DISCUSSION

The management of coagulation disorders has still been a major concern in thoracic aortic surgery. Most thoracic aortic surgeries, such as aortic arch surgery, require hypothermia for brain protection, which is associated with a long CPB time and may cause dysfunction of the platelets and coagulation system. Surgery for the thoracoabdominal aorta is performed via a large spiral incision, which makes a large and invasive surgical field, and creates a large foreign body surface for blood. The long cardiopulmonary bypass, hypothermia and large invasive surgical fields are all associated with the consumption of coagulation factors and dysfunction of the coagulation system, and may lead to intraoperative coagulopathy. Therefore, maintaining coagulation is mandatory to ensure that a safe surgery can be performed and to reduce the amount of blood transfusion required during thoracic aortic surgery.

The causes of coagulopathy during thoracic aortic surgery are numerous ; [6] however, hypofibrinogenemia is one of the major factors leading to coagulopathy. The present study demonstrated that more than half of the enrolled cases showed hypofibrinogenemia (< 150 mg/dl SFL) at CPB termination. Of note, 13% of all cases showed severe hypofibrinogenemia under 100 mg/dl, which generally causes critical coagulopathy.

Many studies have reported the perioperative fibrinogen levels during cardiac surgery[7-9] and have indicated that lower postoperative fibrinogen levels were associated with more extensive intraoperative blood loss. However, there have been few studies that have reported the intraoperative fibrinogen levels during surgery, especially during aortic surgery.[10,11] In these points, the present study contributes new information.

The administration of fibrinogen concentrate appears to be an optimal way to treat hypofibrinogenemia; however, the intraoperative use of fibrinogen concentrate for hypofibrinogenemia has not yet been approved in most countries. Therefore, FFP is a realistic alternative for fibrinogen products. To improve the coagulation under hypofibrinogenemia, however, a large volume of FFP transfusion would be necessary; furthermore, it takes a longer time for a full recovery of the SFL to be reached after the administration of FFP. Therefore, fibrinogen concentrate is the best way to increase the SFL promptly, and without volume loading. A quick recovery of the coagulation system should result in better surgical hemostasis and reduce the total amount of blood transfusion required. It may thus result in a reduction of the total medical expenses.

The criteria for when to administer fibrinogen products for intraoperative coagulopathy have not been determined. Based on the guidelines for blood transfusion proposed by the Ministry of Health, Labour and Welfare of Japan, the use of FFP is recommended for hypofibrinogenemia less than 100 mg/dl due to DIC or after a large amount of blood transfusion. In the present study, patients who showed hypofibrinogenemia with a value < 100 mg/dl required a significantly larger amount of fibrinogen products and blood transfusion than did the patients with higher levels. Hypofibrinogenemia under 100 mg/dl must be considered a critical coagulopathy, and should be treated with fibrinogen concentrate to achieve surgical hemostasis.

However, there are still no criteria for the administration of fibrinogen concentrate even at our institution. In fact, surgeons and anesthesiologists discussed the use of fibrinogen products not only based on the serum fibrinogen level, but also the blood clot formation in the surgical field. We generally administer fibrinogen concentrate for hypofibrinogenemia less than 150 mg/dl at the termination of CPB as a temporary criterion. Because the SFL at the termination of CPB are not the lowest value and they generally decreased during surgical hemostasis, it may be necessary to identify different cut-off values or to measure the levels at another time point. There were no significant differences in the total amount of blood products used between patients who showed fibrinogen values of 101–150 mg/dl and 151–200 mg/dl. This may indicate that

fibrinogen concentrate achieved sufficient hemostasis and reduced the use of blood products even in patients with SFL of 101–150 mg/dl. Hypofibrinogenemia less than 150 mg/dl may be a useful value as a cut-off criterion for when to administer fibrinogen concentrate.

The next concern is how much fibrinogen concentrate is required to achieve sufficient surgical hemostasis. The average SFL at ICU admission were 250 mg/dl, which may be the optimal target value for sufficient surgical hemostasis, because a sufficient SFL is necessary upon the neutralization of heparin. When the SFL are restored effectively and promptly at this point, the subsequent coagulation failure could be avoided. However, in cases without sufficient hemostasis, the surgical bleeding is prolonged, and the consumption of coagulation factors continues. This leads to a gradual decrease in the SFL, and leads to a vicious cycle of coagulopathy. Therefore, sufficient SFLs are mandatory before protamine injection, especially after complex and difficult surgeries. A dose of one gram of fibrinogen concentrate theoretically will increase the SFL by 20 mg/dl in a 65 kg patient with 5L of intravascular blood volume. When patients show a SFL of 150 mg/dl at CPB termination, 5 g of fibrinogen concentrate is therefore theoretically required to achieve the target SFL of 250 mg/dl.

The guidelines for blood transfusion also recommend that blood examinations, including fibrinogen, PT and APTT, are mandatory before the use of FFP. We have a quick measurement system to examine the coagulation in our laboratory, and can obtain a prompt response within 30 minutes even at night. We propose that such a quick measurement of the coagulation is mandatory for deciding whether to administer fibrinogen concentrate. The information obtained by this quick measurement of the coagulation is important for the surgical team to understand the patients' coagulation condition. A lack of factors such as fibrinogen or platelets should be noted and remedied before the neutralization of heparin and during surgical hemostasis. When the bleeding tendency is predicted to continue in the surgical field, additional measurements should be performed. Surgeons must understand the mechanisms underlying coagulopathy in order to achieve sufficient surgical hemostasis.

As noted above, fibrinogen concentrate has not been approved for hypofibrinogenemia during surgery in Japan. This situation is similar in many Western countries. Fibrinogen concentrate will be approved in the near future for intraoperative coagulopathy. Prior to this, the safety of the intraoperative use of fibrinogen concentrate should be confirmed. The present study was a retrospective observational study; however, there were observed no complications related to the fibrinogen concentrate. In addition, there is no evidence that fibrinogen concentrate increased the risk of major complications or mortality.

In conclusion, hypofibrinogenemia frequently was observed at the termination of CPB during thoracic aortic surgery. Hypofibrinogenemia is one of the major factors associated with intraoperative coagulopathy. Quick measurement of the coagulation status is mandatory for deciding whether to administer fibrinogen concentrate, and should provide important information to understand the patients' coagulation condition as well. Hypofibrinogenemia of < 150 mg/dl SFL may be a useful criterion to decide whether to administer fibrinogen concentrate. The intraoperative administration of fibrinogen concentrate appears to be an optimal strategy to increase the SFLs effectively and promptly. It can treat coagulopathy and reduce the need for a large blood transfusion, and can help to avoid massive bleeding during thoracic aortic surgery.

DISCLOSURE

All the authors have declared no competing interest.

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Case Report

Thrombus in acute aortic dissection with atrial fibrillation: a treatment dilemma

Abstract

Type B acute aortic dissection (AAD) is often successfully managed with medical therapy, with a lower mortality rate, compared with type A AAD. Although the number of AAD patients complicated with atrial fibrillation (AF) has increased, reflecting an aging society, there have only been a few reports regarding the association of AAD and AF. Furthermore, there is no consensus on anticoagulation therapy in ADD patients complicated with AF, despite the importance of anticoagulation therapy in AF treatment. Here, we discuss a 79-year-old man with type B AAD and chronic AF complicated with the rapid left atrial appendage (LAA) thrombus formation after discontinuation of anticoagulation therapy. Emergent contrast-enhanced computed tomography revealed type B AAD with a partially thrombosed false lumen from the bifurcation of the aorta and the left subclavian artery to above the diaphragm. Ulcer-like projection was observed in the proximal thrombosed false lumen. Ten days after discontinuation of anticoagulation therapy, LAA thrombus was detected on contrast-enhanced computed tomography, which was not observed on admission. After anticoagulation therapy was resumed, the LAA thrombus disappeared, but the partially thrombosed false lumen was enlarged. The second discontinuation of anticoagulation therapy stabilized the dissected aorta and did not cause recurrence of LAA thrombus. In conclusion, clinicians need to balance the prevention of LAA thrombus formation with the complete thrombosis of a false lumen in patients with AAD and AF.

Type B acute aortic dissection (AAD) is often successfully managed with medical therapy, with a lower mortality rate, compared with type A AAD, especially in cases of thrombosed type AAD [1]. Although the number of AAD patients complicated with atrial fibrillation (AF) has increased, reflecting an aging society, there have only been a few reports regarding the association of AAD and AF [2,3]. Furthermore, there is no consensus on anticoagulation therapy in AAD patients complicated with AF, despite the importance of anticoagulation therapy in AF treatment. Here, we discuss a 79-year-old man with AAD and chronic AF complicated with the rapid left atrial appendage (LAA) thrombus formation after discontinuation of anticoagulation therapy, which was given for the prevention of thromboembolism caused by AF.

