

Original
Article

Factors Influencing Permanent Neurologic Dysfunction and Mortality after Total Arch Replacement with Separate Arch Vessel Grafting Using Selective Cerebral Perfusion

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Objectives: The present study was undertaken to identify risk factors for permanent neurological dysfunction (PND) and in-hospital mortality after total aortic arch replacement (TAR) with separate arch vessel grafting using selective cerebral perfusion (SCP) and hypothermic circulatory arrest.

Methods: Between 1998 and 2008, we preformed a TAR on 143 consecutive patients in two centers by identical methods. Of these, 19 (13.3%) were emergency operations, and 46 (32.2%) were open stent-graft placements. Statistical analysis was performed to determine risk factors for PND and mortality, and furthermore, the survival rate was analyzed.

Results: The in-hospital mortality rate was 4.9%, with chronic renal failure ($p = 0.0013$, odds ratio 10.0) as a significant risk factor. Nine patients (6.3%) had PND, with significant risk factors identified as (1) the presence of an old cerebral or silent lacunar infarction on preoperative imaging methods ($p = 0.0458$, odds ratio 8.0) and (2) duration of SCP ($p = 0.0026$, odds ratio 1.036). Long-term survival was the same in patients with or without PND.

Conclusion: The enhanced vulnerability of the brain in patients with a pre-existing old cerebral infarction or silent lacunar infarction is reflected by a high incidence of PND. Chronic renal failure had an impact on in-hospital mortality.

Key words: aortic arch, surgery, neurologic dysfunction, mortality, risk factor

Introduction

Although simple, deep hypothermic circulatory arrest (HCA) suffices in ascending and transverse aortic arch

repair,¹⁻³ there appears to be a benefit in the application of selective cerebral perfusion (SCP) among those patients in whom prolonged episodes of circulatory arrest are required to perform a total arch replacement (TAR).⁴⁻⁷ For more complex arch repairs or extensive aortic arch disease, superior cerebral protective technique is of crucial importance. Recently, success in performing this surgery in Japan, puts the technique in the top of its class worldwide.^{8,9}

The technique of SCP is well-established and safe; however, it is occasionally associated with permanent neurological dysfunction (PND).¹⁰⁻¹² Most PNDs result from stroke, which are usually attributable to an embolus developing during the surgery.¹³ The aim of the present study was to clarify the independent risk factors for PND and in-hospital mortality after TAR, performed by using

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a four-branched graft with the aid of SCP and an open distal technique. Furthermore, long-term survival rates of patients with and without PND were compared.

Patients and Methods

From 1998 to 2008, staff surgeons in the Department of Surgery 2, Faculty of Medicine at University of Miyazaki and the Department of Cardiovascular Surgery at Miyazaki Prefectural Nobeoka Hospital performed TAR with separate arch vessel grafting with the aid of SCP and hypothermic circulatory arrest in 143 consecutive patients, who all gave their informed consent. Details of the SCP and hypothermic technique have been described previously.¹⁴⁾ All three neck vessels were circulated during SCP at a rectal temperature of 20–25 Celsius degrees. We performed the open stent-graft placement, as reported by Kato et al., on patients whose aneurysm extended into the descending thoracic aorta, fairly deeply into the thoracic cavity, to avoid performing a thoracotomy.

For every patient, a preoperative history was taken which included all of the following: age, sex, history of hypertension, smoking, presence of coronary artery disease, history of central neurological event, cerebral infarction on preoperative brain CT or MRI, presence of clot or atheroma in the aneurysm clearly enough to notice on preoperative CT, chronic obstructive pulmonary disease, redo operation, abdominal aortic aneurysm, diabetes mellitus, preoperative shock, chronic renal failure defined as a creatinine level > 2mg/dl, Marfan syndrome, emergency operation, atherosclerotic aneurysm, acute aortic dissection. The intraoperative time variables of duration of cardiopulmonary bypass, aortic cross-clamp, SCP, and circulatory arrest time of the lower body were evaluated. Preoperative and intraoperative risk factors were analyzed for their possible effects on PND and in-hospital mortality. The analysis for PND and in-hospital mortality was conducted separately. PND was defined as new onset of focal injury or global cerebral damage after the operation with correlates in cranial CT. All variables were analyzed by univariate analysis (unpaired 2-tailed *t* test, chi-square test, or Fisher exact tests when appropriate) to determine whether any single factor caused PND and mortality. Variables that achieved a *p* value of less than 0.2 in the univariate analysis were examined with multivariate analysis by forward stepwise logistic regression to evaluate independent risk factors for PND and in-hospital mortality. Actuarial survival curves

were estimated using the Kaplan-Meier method and compared with log-rank test. Statistical analysis was performed with SPSS 6.1 for UNIX (SPSS, Inc, Chicago, Ill, USA).

