Surgery for Aortic Disease

Neurological Outcomes After Immediate Aortic Repair for Acute Type A Aortic Dissection Complicated by Coma

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Background—Management of acute type A aortic dissection (AADA) complicated by coma remains controversial. We analyzed our experience in managing AADA complicated by coma to determine the relationship of duration of preoperative coma to postoperative neurological recovery.

Methods and Results—Between September 2003 and October 2010, 181 patients with AADA were treated, including 27 presenting with coma (Glasgow Coma Scale <11) on arrival. Twenty-one patients were repaired immediately (immediate group); time from onset of symptoms to operating room was <5 hours. For brain protection, deep hypothermia with antegrade cerebral perfusion was used, and postoperative therapeutic hypothermia with magnesium treatment was performed. Six patients initially were managed medically, and 3 of them were followed by eventual repair because time from onset was >5 hours (delayed group). The preoperative National Institutes of Health Stroke Scale score was 31.4±6.6 in the immediate group and 28.3±9.5 in the delayed group. Hospital mortality was 14% in the immediate group and 67% in the delayed group. Full recovery of consciousness was achieved in 86% of patients in the immediate group and in 17% in the delayed group. In immediate group, the postoperative National Institutes of Health Stroke Scale score significantly improved to 6.4±8.4, cumulative survival rate was 71.8% in 3 years, and independence in daily activities was achieved in 52% (11/21).

Conclusions—Aortic repair, if performed immediately from the onset of symptoms, showed satisfactory recovery of consciousness and neurological function in patients with AADA complicated by coma. In this patient population, immediate aortic repair is warranted. (Circulation. 2011;124[suppl 1]:S163–S167.)

Key Words: aortic aneurysm ■ aneurysm, dissecting ■ cerebral ischemia ■ stroke ■ coma

Preoperative coma or stroke is an independent predictor of late mortality and considered a contraindication to surgery because of the risk of precipitating hemorrhagic cerebral infarction and a poor long-term outcome.1–3 Recent studies have shown that surgical repair of acute type A aortic dissection (AADA) can be performed in the setting of preoperative stroke with acceptable mortality.4,5 However, the severity of neurological injury after aortic repair remains a primary concern.6–8

In the case of an acute thrombotic stroke, the interval from onset of symptoms to return of cerebral blood flow are key factors in determining the severity of permanent brain injury.9,10 In addition, prompt thrombolytic treatment is effective without posing an unacceptable hemorrhagic risk.11,12 Therefore, we postulated that if aortic repair was performed within several hours of the onset of symptoms, favorable neurological outcomes could be obtained among patients with preoperative coma. The purpose of this study was to analyze our single-center results of immediate aortic repair for patients with AADA complicated by coma to determine the relationship of duration of preoperative coma to postoperative neurological recovery.

Methods

Patient Characteristics

Between September 2003 to October 2010, 181 consecutive patients presented with AADA to our institute, and 27 patients experienced preoperative coma. The mean age of the patients was 71.9 years (range, 44 to 91 years), and 33% were men. Among the 27 patients with preoperative coma, 21 had immediate aortic repair, 3 received medical treatment initially and eventually underwent aortic repair, and 3 died during initial medical treatment (all were neurologically devastated).

Neurological Evaluation

To evaluate the effect on neurological outcomes, 3 neurological scales were used: the Glasgow Coma Scale (GCS), the National...
The GCS was used to assess level of consciousness, and the NIHSS was used to quantify the clinical severity of the stroke, which includes the levels of consciousness, language, neglect, visual field loss, extracranial movement, motor strength, ataxia, dysarthria, and sensory loss. Both GCS and NIHSS were used for preoperative and early postoperative evaluation. For evaluation of late outcomes, mRS was used to determine the degree of dependence in the daily activities of patients with neurological injury. Coma was defined on arrival at the hospital as <11 on the GCS, with a mean GCS score of 6.5 (range, 3 to 10). Patients with a transient consciousness disturbance were not included in this study. Initial clinical diagnosis was performed by the Hyogo Emergency Medical Center team, neurologists from the Kobe Red Cross Hospital Stroke Center team, and neurologists from the Hyogo Emergency Medical Center.