A 79-year-old man with chronic AF was admitted to the hospital for severe back pain. His blood pressure was 176/88 mm Hg and had an irregular heart rate of 71 beats/min at presentation. Emergent contrast-enhanced computed tomography (CECT) revealed type B AAD with a partially thrombosed false lumen from the bifurcation of the aorta and the left subclavian artery to above the diaphragm (Figs. 1A and 2A, D). Ulcer-like projection was observed in the proximal thrombosed false lumen. We discontinued administration of warfarin and started administration of antihypertensive drugs, which included a β-blocker and intravenous morphine hydrochloride. The patient's pain and blood pressure was controllable. Laboratory examination after admission showed that prolonged prothrombin time was normalized after warfarin discontinuation, but that the elevation of D-dimer levels was sustained. Follow-up CECT performed 3 and 10 days after admission did not reveal any extension or enlargement of the dissected aorta. However, LAA thrombus was detected on CECT 10 days after admission, which was not observed before (Fig. 1A, B). After concurrent administration of heparin and warfarin, the LAA thrombus completely disappeared on day 18 without any embolic events (Fig. 1C). However, the partially thrombosed false lumen was enlarged and exerted pressure on the true lumen (Fig. 2A-F), despite stabilization of blood pressure and cautious rehabilitation. With respect to anticoagulation therapy, we needed to take balance between the prevention of an LAA thrombus and the complete thrombosis in the false lumen; therefore, we decided to again discontinue anticoagulation therapy. Fortunately, careful follow-up CECT and echocardiogram showed that discontinuation of anticoagulation therapy stabilized the dissected aorta without enlargement of the false lumen or extension of the dissected aorta and did not cause recurrence of an LAA thrombus. After confirmation of false lumen stabilization, we restarted warfarin on day 42 after AAD onset, and AAD remained stable without enlargement of the false lumen.

Although there are no current recommendations regarding the use of anticoagulants for patients with AAD, many physicians believe it would have a negative effect on thrombosis formation and the healing process in the dissected aorta's false lumen. On the other hand, Song et al [4] have also reported favorable effects of early anticoagulation on the AAD; therefore, the effect of anticoagulation on AAD remains unknown. To the best of our knowledge, this is the first description of the rapid formation of LAA thrombus in a patient with AAD. This case emphasizes the careful management required for patients with AAD and AF. Clinicians need to balance the prevention of LAA thrombus formation with the complete thrombosis of a false lumen in patients with AAD and AF. In patients who have a partially thrombosed false lumen with ulcer-like projections, discontinuing anticoagulants may prevent enlargement of the false lumen of the dissected aorta, at least during the acute phase. However, AAD is associated with hypercoagulation reaction, as evidenced by a significant elevation in coagulation marker. If rapid formation of LAA thrombus is observed, anticoagulation therapy needs to be started with careful follow-up of the dissected aorta. We also need to keep in close communication with the cardiovascular surgery team to prepare for emergent surgical intervention, including surgical or thoracic endovascular aortic repair.

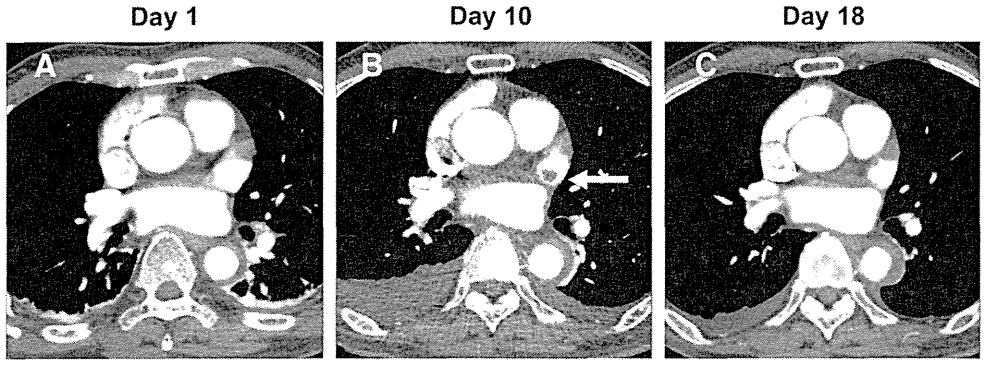

Fig. 1. Contrast-enhanced computed tomography showing thrombus in the LAA (B, arrow) on day 10 after AAD, which was not observed on admission (A). C, After resumption of anticoagulation therapy, LAA thrombus disappeared on day 18.

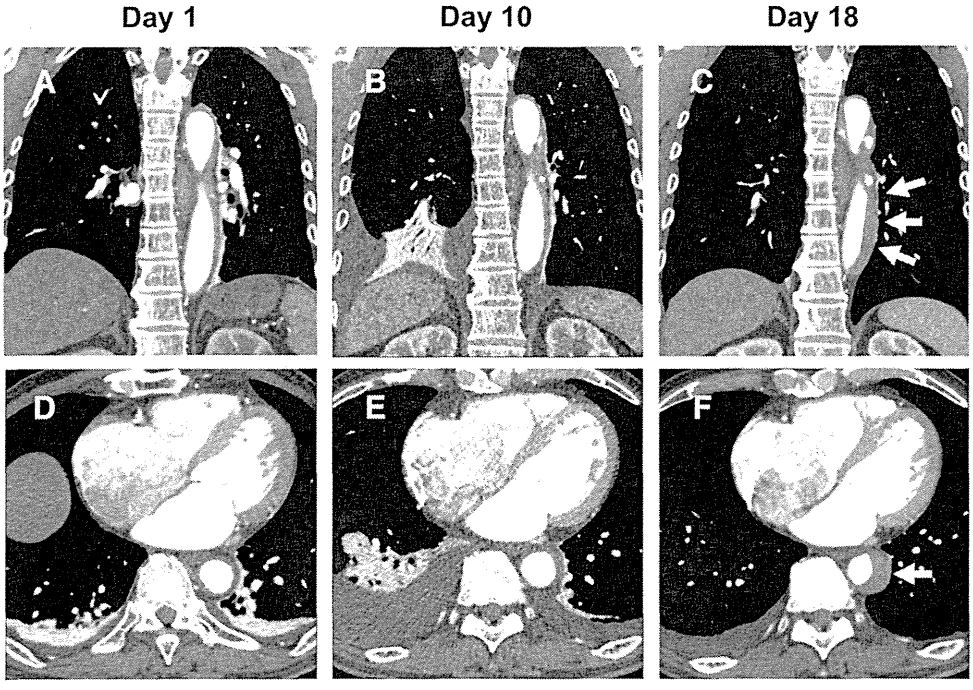

Fig. 2. Comparison of thrombosed aortic dissection seen on CECT on days 1 (A and D), 10 (B and E), and 18 (C and F). C and F, A partially thrombosed false lumen was enlarged (arrows) after resumption of anticoagulation therapy.

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Embolism is emerging as a major cause of spinal cord injury after descending and thoracoabdominal aortic repair with a contemporary approach: magnetic resonance findings of spinal cord injury†

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Abstract

OBJECTIVES: We reviewed magnetic resonance (MR) findings of the spinal cord in patients who had a spinal cord injury after descending and thoracoabdominal aortic repair, to speculate the specific cause of the injury.

METHODS: Between 2000 and 2012, 746 patients underwent descending or thoracoabdominal aortic surgery: 480 received an open repair with adjuncts of spinal cord protection [distal perfusion, cerebrospinal fluid (CSF) drainage, reattachment of intercostal arteries and hypothermia] and 266 received an endovascular repair. Twenty-six (3.5%) suffered a spinal cord injury. Of these, 18 (14 open repair and 4 endovascular repair) underwent postoperative spinal cord MRI. Preoperative identification of the Adamkiewicz artery (ARM) was obtained in all patients except 1. Aortic pathology was dissection in 2 and non-dissection in 16 patients.

RESULTS: There were 3 types MRI finding: sporadic infarction involving a range of spinal cord (sporadic); focal and asymmetrical infarction within a few segments of vertebra (focal); and diffuse and symmetrical infarction around the level of the ARM (diffuse). In endovascular repair, sporadic infarction was observed in all patients (4 of 4). In open repair, sporadic infarction was observed in 3 (21%), focal infarction in 7 (50%) and diffuse infarction in 4 (29%). In all patients who had sporadic or focal infarction, the aortic pathology was non-dissection.

CONCLUSIONS: From these findings, embolism is 1 of the major causes of spinal cord injury in the era of adjuncts to optimize spinal cord haemodynamics during aortic repair.

Keywords: Spinal cord injury • Aortic repair • Embolism

INTRODUCTION

Spinal cord injury (SCI) remains a devastating problem in descending and thoracoabdominal aortic repair. In 1988, Crawford reported that the use of distal aortic perfusion significantly reduced the incidence of SCI [1]. Spinal fluid drainage has been proved to be effective for spinal cord protection [2]. With these adjuncts combined with mild hypothermia, the incidence of SCI has been reduced to 3.5–5.0% in recent reports [3, 4]. Deep hypothermia, which is one of the most promising methods for organ protection, also provides excellent results with a low incidence of SCI [5, 6]. Preoperative identification of the Adamkiewicz artery (ARM) and collateral arteries to the anterior spinal artery by magnetic resonance (MR) angiography or computed tomographic angiography has given a better understanding of the circulation in the spinal cord [7, 8], which has contributed to lowering the incidence of SCI. In 1990, Mawad *et al.* [9] reported the MRI findings of SCI after thoracoabdominal aortic repair, which showed symmetrical high intensity of various degrees according to the severity of ischaemia. Since then, various adjuncts have evolved and the strategy for spinal cord protection has changed over time. To investigate the cause of SCI in patients who underwent aortic repair with a contemporary approach with various adjuncts for spinal cord protection, we reviewed MRI findings of SCI in these patients.

PATIENTS AND METHODS

Between 2000 and 2012, 746 patients underwent descending or thoracoabdominal aortic repair. Four hundred and eighty had open repair and 266 had endovascular repair. Of these, 233 (49%) had aortic dissection. In open repair, the mean age was 63 ± 10 years and 344 (71%) were men. In endovascular repair, their mean age was 75 ± 9 years and 64 (24%) were men.

†Presented at the Postgraduate Course of the 27th Annual Meeting of the European Association for Cardio-Thoracic Surgery, Vienna, Austria, 6 October 2013.