Results

Of 143 patients, 100 (69.9%) were male and 43 (30.1%) were female; the median age was 70.4 ± 8.2 years (range of 36–85 years). Nineteen patients (13.3%) underwent emergency surgery within 24 hours of admission, including two patients with catastrophic circulatory status in need of cardiopulmonary support before the operation. Preoperative shock appeared in 4 patients (2.3%) who had a systolic blood pressure below 80 mmHg under full support of inotropic drugs. The underlying aortic pathology was arteriosclerosis in 97 patients (67.8%) including 5 with ruptured aneurysm, chronic dissection in 30 patients (21.0%) and acute aortic dissection in 14 patients (9.8%), and infective aneurysm in 2 patients (2.2%). The presence of clot or atheroma was confirmed by computed tomography (CT) in 66 patients (46.2%).

Preoperative associated diseases included hypertension in 118 patients (80.3%), presence of coronary artery disease in 26 patients (18.2%), history of a central neurological event in 22 patients (15.4%), chronic obstructive pulmonary disease in 9 patients (6.3%), abdominal aortic aneurysm in 26 patients (18.2%), diabetes mellitus in 7 patients (4.9%), chronic renal failure in 6 patients (4.2%) with 3 patient requiring hemodialysis, and Marfan syndrome in 3 patients (2.1%). Forty six patients (32.2%) had a history of smoking. Eight patients (5.6%) had undergone previous cardiac or aortic operations through median sternotomy. Cerebral infarction was evaluated either by CT or magnetic resonance imaging (MRI) or both in 125 patients and old cerebral infarction was found in 37 cases (29.6%) or silent lacunar infarction was found in 29 patients (23.2%). Intracranial and extracranial arteries were evaluated in search of presence of occlusive disease by digital subtraction angiography or CT angiography or magnetic resonance angiography in 124 patients and 23 patients (18.4%) proved to have cerebro-vascular disease which was defined as over 50% of stenosis.

Median-sternotomy was made in 134 patients (93.7%) and an additional left anterolateral thoracotomy through the 4th intercostal space was required in 9 patients (6.3%). An axillary artery was used for an arterial line in 57 patients (39.9%). Open stent-graft placement was used in 46 patients (32.2%), instead of distal anastomosis. Con-

Table 1 Results of univariate and multivariate analysis for permanent neurological dysfunction

Variable	Univariate analysis	Multivariate analysis		
	<i>p</i>	<i>p</i>	OR	95%CI
Presence of old cerebral infarction or silent lacunar infarction on imaging methods	0.0650	0.0453	8.0	2.27–116
Presence of cerebro-vascular disease on imaging methods	0.0741	0.3669		
Presence of clots or atheroma	0.1365	0.1577		
Duration of SCP	0.0524	0.0026	1.036	1.010–1.063

OR= odds ratio; CI=confidential interval; min.=minutes; SCP=selective cerebral perfusion

comitant cardiac procedures were performed in 32 patients (22.4%).

The mean CPB time was 226.6 ± 56.9 minutes (145 to 524 minutes), and the mean aortic cross-clamp time was 100.2 ± 34.7 minutes (39 to 242 minutes). The mean SCP time was 109.4 ± 36.8 minutes (40 to 275 minutes), and circulatory arrest time of the lower body was 47.9 ± 15.1 minutes (26 to 105 minutes).

