3)	26 (20.2)	
<40	6 (6.7)	8 (6.2)	
Cognitive decline (HDS < 24)	3 (3.4)	11 (8.5)	0.164
MRI (brain)			
Normal or leukoaraiosis	50 (56.2)	95 (73.6)	0.022
Some small infarctions	28 (31.5)	22 (17.1)	
Multiple or broad infarctions	11 (12.4)	12 (9.3)	
MRA (carotid artery)			
Normal or mild	80 (89.9)	112 (86.8)	0.633
Moderate	2 (2.2)	6 (4.7)	
Severe or obstruction	7 (7.9)	11 (8.5)	
MRA (cerebral artery)			
Normal or mild	73 (82.0)	112 (86.8)	0.623
Moderate	15 (16.9)	16 (12.4)	
Occluded	1 (1.1)	1 (0.8)	
Ascending aortic atherosclerosis			
Normal or mild	60 (67.4)	109 (84.5)	0.003
Moderate	12 (13.5)	13 (10.1)	
Severe or diffuse	17 (19.1)	7 (5.4)	
EuroSCORE ^b	4.6 ± 2.1	4.1 ± 1.8	0.036

Cr, creatinine; HDS, Hasegawa dementia scale; MRI, magnetic resonance imaging; MRA, magnetic resonance angiography

^aValues in parentheses represent percentages within the group

^bExpressed as means ± SD

Table 2. Perioperative data and cardiac complications in the two groups^a

	Off-pump (<i>n</i> = 89)	On-pump (<i>n</i> = 129)	<i>P</i> value
Distal grafts ^b	2.4 ± 0.8	3.4 ± 0.9	<0.001
Surgery duration (h) ^b	4.9 ± 1.0	5.9 ± 1.1	<0.001
Cardiac complications			
Coronary spasm	3 (3.4)	1 (0.8)	0.307
Myocardial infarction	6 (6.7)	0	0.004
Atrial fibrillation	15 (16.9)	26 (20.2)	0.540
Intraaortic balloon pump	1 (1.1)	8 (6.2)	0.086
Blood transfusion	66 (74.2)	116 (89.9)	0.002
Reoperation for bleeding	2 (2.2)	7 (5.4)	0.315
Ventilation time (h) ^b	14.1 ± 9.1	18.0 ± 14.0	0.022
Postoperative stay (days) ^b	23 ± 16	24 ± 13	0.878

^aValues in parentheses represent percentages within the group

^bExpressed as means ± SD

Table 3. Neurologic complications and neuropsychological test scores in the two groups^a

Variable	Off-pump (n = 89)		On-pump (n = 129)		P value
Operative mortality	1 (1.1)		0		0.408
Neurologic					
Stroke	0		3 (2.3)		0.272
NP dysfunction	10 (11.2)		29 (22.5)		0.024
Test	Preoperative	1 Week	Preoperative	1 Week	P value
HDS ^b	27.0 ± 2.6	27.3 ± 2.7	27.0 ± 2.5	26.7 ± 3.0	
20% Decline		0		5 (3.9)	0.081
Kana pick-out test ^b	19.9 ± 11.7	18.0 ± 10.5*	17.8 ± 10.4	16.1 ± 9.9*	
20% Decline		26 (29.2)		45 (34.9)	0.380
Digit symbol test ^b	33.7 ± 11.4	29.7 ± 11.0*	30.6 ± 11.2	27.3 ± 11.0*	
20% Decline		16 (18.0)		28 (21.7)	0.500
Digit span test ^b	12.3 ± 3.1	11.0 ± 3.3*	11.5 ± 3.4	10.2 ± 3.3*	
20% Decline		23 (25.8)		39 (30.2)	0.481

* P < 0.05 vs preoperative score

NP, neuropsychological; HDS, Hasegawa dementia scale

^aValues in parentheses represent percentages within the group^bExpressed as means ± SD**Table 4.** Univariate analysis of neuropsychological dysfunction^a