Operative procedures

In open repair, we used 2 methods for spinal cord protection during the period: mild hypothermia (30–32°C) with distal perfusion, spinal fluid drainage and reattachment of intercostal arteries under the guidance of motor evoked potentials (MEPs); and deep hypothermia (18–20°C). Since 2000, we have performed preoperative identification of ARM [10] and 90% could be identified. In patients with preoperatively identified ARM, reattachment of intercostal arteries, including the main source of the ARM, was performed in both methods. We used mild hypothermia with adjuncts in 307 (64%) patients and deep hypothermia in 173 (36%) patients. In mild hypothermia, we used the segmental clamp technique to reduce spinal cord ischaemic time and to close the patent intercostals, which should not be reconstructed immediately after opening the aorta. The target intercostals were decided according to a preoperative ARM study, and we reconstructed 2 or 3 pairs of intercostals around the identified ARM. These were also closed immediately after opening the aorta with balloon-tipped catheters or removable sutures. If ARM could not be identified in the preoperative study, we blindly reattached 2 or 3 pairs of intercostals between Th 8 and Th 12 levels. A spinal fluid drainage tube was inserted preoperatively and drained continuously to keep spinal fluid pressure at 10 mmHg or less if MEPs significantly change.

In endovascular repair, descending aortic repair was performed in 245 and thoracoabdominal aortic repair in 21 patients. Since 2008, we have performed spinal cord protection with spinal fluid drainage, intentional hypertension at the time of deployment and MEPs in high-risk patients who have a long segment of the aorta covered, closing the ARM [11].

The extent of aortic repair, aortic pathology and method of spinal cord protection are shown in Table 1. In all but 1 patient who had SCI and underwent spinal MRI, the left subclavian artery and the bilateral hypogastric arteries were patent. One patient who had emergent surgery had only a plain CT, so their patency was unknown.

Operative results and spinal cord injury

Operative mortality was 3.4% (26/746): 3.5% (18/480) in open repair and 3% (8/266) in endovascular repair. Twenty-six patients (3.5%) had SCI: 4% (19/480) in open repair and 2.6% (7/266) in endovascular repair. Twenty patients had paraparesis, 4 had paraplegia and 2 had monoparesis. Of them, 18 (14 open repair and 4 endovascular repair) had postoperative spinal cord MRI. The other 8 patients did not have spinal cord MRI because of their postoperative conditions.

Table 1: The extent of aortic repair and aortic pathology

	n	Dissection (%)	Deep hypothermia (%)
Open surgery	480	233 (49)	173 (36)
Descending	232	100 (43)	101 (44)
TAAA I	29	15 (51)	12 (41)
TAAA II	59	48 (81)	46 (78)
TAAA III	116	52 (49)	14 (12)
TAAA IV	44	8 (18)	0 (0)
Endovascular repair	266	10 (4)	
Descending	245	6 (2)	NA
TAAA	21	4 (19)	NA

TAAA: thoracoabdominal aortic aneurysm.

Analysis of spinal cord magnetic resonance findings

Spinal MRI was performed in all patients except 1 with SCI 2–4 weeks postoperatively. A patient who had renal failure and paraplegia had spinal MRI 2 months postoperatively. MRI abnormalities in SCI are best demonstrated on T_2-weighted images as high-intensity areas. Two radiologists analysed the MRI findings independently and classified them into 3 types:

Focal type: asymmetrical focal high intensity on axial T_2-weighted images within 2 segments of vertebra (Fig. 1).

Sporadic type: asymmetrical multiple high intensity on axial T_2-weighted images involving more than 3 segments of vertebra (Fig. 2).

Diffuse type: symmetrical high intensity on axial T_2-weighted images (Fig. 3).

The Review Ethics Board of the National Cerebral and Cardiovascular Center approved this study and individual consent for the study was waived.

RESULTS

Age, aortic pathology, the extent of operation, location of ARM, the adjuncts for spinal protection, MRI findings and the location of spinal infarction are shown in Table 2. In open repair, only 4 of 14 (29%) patients had diffuse-type spinal infarction, 7 (50%) had focal infarction and 4 (21%) had sporadic infarction. In endovascular repair, all patients had sporadic infarction. In all patients who had diffuse infarction, the location of the infarction was around the ARM. Aortic pathology was non-dissection in 16 and dissection in 2 patients. With regard to symptoms, 3 patients had paraplegia and the remaining 15 had paraparesis or monoparesis. Two patients who underwent surgery with deep hypothermia had SCI; in 1 who had undergone ascending aorta-to-iliac artery bypass because of lower body malperfusion because of aortic dissection, clamping the bypass graft at the time of thoracoabdominal repair for arterial cannulation caused SCI. In this patient, spinal MRI showed extensive diffuse infarction below the level of ARM. The other had sporadic-type infarction. The incidence of SCI in open surgery was 5.5% (17/307) in patients with mild hypothermia and 1.2% (2/176) in those with deep hypothermia.

DISCUSSION

SCI in aortic surgery has been regarded as provoked by intraoperative and postoperative deterioration of spinal cord circulation. Several authors have reported MRI findings of spinal cord infarction in aortic surgery [12, 13], and we have focused exclusively here on perioperative spinal cord circulation as the cause of ischaemia. However, because the causes of spontaneous spinal cord infarction have been reported [13, 14], we assumed that there would be 2 main causes of spinal cord infarction after aortic repair: infarction developing from ischaemia caused by intraoperative haemodynamic deterioration of the spinal cord, and embolism. Only a few cases of SCI in aortic surgery caused by embolism have been reported [15, 16]. Mawad reported MRI findings

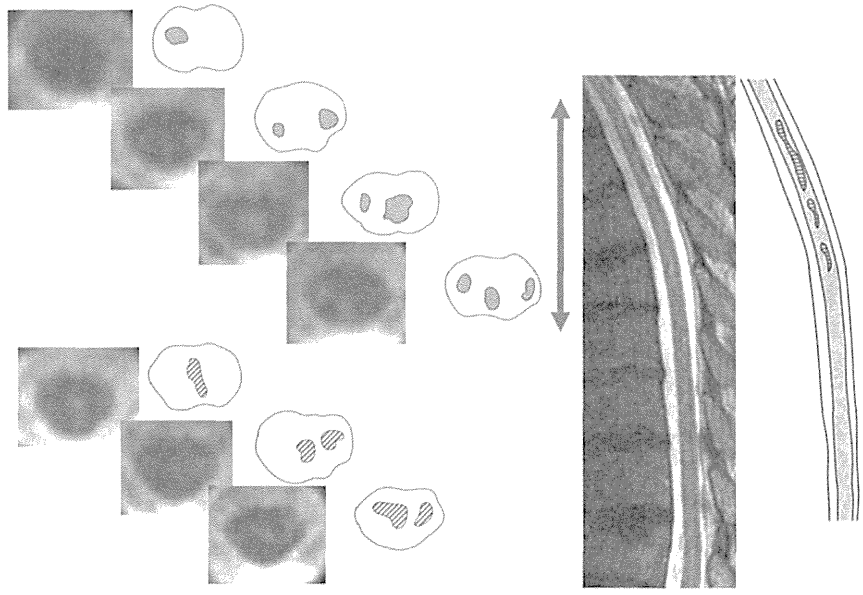

Figure 1: Sporadic type MRI findings: asymmetrical multiple high intensity on axial T_2-weighted images involving more than 3 segments of vertebra. Infarction is shaded on the illustration.

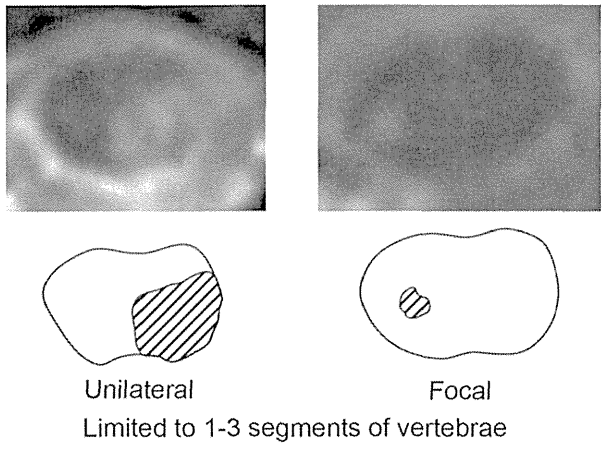

Figure 2: Focal type MRI findings: asymmetrical focal high intensity on axial T_2-weighted images within 2 segments of vertebra. Infarction is shaded on the illustration.

of SCI after thoracoabdominal aortic repair, all of which showed symmetrical high intensity in cross section, classified into 'diffuse type' in this study. These findings are different from those of this study. In Mawad's series, the currently available adjuncts for spinal cord protection had not been used properly at that time; therefore, the main cause of spinal cord infarction would have been haemodynamic deterioration of spinal cord circulation. Three major adjuncts for spinal cord protection, including distal aortic perfusion, mild hypothermia and cerebrospinal fluid drainage, have enabled better outcomes and a lower incidence of SCI, and these adjuncts alleviate intraoperative haemodynamic deterioration of the spinal cord. Despite their evolution, there is a still measurable incidence of SCI.

Over the past 12 years, we have experienced 4 patients with SCI after thoracoabdominal aortic repair who had an autopsy including the spinal cord. In 3 of 4 patients, microscopic findings showed scattered spinal cord infarction with atheroemboli in the anterior spinal artery and its branches, which supports our hypothesis (Fig. 4). The remaining patient showed symmetrical infarction without atheroemboli. Sporadic and focal infarction in MRI findings corresponding to scattered infarction microscopically is thought to be caused by atheroembolism.

In this study, we identified only 20% diffuse infarction, which was caused by haemodynamic deterioration, and the remaining 80% had focal or sporadic infarction, which was mainly caused by atheroemboli. Using the contemporary approach for spinal protection, embolism has become one of the major causes of SCI.