Hospital mortality and morbidity

The in-hospital mortality rate was 4.9%; for elective patients, it was 4.8% (6/124), and for emergent patients, 5.3% (1/19). Causes of death in patients were fatal bleeding in 2, pneumonia in 2, gastro-intestinal bleeding in 1, cardiac failure in 1, and mediastinitis in 1. Nine patients (6.3%) had PND; in 5 it arose from a solitary cerebral infarction (4 patients, right lobe; 1 patient, left lobe; 1 patient, frontal lobe; 4 patients, occipital lobe), in 3, from multiple infarctions, and in 1, from global cerebral damage due to catastrophic shock. Two patients (2/46, 4.3%) had transient paraplegia, after TAR with open stent-graft placement.

Risk analysis for PND

Duration of SCP ($p = 0.0524$), presence of clot or atheroma ($p = 0.1365$), presence of cerebro-vascular disease on preoperative radiographic examination ($p = 0.0741$), and presence of old cerebral infarction or silent lacunar infarction on preoperative imaging method ($p = 0.0650$) achieved a p value of less than 0.2, and they were examined with multivariate analysis. Duration of SCP ($p = 0.0026$, odds ratio = 1.036; 95% CI, 1.010–1.063/min.) and the presence of old cerebral infarction or silent lacunar infarction on imaging method ($p=0.0453$, odds ratio, 8.0) were independent risk factors for PND (**Table 1**).

Risk analysis for in-hospital mortality

Univariate analysis revealed the following significant risk variables: thoracotomy ($p = 0.0054$), chronic renal failure ($p = 0.0015$), operation time ($p = 0.0008$), and CPB time ($p = 0.0002$). Five variables were examined with multivariate analysis and chronic renal failure ($p = 0.0013$, odds ratio = 10.0; 95% CI, 6.06–100) was confirmed as single independent risk factor for in-hospital mortality (**Table 2**).

Long-term mortality and actuarial survival

Long-term survival for all patients was 87.7% at 1 year, 82.3% at 3 years, and 70.9% at 5 years, and there was no significant difference between patients with PND (77.8% at 1 year, 64.8% at 3 years, and 43.2% at 5 years) and without PND (89.1% at 1 year, 84.1% at 3 years, and 73.6% at 5 years) ($p = 0.113$) (**Fig. 1**).

Discussion

With the improvement of cerebral protection methods including retrograde cerebral perfusion,¹⁶⁾ the outcome of TAR has been significantly improved. SCP prevents ischemic damage to the brain during circulatory arrest, so it facilitates complicated aortic arch replacement, resulting in a significant reduction of mortality and morbidity for aortic arch repair.^{7–12)} However, it has some disadvantages including greater complexity, a cumbersome operative field, and an inherent risk for cerebral embolism an inherent risk for cerebral embolism caused by insertion of perfusion cannula for SCP. In this study, we retrospectively examined factors that influence post-operative PND and in-hospital mortality after TAR surgery performed with separate arch vessel grafting during SCP.

There were some major, independent risk factors reported for PND after the aortic arch operation per-

Table 2 Results of univariate and multivariate analysis for mortality

Variable	Univariate analysis	Multivariate analysis		
	<i>p</i>	<i>p</i>	OR	95%CI
Thoracotomy	0.0054	0.3615		
Marfan syndrome	0.1249	0.7734		
Chronic renal failure	0.0015	0.0013	10.0	6.06–100
Duration of operation	0.0008	0.3537		
Duration of CPB	0.0002	0.1497		

OR= odds ratio ; CI=confidential interval;l CPB=cardiopulmonary bypass

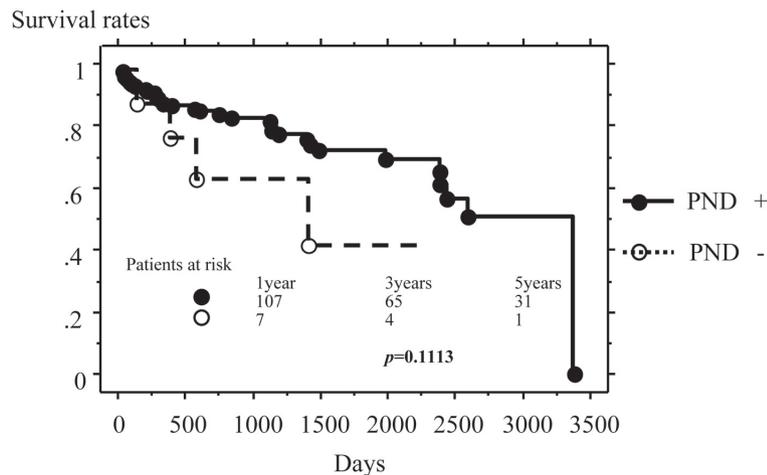


Fig. 1 Comparison of Kaplan-Meier survival curves in patients without PND (solid circle [n = 134]) and with PND (open circle [n = 9])
PND, permanent neurological dysfunction