**Treatment**
When aortic disease was suspected on arrival at the hospital, we performed a CT scan of the aorta and a brain CT scan if any neurological disorder presented and gave a definitive diagnosis. Even if coma presented, the patient was taken to the operating room immediately on diagnosis of AADA. Twenty-one patients with AADA and coma underwent immediate aortic repair (immediate group). However, if a definitive diagnosis was given more than several hours from the onset of symptoms, medical management was chosen initially. Six patients with coma were managed medically, and 3 of the 6 who improved in their GCS level had delayed aortic repair (initially medical group).

**Operative Approach**
The aortic repairs were conducted through median sternotomy, using full heparinization, cardiopulmonary bypass, and profound hypothermic circulatory arrest with antegrade cerebral perfusion. Arterial cannulation was accessed through the femoral artery (n = 24) or both the femoral and axillary arteries (n = 1). The regional oxygen saturation of the forehead was monitored using the INVOS 5100 Cerebral Oximeter (Somanetics, Inc; Troy, MI). Once a nasopharyngeal temperature of 18°C was reached, cardiopulmonary bypass was discontinued, and circulation was arrested. Antegrade perfusion of the left subclavian artery, left common carotid artery, and innominate artery were started by means of direct cannulation into the true lumen from the orifices, and the antegrade perfusion flow was maintained between 10 and 15 mL/kg per minute. The intimal tear was isolated to the proximal transverse aortic arch in 19 patients, and a hemiarch replacement was performed. Five cases of total arch replacement were performed when the intimal tear involved the distal transverse arch. An additional cervical carotid arterial repair was not performed in any patient. After completion of the distal arch reconstruction, antegrade cerebral perfusion was discontinued, and cardiopulmonary bypass flow was resumed, with systemic warming initiated until body temperature reached 35°C. The mean cerebral perfusion time in 24 patients was 73 ± 38 minutes, with a mean cardiopulmonary bypass time of 267 ± 50 minutes.

**Postoperative Care**
All patients were admitted to the intensive care unit and given a course of therapeutic hypothermia using water blankets to keep body temperature <36°C for 24 hours. Magnesium sulfate was infused continuously to maintain an ionized magnesium (Mg++) level between 0.7 and 1.0 mmol/L throughout the operative procedure and during postoperative care. In our protocol, magnesium sulfate solution (0.5 mol/L) was infused at a rate of 3.2 mL/kg per hour for the first 15 minutes followed by 0.05 to 0.4 mL/kg per hour for 24 hours, and Mg++ level was measured every 2 hours.

**Statistical Analysis**
Data collection and analysis were approved by Kobe Red Cross Hospital and Hyogo Emergency Medical Center Committee for the Protection of Human Subjects. Analysis was retrospective. Data were collected from chart reviews by the authors (T.T., T. Hayashi).

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**Figure 1.** Clinical imaging findings of patient 1. **A** and **B**, Preoperative brain CT scan showing brain edema of the right hemisphere of the cerebrum (arrows). **C**, Preoperative contrast-enhanced CT scan showing acute type A aortic dissection and the innominate artery dissection (arrow). **D**, Postoperative CT scan demonstrating clear corticomedullary junction of the right hemisphere of the cerebrum.

**Representative Case Presentation**
A representative CT scan of a 62-year-old comatose woman (GCS 10, NIHSS 21) (Figure 1A through 1C) shows AADA with an obscure corticomedullary junction of the right hemisphere. Immediate total arch replacement was performed. Postoperatively, her brain edema disappeared (Figure 1D). The patient became lucid, and neurological scales were improved (GCS 15, NIHSS 0) at the time of discharge. Seven years after repair, she had no significant disability, and daily activities were quite favorable (mRS, 1). Severity of brain CT scan abnormalities should not be a deterrent to proceeding with early surgical repair.