The source of atheroemboli is obviously aortic atheroma, so which procedure causes the embolism? Intraoperative MEPs serve as useful reference. In all patients who underwent open repair with mild hypothermia, we used MEPs for spinal cord functional monitoring. Of the patients whose MRI showed focal or sporadic infarction, 1 patient showed loss of MEPs (<20% of control) at the time of proximal double clamping outside the aneurysm, and 5 showed loss of MEPs during aortic clamping, including crucial segmental arteries. The MEPs never returned in these patients. Considering these findings, aortic manipulation is a major cause of atheroembolism. Two patients showed no change of MEPs intraoperatively, but they had hemiparesis because of a paralysed thigh and decreased lower leg strength, and their MRI showed a small focal infarction. The MEP device detects evoked potentials only at specific muscles; therefore, it is not reliable if a small part of the spinal cord is injured without segmental ischaemia. Most intercostals in non-dissecting aneurysms are occluded because of parietal thrombus formation; however, some intercostals are patent outside the aneurysm in patients. They can serve as a carrier for emboli at the time of clamping and reperfusion, although this is highly speculative.

In the patients with diffuse-type infarction, infarction occurred around the level of ARM in all patients and, in the patients with focal-type infarction, 14% (1/7) had infarction involving the level

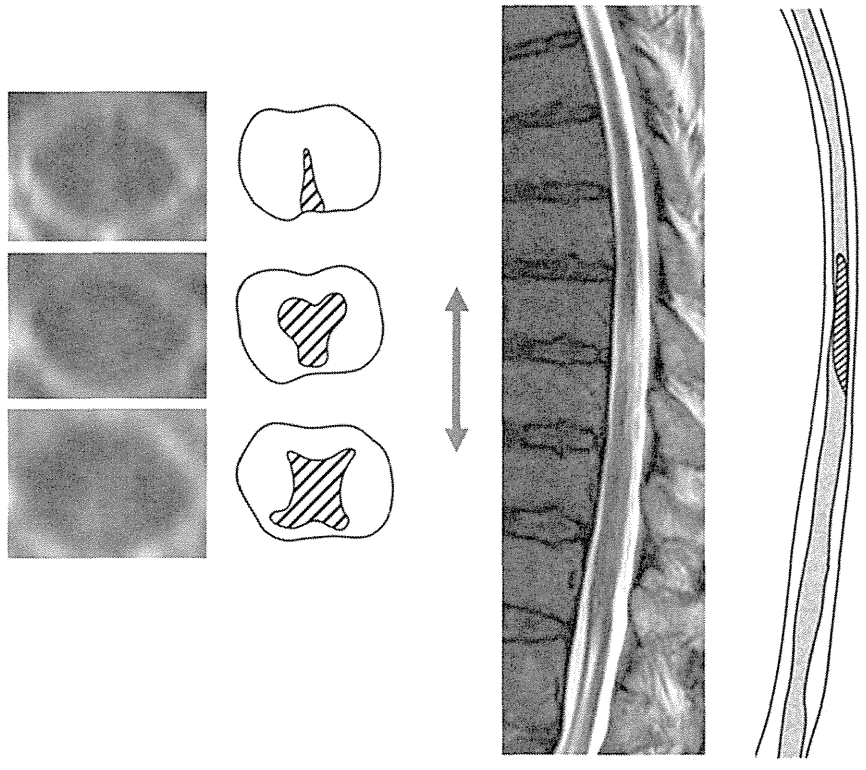

Figure 3: Diffuse type MRI findings: symmetrical high intensity on axial T_2-weighted images. Infarction is shaded on the illustration.

of ARM, but in the sporadic type, the level of ARM was not involved in spinal cord infarction.

There is a possibility that ARM is a crucial source of spinal cord circulation; however, few published data show that ARM has a crucial role in spinal cord protection in thoracoabdominal aortic surgery. This study includes only a few patients with diffuse-type infarction; therefore, data focusing on this subject are necessary.

In endovascular repair, 2 papers have demonstrated a low incidence of SCI [17, 18]. All patients in this study showed sporadic infarction. Atheroemboli might be a more significant factor in endovascular repair, which does not aggravate the global circulation during the procedure.

We have discussed that focal and sporadic types are caused by atheroembolism, and the diffuse type is caused by haemodynamic deterioration; however, the part of the artery that is occluded might influence which type of infarction occurs. In fact, in an autopsy case that showed atheroemboli in the sulcal artery branching to the anterior part of the spinal cord from the anterior spinal artery, infarction involved the anterior part of the grey matter almost symmetrically in a microscopic section. Thus, even the diffuse type on MR might be atheroemboli-driven infarction. It might be too speculative that the type of MRI findings in SCI reflects the aetiology, but atheroemboli cause spinal cord infarction as the autopsies showed, and accumulation of a number of patients would be necessary.

The classic watershed area in the spinal cord had been regarded as the lower cervical and upper thoracic areas, but many articles have reported a low incidence of SCI in these areas, regardless of the cause of SCI. Anatomical variation, including the location of radicular arteries, would cause individual differences in the location of watershed areas. In watershed area infarction during aortic repair, intraoperative occlusion of the artery that has a crucial role in blood supply would cause deterioration of the circulation in that area, spinal cord ischaemia and, finally, infarction followed by ischaemia would occur and the end arteries would be thrombosed. This mechanism was probably the main cause in Mawad's series in 1990, before the era of various adjuncts, which showed diffuse-type infarction in all patients. No patients showed sporadic-type infarction. Although watershed infarction still occurs with the current approach for spinal cord protection, not only haemodynamic stability, but also embolism should be the focus. In horizontal plane of the cord, the radicular arteries form 2 distinct systems of intrinsic blood supply. The first system is a posterolateral and peripheral plexus formed primarily by the 2 posterior spinal arteries that run longitudinally along the posterolateral sulcus of the cord and are richly interconnected by anastomotic channels. This is a centripetal vascular territory with penetrating branches that supply from one-third to one-half of the outer rim of the spinal cord. The second arterial system is a centrifugal system formed by numerous alternating central arteries that arise from the anterior spinal artery, run horizontally in the central sulcus and turn alternately to the right and left. This centrifugal system supplies the central grey matter and an adjacent white matter, which includes the corticospinal tract. Owing to the higher metabolic rate in the grey matter than the white matter and the anatomical arterial distribution, the grey matter, particularly the anterior horn, is vulnerable to hypoperfusion, which corresponds to the severity of ischaemia as Mawad's series showed. In this study, the types of the infarction correlated with the severity of the symptoms: patients with sporadic and the focal types showed severe symptoms and patients with focal type showed mild symptoms, but it might be difficult to speculate the cause of ischaemia only by means of the MRI findings of the spinal cord.

Table 2: Type of spinal magnetic resonance abnormality in patients with spinal cord injury

	Age (years)	Gender	Pathology	Location of aneurysm	Preop ARM	Location of MRI abnormality	Type of MRI abnormality		
Patients who underwent TEVAR									
1	85	M	Non-dissection	Descending	L Th 12th	Th 4–7	Sporadic		
2	89	M	Non-dissection	Descending	NA	Th 4, 8, 10	Sporadic		
3	68	M	Non-dissection	Descending	NA	Th 4–10	Sporadic		
4	81	M	Non-dissection	Descending	L Th 11th	Th-4,5,11–12	Sporadic		
	Age	Gender	Pathology	Deep hypothermia	Preop ARM	Repair involving ARM	Location of MR abnormality	Type of MR abnormality	
Patients who underwent open descending aortic repair									
1	59	M	Dissection	Yes	Th11	No	Th 6–9	Sporadic	
2	82	M	Non-dissection	No	Th9	No	Th 3–12	Sporadic	
3	81	M	Non-dissection	No	Th11	No	Th 7, 12	Focal	
4	58	M	Non-dissection	No	L1	No	Th 5	Focal	
5	85	M	Infection	No	Th10	Yes	Th 6–10	Diffuse	
	Age	Gender	Pathology	Extent	Deep hypothermia	Preop ARM	Repair involving ARM	Location of MR abnormality	Type of MR abnormality
Patients who underwent open thoracoabdominal repair									
1	88	F	Non-dissection	II	No	Th11	Yes	Th 4–12	Sporadic
2	72	M	Non-dissection	I	No	Th8	Yes	Th 5–8	Focal
3	61	F	Non-dissection	II	No	Th11	Yes	Th 5, 6	Focal
4	71	M	Non-dissection	III	No	Th9	No	Conus	Focal
5	79	M	Non-dissection	III	No	Th8	No	Conus	Focal
6	68	M	Non-dissection	III	No	Indefinite	NA	Conus	Focal
7	69	M	Non-dissection	II	No	Th12	Yes	Th12	Diffuse
8	34	M	Dissection	II	Yes	Th11	Yes	Th10-Conus	Diffuse
9	74	M	Non-dissection	III	No	Th10	Yes	Th 9, 10	Diffuse

ARM: Adamkiewicz artery; M: male; F: female.