	NP dysfunction (n = 39)	No NP dysfunction (n = 179)	P value
Age (years) ^b	71.8 ± 5.5	71.1 ± 5.6	0.507
Sex (male/female)	27/12	125/54	0.941
Hypertension	30 (76.9)	140 (78.2)	0.860
Diabetes mellitus	17 (43.6)	72 (40.2)	0.698
Hyperlipidemia	21 (53.8)	93 (52.0)	0.830
Peripheral vascular disease	3 (7.7)	30 (16.8)	0.217
Cerebrovascular disease	7 (17.9)	28 (15.6)	0.722
Renal insufficiency (Cr ≥ 1.9 mg·dl ⁻¹)	4 (10.3)	21 (11.7)	>0.999
Smoking	23 (59.0)	110 (61.5)	0.774
Cognitive decline (HDS < 24)	2 (5.1)	12 (6.7)	>0.999
Multiple cerebral infarctions	10 (25.6)	12 (6.7)	0.002
Carotid artery stenosis ≥50%	6 (15.4)	20 (11.2)	0.752
Cerebral artery stenosis ≥50%	9 (23.1)	24 (13.4)	0.182
Severe aortic atherosclerosis	5 (12.8)	19 (10.6)	0.613
Duration of surgery (min) ^b	337 ± 65	328 ± 70	0.449
Use of cardiopulmonary bypass	29 (74.4)	100 (55.9)	0.033
Aortic manipulation	29 (74.4)	110 (61.5)	0.129
Blood transfusion	34 (87.2)	148 (82.7)	0.636

NP, neuropsychological; Cr, creatinine; HDS, Hasegawa dementia scale

^aValues in parentheses represent percentages within the group^bExpressed as means ± SD

perioperative myocardial infarctions. Multivariate analysis confirmed that the independent risks for NP dysfunction were multiple cerebral infarctions and use of CPB.

NP dysfunctions are reported to occur in up to 60% of on-pump CABG patients in the first week [5,12]. In the present study, the incidence of NP dysfunction was lower than that in other reported series. We used a brief battery of tests, administered within 15 min, including four tests appropriate for Japanese people. In addition,

in one of four tests, HDS showed no deterioration in either group, which supported this low incidence.

Recently, attention has been paid to delirium, which is associated with NP dysfunction [13]. The patients should be monitored closely for early signs of neurological dysfunction, and early NP evaluation is important to identify those patients. Furthermore, early NP dysfunction has also been shown to correlate with a later decline in NP function [12,14]. In addition, Murkin et al. [15] have recommended assessment at a stable period,

ideally 3 months postoperatively. Future investigations of longitudinal follow-up and defining NP outcomes are necessary.

Prior CVD is strongly associated with stroke after CABG [16]. Patients with PVD have atheromatous involvement of the large arteries, including the aorta and carotid arteries, and have been shown to be at risk of adverse neurologic outcomes [17]. John et al. [3] have demonstrated that smoking is a significant risk factor for stroke. These risk factors were prevalent among the patients with systemic atherosclerosis, and are likely to be associated with a higher incidence of thromboembolic events during CPB in these patients.

Aortic atherosclerosis is also a risk factor for postoperative stroke [18,19], and our previous study also demonstrated that severe atherosclerosis of the ascending aorta increased the risk of postoperative stroke and NP dysfunction in elderly patients after on-pump CABG [10]. Many investigators have demonstrated that cerebral embolization occurs during CPB, especially during aortic cannulation, clamping, and clamp removal [20,21]. In addition, embolic debris after the use of anastomotic devices is also evident in off-pump CABG [22]. In the present study, no stroke occurred in seven on-pump patients with severe aortic atherosclerosis in whom surgical modifications or aortic no-touch technique were used, although one of these patients developed NP dysfunction. Therefore, recognition of significant aortic disease, using epiaortic ultrasonography and technical modifications, is important to decrease stroke and NP dysfunction.