formed during SCP, that is, preoperative hemodynamic instability,¹¹⁾ urgency status,^{12, 17)} history of cerebrovascular accident,^{8, 9, 12, 17)} male,⁸⁾ and older age (>60 years).¹⁷⁾ These factors were important for us to consider before performing the surgery. The presence of an old infarction or silent lacunar infarction was a significant predictor for postoperative PND in our study. The morbidity of an old infarction or silent lacunar infarction in patients with aortic arch disease is unclear because the brain CT or MRI is not performed for some patients with aortic arch disease, and it is not always essential. We performed a brain investigation for 125 hemodynamic stable patients and showed that 52.8% of the patients suffered from an old infarction or silent lacunar infarction. Although we could not verify the history of central neurological event as a significant predictor for PND because of the small patient number, an old infarction or silent lacunar infarction observed in the preoperative imaging method is considered to be a positive predictor for PND.

Time variables concerning the operation and operative method are other independent risk factors for PND, such as CPB time,⁹⁾ distal anastomosis below the left pulmonary artery,¹⁷⁾ and approach through a left thoracotomy.¹¹⁾ The open stent-graft placement is a useful technique to avoid both a left thoracotomy and distal anastomosis below the pulmonary artery.^{14, 15)} An important relation between the extent of the replacement of the aorta and occurrence of stroke was observed during aortic arch operation using HCA.²⁾ This may reflect an adverse impact of suboptimal cerebral protection during an extensive repair using HCA because temporally neurologic dysfunction occurs linearly in relation to the duration of HCA.¹³⁾ Many research groups have reported that the duration of SCP had no influence on the postoperative neurological outcome,^{8, 9, 11, 12, 17)} and we concur that postoperative PND is probably more related to the length of time required to reconstruct the complex anatomy of the aortic arch, rather than the use of SCP.

However, Hagl and colleagues⁶⁾ demonstrated that in the case of patients with very prolonged SCP (>80 minutes), an increased duration of SCP was a risk factor for neurologic morbidity, and they speculated that an embolus that blocks flow to a small defined area may lead to a clinically detectable stroke only if an additional prolonged period without adequate perfusion to surrounding tissues occurs. Sakurada and colleagues⁴⁾ revealed that SCP can extend the safe duration of circulatory arrest up to 90 minutes. Harrington and colleagues¹⁸⁾ showed that middle cerebral artery velocity (MACV) increased significantly before and after the arrest both in SCP and HCA groups, and the increase of the post-arrest MACV was much greater in the SCP group. They suggested that the significance of this finding was unknown but could increase vulnerability to any embolic load.

Arch vessel cannulation also carries a risk of cerebral embolization. The trifurcated graft technique of Spilvogel and colleagues¹⁰⁾ can avoid arch vessel cannulation for SCP. Although the lack of randomized trials and the high variety of inclusion criteria in the different studies do not allow a general recommendation for the use of the axillary artery as cannulation site,¹⁹⁾ the utmost meticulous and careful maneuver including cannulation site must be adopted in SCP to avoid cerebral embolic events.

Significant independent risk factor for in-hospital mortality in our study was preoperative renal dysfunction. It has previously been identified as a risk factor for mortality.^{8, 20)} Shah and colleagues³⁾ demonstrated that the mortality increased exponentially with a decreasing glomerular filtration rate after the transverse aortic arch had been repaired.

Conclusion

The results of an open distal technique for TAR with separate arch vessel grafting during SCP were satisfactory. A pre-existing, old cerebral or lacunar infarction and an increased duration of SCP are risk factors for PND. Chronic renal failure was a significant risk factor for in-hospital mortality. However, PND did not affect long-term survival after TAR.

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