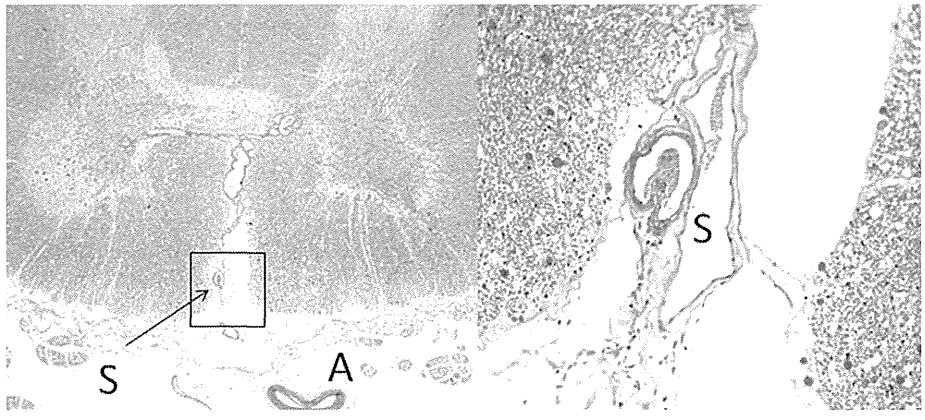

Figure 4: (**A**) Atheroemboli in the sulcal artery branching from the anterior spinal artery. (**B**) Magnification of the area indicated in (A). A: anterior spinal artery, *S: sulcal artery.*

Given that it has been reported that cerebral atheroembolism often occurs during extracorporeal circulation and aortic clamping, even if the patient is asymptomatic postoperatively [19, 20], spinal atheroembolism can potentially occur, but whether it is symptomatic depends on the extent and site of infarction. Reconstructed segmental arteries and vertebral and hypogastric arteries would reperfuse the spinal cord or the collateral artery would restore blood flow if the segmental arteries were occluded in the spinal cord [21], but intraoperative bleeding that would result in systemic hypotension and back-bleeding from the segmental arteries would reduce pressure on the anterior spinal artery, and vasoconstrictor in open surgery would impair blood flow from the arteries. Both atheroembolism and haemodynamic deterioration would adversely affect spinal cord circulation in open surgery. The association with atheroembolism but with less haemodynamic deterioration would be a major reason for the low incidence of SCI in endovascular repair. Therefore, avoiding multiple segmental aortic clamping to prevent atheroembolism seemed to be one of the major reasons for the low incidence of SCI in deep hypothermia, which provides longer ischaemic tolerance of organs and prevents reperfusion injury [22].

In conclusion, the incidence of SCI was lowered with a contemporary approach using various adjuncts to maintain intraoperative spinal cord circulation; however, embolism became a focal issue regarding SCI in descending and thoracoabdominal aortic repair.

STUDY LIMITATIONS

This is a study based only on the analysis of 18 MRI and 4 autopsies. The number of patients is small, and only 3 cases showed direct evidence of spinal cord infarction caused by embolism, proved by autopsies. The others are speculations from circumstantial evidence. Although there might be other reasons for SCI in these cases, some patients must have had embolism-driven infarctions, as shown in the autopsies. We need to accumulate more patients to investigate the specific causes of SCI and hope that this paper will help to lower the incidence of SCI, even if only slightly.

Conflict of interest: none declared.

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Risk Model of Cardiovascular Surgery in 845 Marfan Patients Using the Japan Adult Cardiovascular Surgery Database

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SUMMARY

The aim of this study was to evaluate the short-term operative results of patients with Marfan syndrome who underwent thoracic or abdominal aortic surgery in a 4-year period in Japan. Data were collected from the Japan Cardiovascular Surgery Database (JCVSD). We retrospectively analyzed the data of 845 patients with Marfan syndrome who underwent cardiovascular surgery between January 2008 and January 2011. Logistic regression was used to generate risk models. The early mortality rate was 4.4% (37/845). Odds ratios (OR), 95% confidence intervals (CI), and *P* values for structures and processes in the mortality prediction model were as follows: renal insufficiency (OR, 11.37; CI, 3.72-34.66; $P < 0.001$); respiratory disorder (OR, 11.12; CI, 3.20-38.67; $P < 0.001$); aortic dissection (OR, 13.02; CI, 2.80-60.60; $P = 0.001$); pseudoaneurysm (OR, 11.23; CI, 1.38-91.66; $P = 0.024$); thoracoabdominal aneurysm (OR, 2.67; CI, 1.22-5.84; $P = 0.014$); and aortic rupure (OR, 4.23; CI, 1.26-14.23; $P = 0.002$). The mortality prediction model had a C-index of 0.82 and a Hosmer–Lemeshow *P* value of 0.56. In conclusion, this study demonstrated that renal insufficiency and respiratory disorder had great impact on the operative mortality of Marfan patients undergoing cardiovascular surgery. Because patients with aortic dissection or aortic rupture showed high operative mortality, close follow-up to avoid emergency operation is mandatory to improve the operative results. Achieving good results from surgery of the thoracoabdominal aorta was quite challenging, also in Marfan patients. (Int Heart J 2013; 54: 401-404)

Key words: JACVSD

Marfan syndrome (MFS) is the most common multisystem disorder of connective tissue that affects 1 in 5000 individuals.[1)] It is inherited as an autosomal dominant trait and displays a variety of clinical manifestations in the ocular, musculoskeletal, and cardiovascular systems. Aortic root aneurysm and subsequent aortic dissection are the leading cause of morbidity and mortality in MFS patients. Aortic aneurysm in MFS is typically pear-shaped and involves progressive dilatation of the sinus of Valsalva. Early diagnosis and advances in surgical treatment, in particular the Bentall procedure and more recently the valve-sparing procedure, have significantly improved life expectancy in MFS.[2)] There has been no report of any nationwide study in Japan, presumably because the number of operations on MFS patients at each institute is limited. In the present study, risk analysis was performed for MFS patients who had undergone cardiovascular surgery between January 2008 and January 2011, using the Japan Adult Cardiovascular Surgery Database (JACVSD).

METHODS

Study population: The JACVSD was initiated in 2000 to estimate surgical outcomes after cardiovascular procedures in many centers throughout Japan. The JACVSD adult cardiovascular division currently captures clinical information from nearly half of all Japanese hospitals (235 hospitals) performing cardiovascular surgery. The data collection form has a total of 255 variables (definitions are available online at http://www.jacvsd.umin.jp), and these are almost identical to those in the STS National Database (definitions are available online at http://sts.org). The JACVSD has developed software for the Web-based data collection system through which the data manager of each participating hospital submits their data electronically to the central office. Although participation in the JACVSD is voluntary, data completeness is a high priority. Accuracy of the submitted data is maintained by a data audit that is achieved by monthly visits by administrative office members to the participating hospital to check data against clinical records. Data validity is further confirmed by an independent comparison of the volume of cardiac surgery at a particular

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hospital entered in the JACVSD versus that reported to the Japanese Association for Thoracic Surgery annual survey.[3]

We examined all MFS patients who had undergone cardiovascular surgery between 1 January 2008 and 31 December 2011. First, those JACVSD records that were obtained without informed consent were excluded from this analysis. Records with missing age (or which were out of range), sex, or 30-day status were also excluded. After this data cleaning, the population for this risk model analysis consisted of 845 patients from 235 participating sites throughout Japan.

Endpoints: The primary outcome measure of the JACVSD was 30-day operative mortality, which was defined exactly the same as the 30-day operative mortality in the Society of Thoracic Surgeons National Database. This includes any patient who died during the index hospitalization, regardless of the length of hospital stay, and any patient who died within 30 days of the operation after being discharged from the hospital. By using the definition from a previous study,[4,5] major morbidity was defined as any of the following 5 postoperative in-hospital complications: stroke, reoperation for any reason, need for mechanical ventilation for more than 24 hours after surgery, renal failure, or deep sternal wound infection.

Statistical analysis: The statistical model was multiple logistic regression; variables entered in the model were selected from all variables shown in Table I using bivariate tests. The chi-square test analyzed categoric covariates, and the unpaired *t* test or Wilcoxon rank-sum test was used for continuous covariates. A multivariate stepwise logistic regression analysis was then performed for each outcome. Stability of the model was checked every time a variable was eliminated. When all statistically nonsignificant variables had been eliminated from the model, "goodness-of-fit" was evaluated and the area under the receiver operating characteristic (ROC) curve was used to assess how well the model could discriminate between patients who lived and patients who had died. To evaluate model calibration, the Hosmer–Lemeshow test was applied.[6]

Results

Patient characteristics: Patient characteristics and outcomes of each procedure are shown in Table I. Patient median age was 41.9 ± 13.9 years, and the percentage of male patients was as 59.7%.

Early mortality and morbidity: As shown in Table II, 30-day operative mortality rates and composite rates for mortality or major morbidity were 4.4% and 23.0% respectively.

Model results and performance: Multiple regression analyses for all patients identified 6 preoperative risks affecting operative mortality (Table III). Preoperative comorbid conditions such as high creatinine levels ≧ 3.0 mg/dL or severe chronic lung disease significantly increased the surgical risks. Types of aortic disease such as dissecting aortic aneurysm, pseudoaneurysm, and thoracoabdominal aneurysm, and also mode of surgery such as emergency surgery for rupture of the aneurysm did as well. Model performance was evaluated using the C-index (area under the ROC curve) as a measure of model discrimination and the Hosmer–Lemeshow test as a measure of "goodness-of-fit." The C-index was 0.82 for the mortality model and 0.76 for the composite mortality or morbidity model; the Hosmer–Lemeshow test *P* value was 0.56 for the mortality model and 0.35 for the composite mortality or morbidity model. Details of model performance metrics are shown in Table IV.