CPB may cause cerebral injury by embolism, inflammatory response, and hypoperfusion. Transcranial Doppler ultrasonography has demonstrated that microemboli are created during CPB [6,19,20]. A diffusion-weighted imaging (DWI) study also indicated that 26% of patients suffered new silent infarctions after CPB [23]. Off-pump CABG would be expected to decrease cerebral embolic load and improve neurologic outcomes. Diegeler et al. [6] demonstrated a significant decrease in microemboli and postoperative NP dysfunction in an off-pump CABG group. Patients with severe aortic atherosclerosis or PVD who undergo off-pump CABG have a significantly lower prevalence of stroke than patients who undergo on-pump CABG [24,25]. In addition, Lev-Ran et al. [26] demonstrated that avoiding side-clamping significantly lowered stroke rate in off-pump CABG. In the present study, 1 of 13 off-pump patients with aortic manipulation developed NP dysfunction. By avoiding surgical maneuvers on the ascending aorta in off-pump patients, the incidence of cerebral embolization should decrease even further. Additional studies are needed to assess the correlation between postoperative DWI abnormalities and neurologic dysfunction.

The presence of multiple cerebral infarctions was an independent predictor of NP dysfunction in the present study. Although off-pump CABG appeared to eliminate microemboli, ten off-pump patients in this study developed postoperative NP dysfunction. Seven of these patients had cerebral infarctions and five patients were asymptomatic. Our earlier study demonstrated that silent infarctions were common in CABG patients and are associated with an increased risk of NP dysfunction and stroke [27]. Kobayashi et al. [28] have demonstrated that silent lacunar lesions are related to decreased cerebral circulation, and Maeda et al. [29] have shown that cerebral ischemic disorders tend to impair the cerebral autoregulation mechanism. The heart must be displaced during off-pump CABG to expose the anastomotic sites, which causes hemodynamic instability. It is important to maintain mean artery pressure during surgery. Preoperative cerebral evaluation is useful to identify patients with an elevated risk of postoperative NP dysfunction.

A recent metaanalysis of off-pump versus on-pump CABG demonstrated that the mean number of distal vessels anastomosed and the incidence of myocardial infarction was comparable [9]. In the present study, the surgeon was still gaining experience with off-pump techniques during the early part of data collection. Therefore, on average, 1.0 fewer grafts and a higher rate of imprecise anastomoses may have led to an increased risk of postoperative myocardial infarction in the off-pump group. Although a recent study has demonstrated reduced graft patency rates 3 months after off-pump compared with rates after on-pump CABG [30], there are few reports that have examined graft patency grading. Further studies are required to address concerns about the fate of early graded grafts and the need for reintervention over the long term after off-pump surgery.

We note two limitations of our study. The first limitation is that this was a nonrandomized study. Elderly patients with severe systemic atherosclerosis may benefit from off-pump CABG. Therefore, a randomized study comparing off-pump and on-pump CABG would be difficult to perform in these patients. The second limitation is that we have not taken account of the impact of aortic arch atheromas. An association between aortic arch atheromas and postoperative stroke has been demonstrated [31]. Further studies are required to confirm the relationship between aortic arch atheromas and NP dysfunction in patients with systemic atherosclerosis.

In conclusion, off-pump CABG reduces postoperative NP dysfunction in elderly patients with severe systemic atherosclerosis compared to on-pump CABG with more vessels grafted and better graft quality.

Acknowledgments. The authors thank Dr. Jon Moon for editorial advice and Dr. Akira Kitagawa for statistical assistance.

