Multivariate analysis of predictors of late stroke after total aortic arch repair

Kaoru Matsuura, Hitoshi Ogino*, Hitoshi Matsuda, Kenji Minatoya, Hiroaki Sasaki, Toshikatsu Yagihara, Soichiro Kitamura

Department of Cardiovascular Surgery, National Cardiovascular Center, 5-7-1 Fujishirodai, Suita, Osaka 565-8565, Japan

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Abstract

Objective: The number of aortic surgeries has recently increased, with improvement of outcome due to the development of various novel operative techniques and adjuncts. Although the postoperative incidence of stroke, the most severe complication of aortic surgery, is still a matter of concern and has been described well previously, late stroke after aortic arch repair has not been described well. We assessed the incidence and predictors of late stroke after total aortic arch repair. Methods: From January 1993 to December 2003, 470 patients underwent total aortic arch repair in our institution. All patients, whether undergoing elective, urgent, or emergent aortic arch repair, were included. Emergent operation was required for 115 patients because of rupture or acute type A dissection. For brain protection, retrograde cerebral perfusion was used in 27% (125) and selective cerebral perfusion in 75% (353) of cases. The follow-up period was 32.5 ± 31.5 months. Late stroke was defined as stroke occurring more than 30 days postoperatively. Results: The incidence of early postoperative stroke was 4.9% (23/470), while that of late postoperative stroke was 6.0% (28/470). On univariate analysis, postoperative atrial fibrillation (P = 0.014), preoperative prevalence of craniocervical lesions (P = 0.0001), and advanced age (P = 0.046) were each significantly related to late stroke. A Cox proportional hazards model detected postoperative atrial fibrillation (P = 0.013, OR = 3.02, 95% CI: 1.26–7.24) and preoperative prevalence of craniocervical lesions (P = 0.0001, OR = 5.37, 95% CI: 2.30–12.52) as predictors of late stroke. Conclusions: Postoperative atrial fibrillation and preoperative prevalence of craniocervical lesions were found to be risk factors for late stroke after total aortic arch repair.

Keywords: Aorta; Surgery; Stroke; Complication

1. Introduction

The number of aortic surgeries has recently increased, with improvement of outcome due to the development of operative techniques, adjuncts, and postoperative care [1-5]. Although the mortality rate of aortic arch repair has recently decreased, the occurrence of stroke, the most severe complication of this type of surgery, is still a matter of concern [6-8]. Aortic arch surgery requires the use of cerebral protection, and over the past decades many surgeons have attempted to refine methods for it. We have recently used selective cerebral perfusion (SCP) for this purpose. Though many studies of aortic arch surgery have focused on the perioperative period, they have failed to include long-term follow-up of neurological outcome. The present study was designed to investigate the late neurological outcome of aortic arch surgery and to determine predictors of late stroke.

2. Materials and methods

2.1. Patients

Between January 1993 and December 2003, a total of 470 consecutive patients with atherosclerotic aortic arch aneurysm (n = 317) or aortic dissection (n = 153) underwent aortic arch repair in a single institution. All patients, whether undergoing elective, urgent, or emergent aortic arch repair, were included. Emergent operation was required for 115 patients because of rupture or acute type A dissection. Baseline demographic and clinical data were available for all of the patients. Initial data were collected from the case records, and follow-up data by contacting physicians performing close follow-up of the patients. The mean age at time of operation was 68.6 ± 10.3 years.

Preoperative medications were continued up to the day of operation, except non-steroidal anti-inflammatory drugs, which were discontinued one week preoperatively, and digoxin which was discontinued 3 days preoperatively.

Preoperative examination to detect craniocervical vascular lesions was regularly performed. Cervical ultrasonography and brain computed tomography (CT) examination were routinely carried out in all patients. For patients with suspicious lesions, magnetic resonance angiography (MRA) was performed to detect craniocervical vascular lesions.
For the purpose of this study, craniocervical vascular lesions were defined as those with >75% stenosis.

2.2. Operation

All operations were performed through a median sternotomy under standard general anesthesia. Cardiopulmonary bypass was established with arterial cannulation and bicaval drainage. The sites of arterial cannulation were the axillary artery and femoral artery (n=244), femoral artery alone (n=96), ascending aorta alone (n=65), axillary artery and ascending aorta (n=47), aorta and axillary artery and femoral artery (n=12), and ascending aorta and femoral artery (n=6). Myocardial protection was achieved using intermittent ante-grade cold-blood cardioplegia. For intraoperative brain protection, retrograde cerebral perfusion (SCP) was used in 73% (n=345) of patients. Both were used in eight patients. The cannulation sites for selective cerebral perfusion were as follows: right axillary artery and left carotid artery (n=249), right axillary artery and left carotid and subclavian arteries (n=46), brachiocephalic artery and left carotid artery (n=56), and brachiocephalic artery and left carotid and subclavian arteries (n=2). The patients were cooled to a core body temperature of 15–28°C during the study period, all of the graft replacements were performed with separate anastomoses using quadrifurcated grafts.