Discussion

A clinical diagnosis of MFS is made according to the Ghent nosology when major manifestations are present in 2 organ systems and a third organ system is involved.[7] The cardinal features of MFS involve the ocular, cardiovascular, and skeletal systems,[1] but aortic enlargement and dissection, mostly of the ascending aorta, are the primary cause of early death.[8] In

Table I. Patient Characteristics ($n = 845$)

Variable	*n*	%
Male sex	507	59.7
Age (years)	41.9 ± 13.9	
Redo	326	38.4
Aortic dissection	487	57.4
Pseudoaneurysm	30	3.5
Rupture	24	2.8
Dilatation	560	66
Aortic root	432	50.9
Ascending aorta	359	42.3
Aortic arch	254	29.9
Descending aorta	165	19.4
Thoracoabdominal	118	13.9
Abdominal aorta	23	2.7
CABG	62	7.3
Mechanical valve	268	31.6
Bioprosthetic valve	48	5.7
Aortic regurgitation ≧ 2	371	43.7
Aortic regurgitation ≧ 3	245	28.9
Emergent operation	169	19.9
NYHA class ≧ 2	244	28.7
LVEF < 50%	18	2.1
Endocarditis	19	2.2
Hypertension	356	41.9
Associated coronary disease	18	2.2
History of myocardial infarction	19	2.2
Smoking	104	12.2
COPD	83	9.8
Diabetes	17	2
Renal insufficiency	24	2.8
Cerebrovascular accident	45	5.3
Aortic valve stenosis	4	0.5
Preoperative congestive heart failure	77	9.1
Prior cardiac operation	50	5.8
Hypercholesterolemia	89	10.5

Table II. Procedural Outcomes ($n = 845$)

	30-day operative mortality (%)	Composite results (%)
All patients	4.4	23
Thoracic aneurysm		
Root	2.1	23.1
Ascending	3.5	31
Arch	5.4	45.1
Descending	8.6	36.4
TAAA	12.4	68.6

Table III. Description of each prediction model ($n = 845$)

	30-day operative mortality				Composite mortality or major morbidity			
			95%CI				95%CI	
	P	OR	Lower	Upper	*P*	OR	Lower	Upper
Age	—	—	—	—	0.033	1.292	1.02	1.64
Gender	—	—	—	—	0.002	1.829	1.26	2.66
Myocardial infarction	—	—	—	—	0.011	3.566	1.34	9.52
Poor LV function	—	—	—	—	0.032	3.105	1.1	8.76
NYHA ≧ 2	—	—	—	—	0.007	1.688	1.15	2.47
Renal failure	0	11.37	3.727	34.66	—	—	—	—
Respiratory insufficiency	0	11.12	3.195	38.67	—	—	—	—
Reoperation	—	—	—	—	0.001	2.02	1.36	3.01
Rupture	0.02	4.225	1.256	14.22	0	6.975	2.61	18.7
Acute aortic dissection	—	—	—	—	0	2.339	1.53	3.59
Dissecting aortic aneurysm	0.001	13.02	2.796	60.6	—	—	—	—
Pseudoaneurysm	0.024	11.23	1.377	91.66	—	—	—	—
Aortic arch	—	—	—	—	0	2.376	1.61	3.51
Thoracoabdominal aneurysm	0.014	2.668	1.22	5.835	0	3.511	2.12	5.81

Table IV. Performance of each prediction model ($n = 845$)

	30-day operative mortality	Composite mortality or major morbidity
C-statistic	0.82	0.76
Hosmer-Lemeshow test	0.56	0.35

1968, Bentall reported a technique for the combined treatment of diseases of the aortic valve and the segment of the ascending aorta using a valvulated tube in which the coronary artery ostia were reimplanted.[2] In the years since, this technique has gone through several modifications and has become the procedure of choice for the treatment of aortic valve disease associated with the involvement of the ascending aorta.[9-12] Thus, the life expectancy of patients with MFS has dramatically improved from about 45 years in 1972[8] to 72 years in 1995.[13]

This study demonstrated that the 30-day operative mortality of aortic root surgery including both dissecting and nondissecting aneurysm in MFS patients was 2.1%. The JATS publishes an Annual Report of all Registry data, and the most recent version reported that the 30-day operative mortality of aortic root surgery performed for acute dissecting aneurysm and nondissecting, unrupturred aneurysm was 16.3% and 2.7%, respectively.[1] The better results in our study than the JATS Registry report might be attributed to the younger ages, less atherosclerotic changes of the aortic wall, and less opportunity for accompanying diseases in MFS patients. However, the operative mortality of thoracoabdominal aneurysm in MFS patients was 12.4%, which is not better than the number reported in the JATS Registry report; the 30-day operative mortality of thoracoabdominal procedures for chronic Stanford type B aortic dissection and nondissecting unruptured thoracoabdominal aneurysm was 10.7% and 6.9%, respectively.[1] It is likely that the thoracoabdominal aneurysms in MFS patietns in our study included more extensive types than the JATS Registry report, although classification of thoracoabdominal aneurysms was not clarified in either study.

There were two important variables affecting both the 30-day operative mortality rates and the composite results; ruputure for operative indication (OR, 3.67; 95% CI, 2.80 to 4.81 and OR, 3.67; 95% CI, 2.80 to 4.81) and thoracoabdominal aortic aneurysm (OR, 3.67; 95% CI, 2.80 to 4.81 and OR, 3.67; 95% CI, 2.80 to 4.81). Other factors, like preoperative high creatinine levels ≧ 3.0 mg/dL, severe chronic lung disease, dissecting aortic aneurysm, and pseudoaneurysm were also significant risk factors for the 30-day operative mortality in our study.

Aortic root dilatation, with subsequent aortic valve regurgitation, aortic dissection, or rupture, is a common and morbid cardiovascular abnormality in MFS patients.[14] As shown in our study, because the morbidity and mortality rates in MFS patients undergoing elective root surgery is low, and besides, emergency operation for aneurysmal rupure or acute dissection worsens the clinical results, early recognition of the disorder, identification of presymptomatic patients, and subsequent institution of surgical therapy is mandatory to reduce the frequency of catastrophic aortic events.

Symptomatic aneurysms have a much worse prognosis than asymptomatic ones, and should be resected regardless of size. There is an operative mortality of up to 20% for acute ascending aortic dissection in MFS. MFS patients who suffer aortic dissection have a significantly reduced long term survival, reported at 50–70% at 10 years.[15] These facts emphasise the importance of prophylactic aortic surgery before aortic dissection occurs in MFS. Recent guidelines have suggested that prophylactic aortic surgery be performed in adults with MFS when the aortic root diameter exceeds 5 cm.[15] Aortic surgery should also be considered in MFS when the aortic root exceeds 4.5 cm and there is a family history of aortic dissection, when there is rapid aortic growth (> 5–10 mm per year), and when significant aortic insufficiency is present. Aortic diameter should be measured serially by a transthoracic echocardiogram at multiple levels and compared to normal values based on age and body surface area. Unfortunately, there is no information about size criteria for operative indication in the study. Because Japanese people are generally smaller than people in western countries and the size of the vasculature might be accordingly smaller, further investigation is warranted to elucidate the true criteria of aortic size for operative indication in Japanese people.

Our study found that the operative mortality of thoracoabdominal aneurysm in MFS patients was not better than the JATS Registry report in the general population. Although en-

dovascular treatment has been demonstrated to be effective in type B aortic dissection and descending thoracic aneurysms in non-Marfan patients, it may have limited durability in MFS patients, because the aorta is prone to dilate in these connective tissue disorders.[16,17]

The validity of our study is limited because the odds ratio of several factors for the 30-day operative mortality were quite high (> 10) and suboptimal. These high odds ratios are attributed to the small number of each factor and therefore the figures themselves are not reliable, although these factors surely affect the results significantly. Additional limitation is that we did not divide our data into analyzing and validation data sets because of the relatively small volume of data. It would be possible to perform a validation of our risk model by dividing into the 2 data sets when the volume of data becomes large enough.

In conclusion, we have reported a risk stratification study on cardiovascular surgery that uses a nationwide cardiovascular surgery database. By analyzing 845 patients, the 30-day operative mortality rate was 4.4%. Renal insufficiency and respiratory disorder had great impacts on the operative mortality of MFS patients undergoing cardiovascular surgery. Because patients with aortic dissection or aortic rupture showed high operative mortality, close follow-up to avoid emergency operation is mandatory to improve the operative results in MFS patients. Achieving good results from surgery of the thoracoabdominal aorta was also quite challenging in MFS patients.

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Cerebral blood flow after hybrid distal hemiarch repair

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Abstract

OBJECTIVES: Aortic arch disease can be treated with hybrid repair (extra-anatomic bypass plus placement of aortic endoprostheses), but there is controversy about whether a bypass from one relatively small vessel will provide adequate blood flow to the entire brachiocephalic system. We, therefore, compared flow volumes before and after hybrid repair.

METHODS: We reviewed the records of 16 patients who underwent a hybrid distal hemiarch repair between October 2010 and May 2012. The procedure consisted of debranching of the left subclavian and left common carotid arteries, creation of a bypass to these vessels from the right subclavian artery by using a T-shaped synthetic graft, and placement of a stent graft. Preoperative and postoperative measurements of blood flow volume in the carotid and vertebral arteries and of regional cerebral blood flow were performed in ~70% of the patients.

RESULTS: Perioperative complications were one new-onset, fatal acute aortic dissection and two minor strokes. No major endoleaks occurred. Postoperatively, mean flow volumes in the right and left common carotid arteries, right and left internal carotid arteries, and right and left vertebral arteries were 423 and 393, 271 and 189, and 87 and 80 ml/min, respectively. Regional cerebral blood flow in the territories of the anterior, middle and posterior cerebral arteries was not significantly different from preoperative levels, as assessed both with and without administration of acetazolamide.

CONCLUSIONS: Hybrid distal hemiarch repair preserved regional cerebral blood flow and vasoreactivity, although flow in the common and internal carotid arteries was right-side dominant postoperatively.