References

1. Stump DA, Jones TJJ, Rorie KD (1999) Neurophysiologic monitoring and outcomes in cardiovascular surgery. *J Cardiothorac Vasc Anesth* 13:600–613
2. Tuman KJ, McCarthy RJ, Najafi H, Ivankovich AD (1992) Differential effects of advanced age on neurologic and cardiac risks of coronary artery operations. *J Thorac Cardiovasc Surg* 104:1510–1517
3. John R, Choudhri AF, Weinberg AD, Ting W, Rose EA, Smith CR, Oz MC (2000) Multicenter review of preoperative risk factors for stroke after coronary artery bypass grafting. *Ann Thorac Surg* 69:30–36
4. Goto T, Baba T, Yoshitake A, Shibata Y, Ura M, Sakata R (2000) Craniocervical and aortic atherosclerosis as neurologic risk factors in coronary surgery. *Ann Thorac Surg* 69:834–840
5. Zamvar V, Williams D, Hall J, Payne N, Cann C, Young K, Karthikeyan S, Dunne J (2002) Assessment of neurocognitive impairment after off-pump and on-pump techniques for coronary artery bypass graft surgery: prospective randomized controlled trial. *BMJ* 325:1268–1272
6. Diegeler A, Hirsch R, Schneider F, Schilling LO, Falk V, Rauch T, Mohr FW (2000) Neuromonitoring and neurocognitive outcome in off-pump versus conventional coronary bypass operation. *Ann Thorac Surg* 69:1162–1166
7. Lee JD, Lee SJ, Tsumhima WT, Yamauchi H, Lau WT, Popper J, Stein A, Johnson D, Lee D, Petrovitch H, Dang CR (2003) Benefits of off-pump bypass on neurogenic and clinical morbidity: a prospective randomized trial. *Ann Thorac Surg* 76:18–26
8. Stamou SC, Jablonski KA, Pfister AJ, Hill PC, Dullum MKC, Bafi AS, Boyce SW, Petro KR, Corso PJ (2002) Stroke after conventional versus minimally invasive coronary artery bypass. *Ann Thorac Surg* 74:394–399
9. Cheng DC, Bainbridge D, Martin JE, Novick RJ (2005) Does off-pump coronary artery bypass reduce mortality, morbidity, and resource utilization when compared with conventional coronary artery bypass? A meta-analysis of randomized trials. *Anesthesiology* 102:188–203
10. Goto T, Baba T, Matsuyama K, Honma K, Ura M, Koshiji T (2003) Aortic atherosclerosis and postoperative neurological dysfunction in elderly coronary surgical patients. *Ann Thorac Surg* 75:1912–1918
11. FitzGibbon GM, Leach AJ, Keon WJ, Burton JR, Kafka HP (1986) Coronary bypass graft fate: angiographic study of 1179 vein grafts early, 1 year, and 5 years after operation. *J Thorac Cardiovasc Surg* 91:773–778
12. Newman MF, Kirchner JL, Phillips-Bute B, Gaver V, Grocott H, Jones RH, Mark DB, Reves JG, Blumenthal JA (2001) Longitudinal assessment of neurocognitive function after coronary artery bypass surgery. *N Engl J Med* 344:395–402
13. Ely EW, Shintani A, Truman B, Speroff T, Gordon SM, Harrell FE Jr, Inouye SK, Bernard GR, Dittus RS (2004) Delirium as a predictor of mortality in mechanically ventilated patients in the intensive care unit. *JAMA* 291:1753–1762
14. Dijk DV, Moons KGM, Keizer AMA, Jansen EWL, Hijman R, Diephuis JC, Borst C, Jaegere PPT, Grobbee DE, Kalkman CJ (2004) Association between early and 3 month cognitive outcome after off-pump and on-pump coronary bypass surgery. *Heart* 90:431–434
15. Murkin JM, Newman SP, Stump DA, Blumenthal JA (1995) Statement of consensus on assessment of neurobehavioral outcomes after cardiac surgery. *Ann Thorac Surg* 59:1289–1295
16. Hogue CW Jr, De Wet CJ, Schechtman KB, Davila-Roman VG (2003) The importance of prior stroke for the adjusted risk of neurologic injury after cardiac surgery for women and men. *Anesthesiology* 98:823–829