**Patient Characteristics and Postoperative Mortality and Morbidity**
Preoperative patient characteristics, procedures, and operative mortality and morbidity are listed in Table 1. In-hospital mortality was 14.3% (3/21) in the immediate group. Cause of death included rupture of the descending aorta (postoperative day 5), acute myocardial infarction (postoperative day 35), and massive brain edema (postoperative day 14). In contrast, 66.7% (4/6) in the initially medical group died, including 3 patients who were neurologically devastated and 1 who died.
after delayed aortic repair. Postoperative brain CT scans were performed in all patients, and none showed intracerebral hemorrhage.

Complete recovery of consciousness, assessed by GCS, was achieved postoperatively in 71% (15/21) of patients within 14 days, and only 3 patients remained in a state of partial consciousness during the follow-up period in the immediate group (Figure 2). Therefore, 86% (18/21) completely regained consciousness, and there was a significant statistical improvement in consciousness ($P<0.0001$). By contrast, in the initially medical group, only 1 patient became lucid postoperatively.

Postoperative functional recovery, assessed by improvement of NIHSS and mRS, were significantly improved in the immediate group. Postoperative NIHSS score was 6.4±8.4, which was significantly lower than the preoperative NIHSS score ($P<0.0001$) (Figure 3). However, major neurological deficit was observed in 33% (6/18) of patients, which included aphasia with left hemiplegia in 2, left hemiparesis in 2, monoparesis in 1, and quadriplegia with consistent coma in 1.

Relations between preoperative carotid involvement and postoperative neurological outcomes in the immediate group are listed in Table 2. Carotid arterial dissection was presented in 81% of the patients, including unilateral involvement in 43% and bilateral involvement in 38%, and carotid ultrasound study demonstrated complete occlusion of the right carotid artery in 2 patients. There was no significant difference in postoperative neurological outcomes among unilateral, bilateral, and no dissection of the carotid artery.

In the immediate group, the mean follow-up period was 34.5±25.1 months, and the cumulative survival rate was 71.8% in 3 years. The mRS in the follow-up periods was 2.4±1.9, and independence in activities of daily life (mRS $<3$) was achieved in 52% (11/21).

**Discussion**

Coma or stroke as part of the clinical presentation of AADA generally has been considered a major contraindication in emergency repair, which requires systemic anticoagulation for cardiopulmonary bypass because it risks making the neurological injury worse.1–3,15,16 Several authors reported a strong correlation between mortality rate and stroke in patients with AADA. Cambria et al1 reported that 6 of 7 patients with preoperative cerebral infarction and aortic dissection

<table>
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<th>Table 1. Patient Characteristics</th>
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<td>Age, y</td>
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<tr>
<td>Male sex</td>
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<tr>
<td>GCS</td>
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<tr>
<td>Shock on arrival</td>
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<tr>
<td>Pericardial effusion</td>
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<tr>
<td>Carotid dissection</td>
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<tr>
<td>NIHSS</td>
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<tr>
<td>Aortic repair performed</td>
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<tr>
<td>Time from onset to OR, minutes</td>
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<tr>
<td>Operative procedure</td>
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<tr>
<td>Total arch replacement</td>
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<td>Hemiarch replacement</td>
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<td>Posttreatment</td>
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<td>In-hospital mortality</td>
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<tr>
<td>Intracerebral hemorrhage</td>
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<tr>
<td>Full recovery of consciousness</td>
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<td>NIHSS at discharge</td>
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<td>mRS</td>
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<td>mRS 0-2</td>
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<td>mRS 3-6</td>
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Data are presented as mean±SD or n (%). GCS indicates Glasgow Coma Scale; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; NS, not significant; OR, operating room.

*P<0.0001 compared with preoperative consciousness.
†P<0.0001 compared with preoperative NIHSS.

Figure 2. Recovery of the consciousness: changes in GCS of all patients in the immediate group. The elements of the GCS are indicated in online-only Data Supplement Table 1. GCS indicates Glasgow Coma Scale.