2.3. Definitions of AF and stroke

All medical records, including electrocardiograms and telemetry strips, were reviewed. Postoperative AF was defined as an acute, sustained episode (over 10 min) of AF requiring intervention in the hospital. Postoperative stroke was defined as a new, clinically evident, temporary or permanent, focal deficit. Only neurological deficits confirmed by brain CT scan by an independent neurologist were considered strokes. Early postoperative stroke was defined as such an event occurring within 30 days postoperatively, and late postoperative stroke as an event occurring after that. For patients who had been followed on an outpatient basis in other hospitals, follow-up was completed by contacting the current physician. All late postoperative strokes were confirmed by brain CT scan by an independent neurologist. The mean follow-up period was 32.5 ± 11.5 months.

2.4. Statistical analysis

All values are the mean ± SD. Differences between patient groups were tested by univariate analysis (χ² test, two-tailed t-test, Fisher’s exact test, or Mann-Whitney U test as appropriate). Findings of P < 0.05 were considered significant. A Cox proportional hazards model was used to determine predictors of stroke based on the baseline characteristics. The model included variables selected based on clinical importance or significant relationship to stroke on univariate analysis. Freedom from stroke was estimated using the Kaplan-Meier method. The logrank test was used for examining the significance of differences in freedom from stroke. All analyses were performed using SAS statistical software® (version 8.02, SAS Institute, Inc., Cary, NC).

3. Results

The demographic characteristics, preoperative medications, and surgical data for patients are presented in Table 1. Complete and reliable information regarding embolic events was obtained. Surgical outcome is described in Table 2. The 30-day mortality was 6.6% (31/470), and hospital mortality was 7.7% (36/470). The actuarial survival rate was 76.4% at 5 years.

Twenty-three patients (4.9%) had atrial fibrillation (AF) preoperatively. They continued to exhibit AF postoperatively and in late follow-up. The incidence of postoperative AF of new onset, most cases of which were temporary, was 50.0% (235/470). The total number of patients who experienced early postoperative AF, whether temporary or permanent, was 258 (54.9%). Anticoagulant therapy with warfarin was used in 33 (12.8%) of these patients. Twenty-nine patients (6.2%) had AF at discharge, and warfarin therapy was performed for 12 (41.3%) of these. Data on the occurrence of chronic AF in the late follow-up period were also collected by contacting physicians performing close follow-up. Forty-one patients (8.7%) had AF at late follow-up, and warfarin therapy was performed for 33 (82.5%) of them.

Early postoperative stroke occurred in 23 patients (4.9%), while late stroke occurred in 28 patients (6.0%), not...
including those who also had early postoperative stroke. Overall postoperative stroke occurred in 51 patients (10.6%). Late stroke was observed in four patients who had AF preoperatively (14.3%), five patients (17.2%) who had AF at the time of discharge, and nine patients who had AF at late follow-up (22.0%).

On univariate analysis, postoperative AF ($P = 0.014$), preoperative prevalence of craniocervical lesions ($P = 0.0001$), and advanced age ($P = 0.046$) were significantly related to late stroke, while warfarin therapy, cerebral perfusion, and type of cerebral protection were not. Table 3 presents the predictors of late stroke. A multivariate Cox proportional hazards model revealed postoperative atrial fibrillation ($P = 0.013$, HR = 3.02, 95% CI: 1.26-7.24) and preoperative prevalence of craniocervical lesions ($P = 0.0001$, HR = 5.37, 95% CI: 2.30-12.5) to be predictors of late stroke. Curves for freedom from stroke stratified by presence of preoperative craniocervical vascular lesions and presence of postoperative AF are shown in Figs. 1 and 2, respectively. Curves were statistically different with or without these two factors (craniocervical vascular lesion; $P < 0.0001$, postoperative AF; $P = 0.0006$).

### Table 2

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Count (Percentage)</th>
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<tr>
<td>30-day mortality</td>
<td>31 (6.6%)</td>
</tr>
<tr>
<td>Hospital mortality</td>
<td>36 (7.7%)</td>
</tr>
<tr>
<td>Early postoperative stroke</td>
<td>23 (4.9%)</td>
</tr>
<tr>
<td>Late postoperative stroke</td>
<td>28 (6.0%)</td>
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<tr>
<td>Overall postoperative stroke</td>
<td>51 (10.9%)</td>
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<tr>
<td>Late death</td>
<td>83 (17.7%)</td>
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### Table 3

<table>
<thead>
<tr>
<th>Risk factors for late stroke</th>
<th>Hazard ratio</th>
<th>95% CI</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.04</td>
<td>0.99-1.01</td>
<td>0.156</td>
</tr>
<tr>
<td>Gender (Female)</td>
<td>0.85</td>
<td>0.30-2.40</td>
<td>0.751</td>
</tr>
<tr>
<td>Body mass index</td>
<td>0.41</td>
<td>0.10-1.54</td>
<td>0.18</td>
</tr>
<tr>
<td>Emergency operation</td>
<td>1.27</td>
<td>0.49-3.27</td>
<td>0.63</td>
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<tr>
<td>Postoperative AF</td>
<td>3.02</td>
<td>1.26-7.24</td>
<td>0.013</td>
</tr>
<tr>
<td>Craniocervical vascular lesion</td>
<td>5.37</td>
<td>2.30-12.52</td>
<td>0.0001</td>
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### 4. Discussion