Keywords: Aortic arch • Brain • Hybrid repair • Cerebral blood flow

INTRODUCTION

Open repair of aortic arch disease remains a challenge, particularly in patients at high risk of operative complications. The endovascular approach is useful for treating complex aortic disease, but its application is limited when the arch is affected because adequate landing zones cannot be obtained without interrupting the supra-arch vessels. Hybrid repair, which includes endovascular aortic repair plus debranching and reconstruction of the supra-arch vessels, may be an option when standard endovascular procedures are not possible for anatomical reasons [1]. Several different hybrid repairs have been described [2]. To treat disease in the distal aortic arch, we preferably perform debranching of the left subclavian artery (SA) and left common carotid artery (CCA) and creation of a bypass to these vessels from the right SA by using a T-shaped synthetic graft. This method is less invasive and simpler than other hybrid procedures, but concerns have been raised about the adequacy of blood flow to the entire brachiocephalic system provided by one relatively small vessel. We, therefore, measured global cerebral blood flow and blood flow in the carotid and vertebral arteries before and after hybrid repair in patients with distal aortic arch disease.

METHODS

We retrospectively reviewed the records of all 16 patients (14 men; mean age, 75.4 years [range 64–86 years]; 5 octogenarians) with aortic disease who underwent a distal hemiarch hybrid repair between October 2010 and May 2012. The repair was elective in 13 cases, urgent in 2, and emergency in 1. Aside from aortic disease, patients in the series had shock due to rupture of an aneurysm ($n = 1$), hemosputum ($n = 1$), congestive heart failure ($n = 1$), chronic obstructive pulmonary disease (COPD) ($n = 2$), cerebral infarction ($n = 2$), dementia ($n = 2$), cancer ($n = 2$), previous aortic surgery ($n = 7$), previous coronary artery bypass surgery ($n = 2$) and previous percutaneous coronary intervention ($n = 5$). Patients in whom preoperative Doppler echocardiography and magnetic resonance imaging assessments showed abnormal findings, such as the occlusion of the right SA and the right carotid artery and poor communication in the Circle of

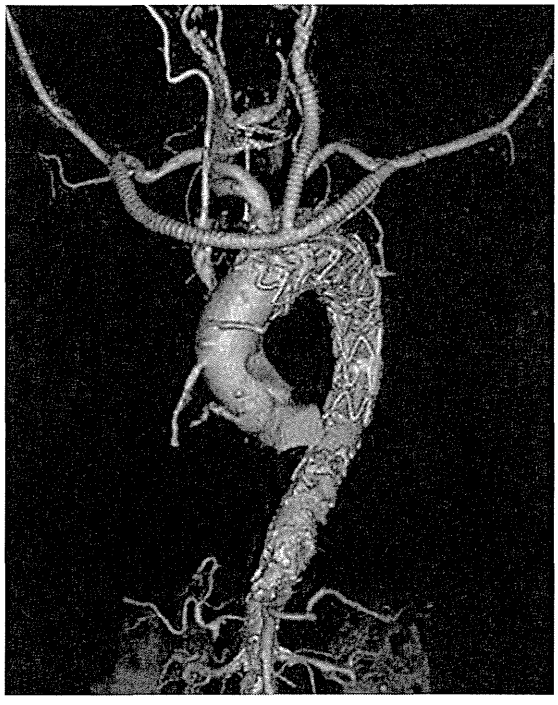

Figure 1: Computed tomographic image of distal hemiarch hybrid repair. A subcutaneous bypass is achieved by using a one-branched (T-shaped) graft. Each end of the graft is anastomosed to a SA in an end-to-side fashion, and the end of the branch is anastomosed to the left CCA in an end-to-end fashion. The proximal stump of the left CCA is then ligated. The proximal end of a covered stent graft is between the brachiocephalic and left common carotid arteries (Zone 1). A bare spring crosses the ostium of the brachiocephalic artery, but does not occlude blood flow.

Willis, were excluded from undergoing the procedure. The Institutional Review Board of Keio University Hospital approved the study, and written informed consent to undergo all procedures associated with the study was obtained from each patient.

The repair procedure was performed with the patient under general anaesthesia. The patient was placed supine, and the left CCA and both SAs were exposed. A ringed, 8-mm diameter, expanded polytetrafluoroethylene (ePTFE) prosthesis (W.L. Gore & Associates, Flagstaff, AZ, USA) with one branch (T-shaped device) was used as the conduit for a subcutaneous bypass (Fig. 1). Each end of the graft was anastomosed to an SA in an end-to-side fashion, and the end of the branch was anastomosed to the left CCA in an end-to-end fashion under simple clamping. The proximal stump of the left CCA was ligated. Neither extracorporeal circulation nor a shunt tube was used. After creation of the bypass, a stent graft (either a GORE TAG Thoracic Endoprosthesis, W.L. Gore & Associates; a Zenith TX2 TAA Endovascular Graft, Cook Medical, Bloomington, IN, USA; a Talent Thoracic Stent Graft, Medtronic, Santa Rosa, CA, USA or a Najuta Endograft, Kawasumi Laboratories, Tokyo, Japan) was deployed through the femoral artery and positioned so that the proximal end of the covered stent graft was in the aortic arch between the brachiocephalic artery and left CCA. All procedures were performed during the same operation.

Measurements of blood flow volume in the CCAs, internal carotid arteries (ICAs) and vertebral arteries (VAs) were done ~1 month postoperatively in 13 patients and preoperatively in 11 of those 13. Blood flow volume was determined by using Doppler sonography. Measurements of regional cerebral blood flow were done postoperatively in 13 patients and preoperatively in 12. Regional cerebral blood flow was determined by means of the graph-plot method employing N-isopropyl-p [I-123] iodoamphetamine (I-123 IMP) single-photon emission computed

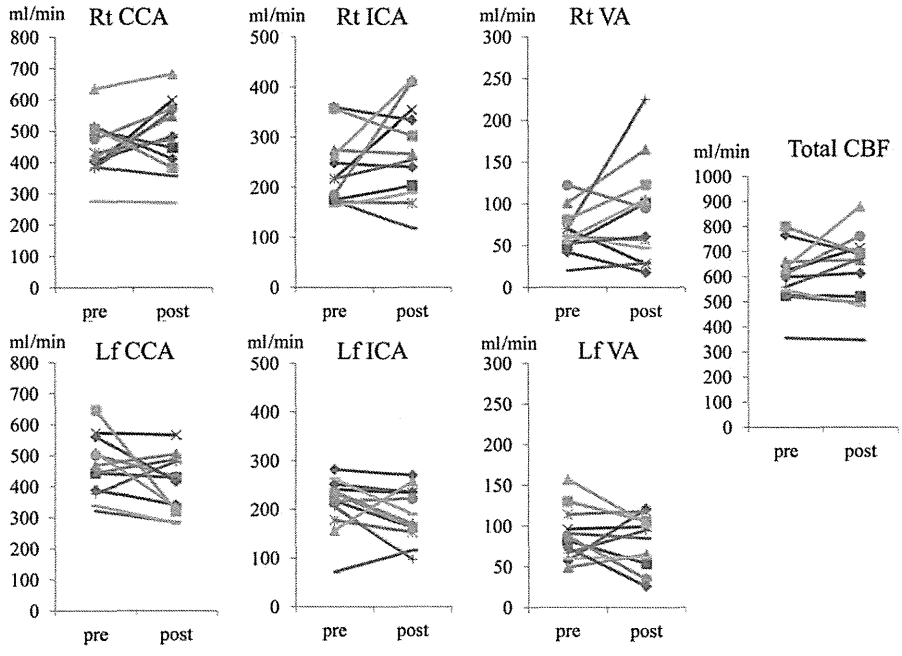

Figure 2: Flow volumes in arteries in individual patients and the calculated total cerebral blood flow before and after hybrid aortic repair. The total cerebral blood flow was calculated as the sum of flow volumes in both ICAs and both vertebral arteries. Rt: right; CCA: common carotid artery; ICA: internal carotid artery; VA: vertebral artery; Lf: left.

tomography (SPECT). This technique permits quantitative assessment of cerebral blood flow without arterial blood sampling [3, 4]. Two SPECT investigations were performed: a baseline study that did not include administration of acetazolamide and, ~10 days later, a study of the response to intravenous acetazolamide (1 g). The I-123 IMP SPECT method measures regional cerebral blood flow as accurately as does positron emission tomography using oxygen 15-labelled water [4], even in areas of hyper-perfusion; therefore, it can be employed for quantitative assessment of cerebral vasoreactivity to acetazolamide.

Statistical analyses of the blood flow assessments were performed by using SPSS software (Version 17.0, SPSS, Inc., Chicago, IL, USA). Results are expressed as the mean ± SD. Student's paired *t*-test was used to compare parametric variables. A *P*-value of <0.05 was considered to represent a significant difference between groups.

Table 1: Mean blood flow volumes in individual arteries and calculated total cerebral blood flow before and after hybrid aortic repair

Artery	Volume before repair (ml/min)	Volume after repair (ml/min)	*P*-value
Rt CCA	443 ± 91	482 ± 117	0.24
Lf CCA	465 ± 99	406 ± 93	0.11
Rt ICA	234 ± 69	271 ± 94	0.17
Lf ICA	213 ± 56	189 ± 55	0.18
Rt VA	66 ± 27	88 ± 62	0.18
Lf VA	89 ± 32	81 ± 32	0.46
ICA + VA	601 ± 117	629 ± 144	0.36

Rt: right; CCA: common carotid artery; Lf: left; ICA: internal carotid artery; VA: vertebral artery.

RESULTS

One of the 16 patients who underwent a hybrid distal hemiarch repair died perioperatively of a new-onset acute aortic dissection. Two patients had a minor stroke postoperatively. No major endoleaks were observed on computed tomographic scanning performed before hospital discharge in the 15 surviving patients. The mean age of the 13 patients (12 men) in whom cerebral blood flow was studied was 74.1 ± 6.0 years (range 64–82 years), with 3 of those patients being octogenarians. Two of the 13 patients had an urgent operation and 11 had an elective procedure.