17. Rihai CS, Sutton-Tyrrell K, Guo P, Keller NM, Jandova R, Sellers MA, Schaff HV, Holmes DR Jr. (1999) Increased incidence of periprocedural complications among patients with peripheral vascular disease undergoing myocardial revascularization in the bypass angioplasty revascularization investigation. *Circulation* 100:171–177
18. Rorch GW, Kanchuger M, Mangano CM, Newman F, Nussmeier N, Wolman R, Aggarwal A, Marschall K, Graham SH, Ley C, Ozanne G, Mangano DT (1996) Adverse cerebral outcomes after coronary bypass surgery. *N Engl J Med* 335:1857–1863
19. Hogue CW Jr, Murphy SF, Schechtman KB, Davia-Roman VG (1999) Risk factors for early or delayed stroke after cardiac surgery. *Circulation* 100:642–647
20. Barbut D, Hinton RB, Szatrowski TP, Hartman GS, Bruefach M, Williams-Russo P, Charlson ME, Gold JP (1994) Cerebral emboli detected during bypass surgery are associated with clamp removal. *Stroke* 25:2398–2402
21. Pugsley W, Klinger L, Paschalis C, Tressure T, Harrison M, Newman S (1994) The impact of microemboli during cardiopulmonary bypass on neuropsychological functioning. *Stroke* 25:1393–1399
22. Van Boven WJ, Berry G, International Council of Emboli Management (ICEM) Study Group (2002) Intraaortic filtration captures particulate debris in OPCAB cases using anastomotic devices. *Heart Surg Forum* (5 Suppl 4):S461–S467
23. Restrepo L, Wityk RJ, Grega MA, Borowicz L Jr, Barker PB, Lacobs MA, Beauchamp NJ, Hillis AE, McKhann GM (2002) Diffusion- and perfusion-weighted magnetic resonance imaging of the brain before and after coronary artery bypass grafting surgery. *Stroke* 33:2909–2915
24. Sharony R, Grossi EA, Saunders PC, Galloway AC, Applebaum R, Ribakove GH, Culliford AT, Kanchuger M, Kronzon I, Colvin SB (2004) Propensity case-matched analysis of off-pump coronary artery bypass grafting in patients with atherosclerotic aortic disease. *J Thorac Cardiovasc Surg* 127:406–413
25. Karthik S, Musleh G, Grayson AD, Keenan DJ, Pullan DM, Dihmis WC, Hasan R, Fabri BM (2004) Coronary surgery in patients with peripheral vascular disease: effect of avoiding cardiopulmonary bypass. *Ann Thorac Surg* 77:1245–1249
26. Lev-Ran O, Braunstein R, Sharony R, Kramer A, Paz Y, Mohr R, Uretzky G (2005) No-touch aorta off-pump coronary surgery: the effect on stroke. *J Thorac Cardiovasc Surg* 129:307–313
27. Goto T, Baba T, Honnma K, Shibata Y, Arai Y, Uozumi H, Okuda T (2001) Magnetic resonance imaging findings and postoperative neurologic dysfunction in elderly patients undergoing coronary artery bypass. *Ann Thorac Surg* 72:137–142
28. Kobayashi S, Okada K, Yamashita K (1991) Incidence of silent lacunar lesion in normal adults and its relation to cerebral blood flow and risk factors. *Stroke* 22:1379–1383
29. Maeda H, Matsumoto M, Handa N, Hougaku H, Ogawa S, Itoh T, Ysukamoto Y, Kamada T (1993) Reactivity of cerebral blood flow to carbon dioxide in various types of ischemic cerebrovascular disease: evaluation by the transcranial Doppler method. *Stroke* 24:670–675
30. Khan NE, De Souza A, Mister R, Flather M, Clague J, Davies S, Collins P, Wang D, Sigwart U, Pepper J (2004) A randomized comparison of off-pump and on-pump multivessel coronary-artery bypass surgery. *N Engl J Med* 350:21–28
31. Kats ES, Tunick PA, Rusinek H, Ribakove G, Spencer FC, Kronzon I (1992) Protruding aortic atheromas predict stroke in elderly patients undergoing cardiopulmonary bypass: experience with intraoperative transesophageal echocardiography. *J Am Coll Cardiol* 20:70–77