The number of aortic surgeries has increased recently. Although operative mortality has decreased, operative morbidity is still a matter of concern [1-5]. Stroke is the most severe complication of aortic arch repair [6-8]. Its severity is related not only to quality of life, but also to increase in risk of postoperative late mortality. The causes of stroke after aortic arch repair have been surmised to be thromboembolic or hypoperfusion. However, it is difficult to distinguish these two causes clinically: inadequate cerebral protection can induce cerebral hypoperfusion, while inappropriate cerebral protection can cause thromboembolic events [6-8]. Previous reports have described refined operative techniques and adjuncts including cerebral protection [9-14]. Our experience has led us to prefer use

of systemic perfusion from the ascending aorta whenever possible as a strategy for arterial cannulation and brain protection and selective cerebral perfusion from the right axillary artery, left common carotid artery, and left subclavian artery. We previously reported the superiority of the selective cerebral perfusion with axillary arterial cannulation in preventing cerebral complications [15,16]. We used quadrifurcated grafts for arch replacement for all patients in this study period.

Operative techniques and adjuncts have developed enough that the late outcome of aortic arch repair must now be examined. Identification of predictors of late stroke is important for describing well. Identification of predictors of late stroke is important for understanding the pathogenesis of this complication as well as for developing strategies to prevent it. The present study found that preoperative prevalence of craniocervical vascular lesions and postoperative AF to be predictors of late stroke. These findings coincide with those reported by Ridderstolpe et al., who described results of risk factor analysis for early and delayed cerebral complications after cardiac surgery, including postoperative supraventricular tachyarrhythmia and previous craniocervical vascular lesions [17].

Archbold et al. investigated the benefit of screening for craniocervical vascular lesions before cardiac surgery [18]. Their literature review revealed craniocervical vascular lesions to be a risk factor for future stroke unrelated to surgery as well as postoperative stroke. Our findings also suggested that screening for craniocervical vascular lesions prior to the aortic arch surgery is essential for reducing
the risk of stroke not only in the early postoperative period but also in the long-term follow-up period. Aortic arch repair can eliminate atheromatous aorta, which can be a source of emboli, or dissecting aorta, which can cause malperfusion. However, patients who have craniocervical vascular lesions which cannot be excluded by the aortic arch repair are still at risk for embolic events or cerebral hypoperfusion after this procedure. We believe this is the main reason why patients who had craniocervical vascular lesions preoperatively had increased risk of late postoperative stroke. In the late postoperative period, careful follow-up using radiographic study of craniocervical vascular lesions is also important for early detection of progression of these lesions. Prompt surgical or medical treatment of these progressive lesions is needed to reduce the risk of stroke.

AF is a well-known cause of thromboembolic stroke. The existence of a relationship between new postoperative onset of AF and stroke after cardiac surgery has been suggested by some authors. Lahtinen et al. investigated 2630 patients who underwent CABG [19]. They found the incidences of new onset of postoperative stroke to be 2.0%, and in 36.5% of these patients group postoperative AF preceded the occurrence of stroke. Bando et al. investigated the risk factors for early and late stroke after mechanical mitral valve replacement, and concluded that restoration of sinus rhythm with a maze procedure nearly eliminated risk of stroke [20]. In the present study, late stroke was observed more frequently in patients who developed persistent AF after surgery than in patients who had only temporary AF. If AF occurs postoperatively, every effort should be made to prevent the persistent AF, which leads to preventing late embolic events.

Anticoagulation therapy for patients who have developed AF is very important in preventing thromboembolic events. In the earlier portion of this study, some of the patients were followed without warfarin but with other anticoagulants including aspirin. However, we now believe that proper use of warfarin is essential to prevent thromboembolic complications in patients with AF at the time of discharge.

Given the findings of the present study, we now aggressively prevent postoperative AF medically and surgically. Surgical treatment of atrial fibrillation was established by Cox et al. and has been refined in the past decade [21]. Our standard criteria for performance of the Maze procedure have been described previously [22]. We routinely use beta blockers or other antiarrhythmic drugs postoperatively. Even if AF occurs, we use cardioversion, performed either medically or electrically. Moreover, for patients with craniocervical vascular lesions, the risk of late stroke must be kept in mind and preventive anticoagulant therapy may be required, in collaboration with a neurologist.

5. Study limitations

We examined patients in a single institution, and the present study was performed in retrospective fashion. The operations were performed by more than one surgeon, and the patients have been followed up by more than one physician.

6. Conclusions

Although the surgical outcome of total aortic arch repair has improved, postoperative incidence of atrial fibrillation and preoperative prevalence of craniocervical vascular lesions were found to be risk factors for late stroke after this procedure.

References