Figure 3. Functional recovery: changes in the NIHSS of the 18 patients who survived aortic repair in the immediate group. The elements of the NIHSS and the mRS are indicated in online-only Data Supplement Tables 2 and 3. mRS indicates modified Rankin scale; NIHSS, National Institutes of Health Stroke Scale.
Table 2. Involvement of the Carotid Dissection and Frequency of Postoperative Neurological Outcomes in the Immediate Group (n=21)

<table>
<thead>
<tr>
<th>Preoperative Carotid Dissection (CT Scan)</th>
<th>Unilateral (n=9, 43%)*</th>
<th>Bilateral (n=8, 38%)</th>
<th>None (n=4, 19%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stenosis of the true lumen</td>
<td>7 (78)</td>
<td>8 (100)</td>
<td>0</td>
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<tr>
<td>Occlusion</td>
<td>2 (12)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Postoperative neurological outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full recovery of consciousness (GCS 15)</td>
<td>8 (89)</td>
<td>7 (88)</td>
<td>3 (75)</td>
</tr>
<tr>
<td>ADL independence (mRS 0-2)</td>
<td>4 (44)</td>
<td>5 (63)</td>
<td>2 (50)</td>
</tr>
</tbody>
</table>

Data are presented as n (%). ADL indicates activities of daily life. Other abbreviations as in Table 1.

*Right carotid artery in 8 patients and left carotid artery in 1 patient.

...died of brain damage after aortic repair. However, Estrera et al reported that surgical repair of AADA could be performed safely when preoperative stroke occurs. In their 14 surgical patients, 80% who underwent surgical repair within 10 hours from onset of stroke had improved neurological status, whereas none operated on beyond 10 hours improved. The present results are comparable with those produced by Estrera et al in which 4 patients were operated on within 5 hours from onset of symptoms, with 3 of them showing marked improvement. In addition, Estrera et al observed no hemorrhagic conversion of ischemic stroke in their 14 surgical patients, despite the use of full anticoagulation. Similarly, we did not observe intracerebral hemorrhage. Pocar et al reported no operative deaths in 5 comatose patients with no postoperative hemorrhagic infarction or severe brain edema. However, they did report that the prevalence of reperfusion injury of the brain can be higher with longer intervals before surgical repair or in older patients. Predicting hemorrhagic conversion during or after aortic repair is difficult. In addition, initial medical management might result in death caused by rupture, cardiac tamponade, or retrograde dissection with coronary artery involvement. Therefore, blood pressure must be kept low, and thrombolytic therapy must be avoided.

In acute ischemic stroke, regional cerebral blood flow and the interval from onset of ischemia to reperfusion are major determinants of severity of the brain infarction. Jones et al reported the concept of the ischemia threshold and reversible ischemia zone (ischemic penumbra) and clearly documented a therapeutic time window in a nonhuman primate model. These results are reflected in the current treatment for acute ischemic stroke. Intravenous recombinant tissue plasminogen activator is beneficial when treatment is initiated within 3 hours of the onset of stroke. If intraarterial thrombolysis is applied, the therapeutic window may extend to several hours. If the concept of the therapeutic time window is applied to brain ischemia caused by AADA, the time from onset until improved cerebral blood flow is a key factor. In the current study, the therapeutic time window (time from onset of symptoms to transporting the patient to the operating room) was determined to be ≤5 hours because 1 patient who presented with coma (GCS 5) and was taken to the operating room 5 hours after onset of symptoms developed massive postoperative cerebral infarction and so underwent emergency cerebral decompression. Relatively poor neurological recovery has been seen when aortic repair is not performed within 5 hours of symptom onset. However, this temporal limitation may not be equal for all patients because regional cerebral blood flow might be affected by several factors, such as severity of carotid arterial obstruction, systemic blood pressure, cardiac output, and thromboembolism. Additional interventions may improve brain protection and recovery.

Brain temperature is an important variable in determining the outcome of cerebral ischemia. The broad principles of therapeutic hypothermia established from animal studies dictate that earlier induction is better than later induction, increased depth of hypothermia increases efficacy, longer treatment duration (12 to 72 hours) is more effective than shorter (<12 hours), and slower rewarming is better than faster rewarming. Our strategy of inducing initial deep hypothermia during repair followed by mild hypothermia in intensive care may enhance the benefits of therapeutic hypothermia. Influx of calcium has been demonstrated to be one of the pathways leading to ischemic neuronal death. Magnesium as a natural calcium antagonist has been shown to be neuroprotective and to reduce the occurrence both of delayed cerebral ischemic events and poor outcomes. Recently, Meloni et al reported that combined mild hypothermia and magnesium treatment has synergistic neuroprotective effects and reduces brain injury when administered several hours after global and focal cerebral ischemia. Based on the findings from their study, our strategy of magnesium infusion combined with therapeutic hypothermia may have contributed to our positive results.

The optimal arterial cannulation site for repair of AADA is still controversial, especially in patients with brain ischemia. The site of cannulation may be important for rapid cooling of the brain. Estrera et al reported that femoral cannulation was attempted first, but if femoral cannulation exhibited inadequate perfusion flow, axillary cannulation was added. We used femoral cannulation first. When cardiopulmonary bypass was started, we checked the arterial pressure of both radial arteries and changes in both frontal cerebral oxygenation for detecting inadequate perfusion. One patient required additional axillary cannulation because complete occlusion of the abdominal aorta was observed in the preoperative CT scan.

The present study has several limitations. First, the sample size was small. Despite the small sample size, we believe that the overall number of affected patients (n=27) was adequate to proceed with an analysis of this topic. Second, there was no control group of patients with AADA presenting with coma who did not undergo surgical repair.

The etiology of coma during AADA is multifactorial. These factors include malperfusion from the dissecting flap occluding the great vessels, thromboembolism in the brain...
circulation from thrombus in the dissecting lumen, and the manifestation of hypoxic encephalopathy because of low cardiac output in patients with cardiac tamponade. For example, 2 patients who presented with complete neurological devastation (GCS 3) had both right-side carotid dissection and pericardial effusion. We took the patients to the operating room as quickly as practicably possible. Therefore, in our study, the etiology of coma was not completely determined before surgery.

In conclusion, aortic repair, if performed within 5 hours from the onset of symptoms, showed satisfactory early and late recovery of consciousness and function for AADA complicated by coma. Immediate aortic repair is warranted even if AADA is complicated by coma.

Acknowledgments

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Disclosures

None.

References

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SUPPLEMENTAL MATERIAL

Supplemental Tables

Table-1. Elements of the Glasgow Coma Scale

**Best eye response (E)**
1. No eye opening
2. Eye opening in response to pain.
3. Eye opening to speech.
4. Eyes opening by himself.

**Best verbal response (V)**
1. No verbal response.
2. Meaking meaningless sounds.
3. Inappropriate words.
5. Oriented.

**Best motor response (M)**
1. No motor response.
2. Extension in response to pain.
3. Flexion in response to pain.
4. Withdrawing from pain.
5. Localizing to pain.
6. Obeys commands.

Table-2. Elements of the National Institutes of Health Stroke Scale (NIHSS)

- Level of Consciousness (LOC): tests stimulation. Graded from 0-3.
- LOC Questions: tests the patient’s ability to answer questions correctly. Graded from 0-2.
- LOC Commands: tests the patient’s ability to perform tasks correctly. Graded from 0-2.
- Visual: tests visual fields. Graded from 0-3.
- Facial Palsy: tests the patient’s ability to move facial muscles. Graded from 0-3.
- Motor Leg: tests motor abilities of the legs. Graded from 0-4.
- Sensory: tests sensation of the face, arms, and legs. Graded from 0-2.
- Best Language: tests the patient’s comprehension and communication. Graded from 0-3.
- Dysarthria: tests the patient’s speech. Graded from 0-2.

**Table-3. Elements of the modified Rankin Scale (mRS)**

0- No symptoms.
1- No significant disability. Able to carry out all usual activities, despite some symptoms.
2- Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.
3- Moderate disability. Requires some help, but able to walk unassisted.
4- Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted.
5- Severe disability. Requires constant nursing care and attention, bedridden, incontinent.
6- Dead.