Figure 2 shows the preoperative and postoperative blood flow volumes in the CCAs and VAs, as well as the calculated total cerebral blood flow, for each of the 13 patients assessed. The mean preoperative and postoperative flow volumes in the right CCA, left CCA, right ICA, left ICA, right VA and left VA in the 12 patients for whom both preoperative and postoperative data were obtained are given in Table 1. Preoperatively, the mean flow volume values for the left and right CCAs were similar ($P = 0.403$), as were those for the left and right ICAs ($P = 0.327$). Postoperatively, mean flow volume was significantly greater in the right CCA compared with the left CCA ($P = 0.025$) and in the right ICA compared with the left ICA ($P = 0.002$). The mean total cerebral blood flow, calculated as the sum of flow volumes in both ICAs and both VAs, was 601 ± 117 ml/min preoperatively and 629 ± 144 ml/min postoperatively. There was no significant difference between preoperative and postoperative total cerebral blood flow ($P = 0.362$).

Individual results of baseline (no administration of acetazolamide) SPECT assessments of regional cerebral blood flow performed preoperatively (11 patients) and postoperatively (13 patients) are shown in Fig. 3. The mean preoperative and postoperative blood flow values (ml/100 g/min) in the territories of the right anterior cerebral artery (ACA), left ACA, right middle

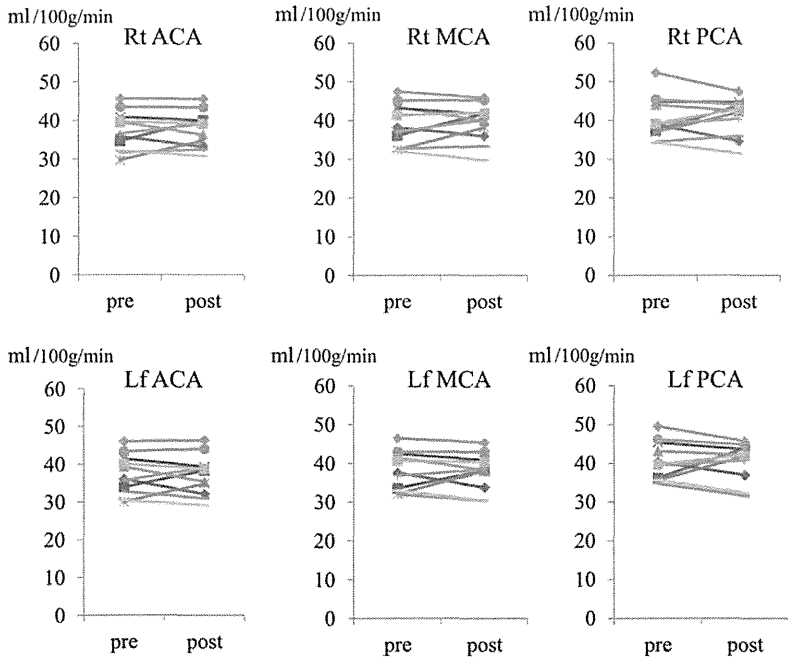

Figure 3: Baseline preoperative and postoperative regional cerebral blood flow in arteries in individual patients, as detected with SPECT. Rt: right; ACA: anterior cerebral artery territory; MCA: middle cerebral artery territory; PCA: posterior cerebral artery territory; Lf: left.

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cerebral artery (MCA), left MCA, right posterior cerebral artery (PCA) and left PCA are given in Table 2.

Values obtained for regional cerebral blood flow on SPECT analysis after administration of acetazolamide in individual patients are shown in Fig. 4. The mean preoperative (11 patients) and postoperative (13 patients) blood flow values (ml/100 g/min) in the territories of the right ACA, left ACA, right MCA, left MCA, right PCA and left PCA are given in Table 3.

So far, none of the patients in the series have had a procedure-related complication, although the patient with COPD died 10 months postoperatively, after progression of the disease. The 2-year actuarial survival rate in the series, calculated with use of Kaplan–Meier analysis by including this patient and the patient who died during initial hospitalization, was 85.2% ± 9.8% (Fig. 5).

Table 2: Baseline mean preoperative and postoperative regional cerebral blood flow values, as detected with SPECT

Artery	Preoperative flow (ml/100 g/min)	Postoperative flow (ml/100 g/min)	*P*-value
Rt ACA	37.2 ± 5.1	37.6 ± 4.6	0.64
Lf ACA	37.2 ± 5.3	37.1 ± 5.3	0.91
Rt MCA	38.9 ± 5.4	39.4 ± 4.9	0.29
Lf MCA	38.0 ± 5.0	37.8 ± 4.8	0.86
Rt PCA	40.6 ± 5.5	40.8 ± 4.9	0.84
Lf PCA	40.5 ± 4.9	40.4 ± 4.8	0.96

Rt: right; ACA: anterior cerebral artery territory; Lf: left; MCA: middle cerebral artery territory; PCA: posterior cerebral artery territory.

DISCUSSION

Recent advances have improved the outcomes of open repair of aortic arch disease, but the procedure remains a challenge, particularly in patients at high risk of complications [5]. Several innovative methods for treating aortic arch disease have been described. With respect to minimally invasive repair, procedures using fenestrated or branched stent grafts have yielded some promising results, but experience with these new endovascular devices is still limited. Hybrid repair is another alternative. In our previous experience with hybrid repair (33 patients), the source of the blood flow for the bypasses was the aorta. However, avoiding sternotomy and cardiopulmonary bypass has several potential advantages for high-risk patients [6, 7]. Because the greatest advantage of a hybrid procedure is its decreased invasiveness compared with open repair, sternotomy should be avoided if possible. In this study, we found evidence that the blood flow provided to the brachiocephalic system via the relatively small SA after a specific hybrid repair is adequate. In our patients who underwent this repair, postoperative total cerebral blood flow was similar to preoperative flow, although postoperative flow volume was significantly greater in the right compared with the left CCA ($P = 0.025$) and the right compared with the left ICA ($P = 0.002$). Moreover, there were no significant differences between preoperative and postoperative cerebral flow volumes (i.e., flow in the ACAs, MCAs and PCAs), with or without acetazolamide administration.

Using colour duplex sonography, Schöning *et al.* [8] measured blood flow volumes in the CCAs, ICAs and VAs in healthy adults and reported mean values of 470, 265 and 85 ml/min (either side), respectively. The mean value for total cerebral blood flow in their investigation was 701 ml/min (corresponding to 54 ± 8 ml/100 g/min), and no variations according to age or sex were

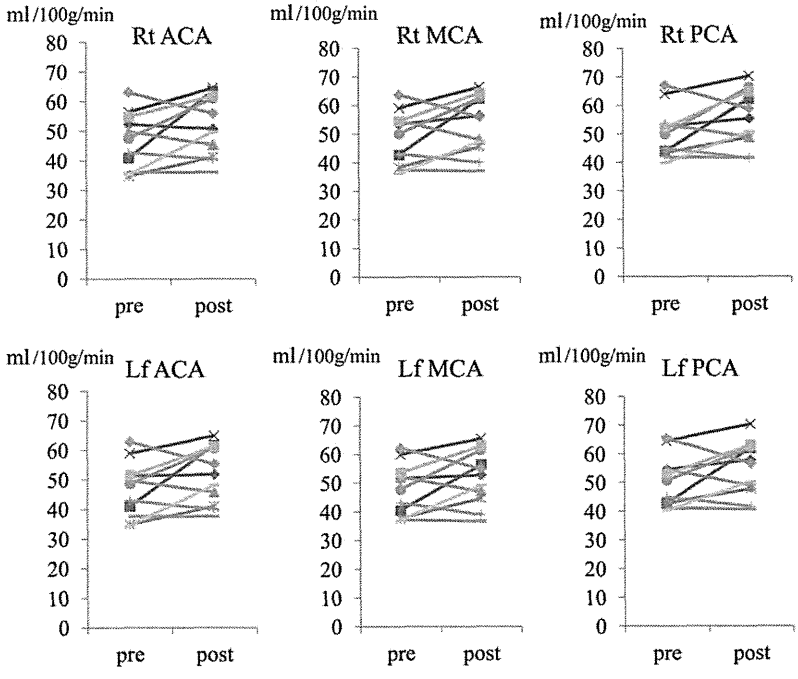

Figure 4: Preoperative and postoperative regional cerebral blood flow in arteries in individual patients after administration of acetazolamide, as detected with SPECT. Rt: right; ACA: anterior cerebral artery territory; MCA: middle cerebral artery territory; PCA: posterior cerebral artery territory; Lf: left.

Table 3: Mean preoperative and postoperative regional cerebral blood flow values, as detected with SPECT after administration of acetazolamide

Artery	Preoperative flow (ml/100 g/min)	Postoperative flow (ml/100 g/min)	*P*-value
Rt ACA	46.7 ± 9.5	51.8 ± 10.2	0.09
Lf ACA	46.7 ± 9.4	51.7 ± 9.8	0.09
Rt MCA	48.5 ± 9.4	53.3 ± 10.2	0.09
Lf MCA	47.5 ± 9.1	51.9 ± 9.5	0.10
Rt PCA	50.3 ± 8.9	55.5 ± 9.9	0.08
Lf PCA	50.4 ± 8.9	54.7 ± 9.5	0.12

Rt: right; ACA: anterior cerebral artery territory; Lf: left; MCA: middle cerebral artery territory; PCA: posterior cerebral artery territory.

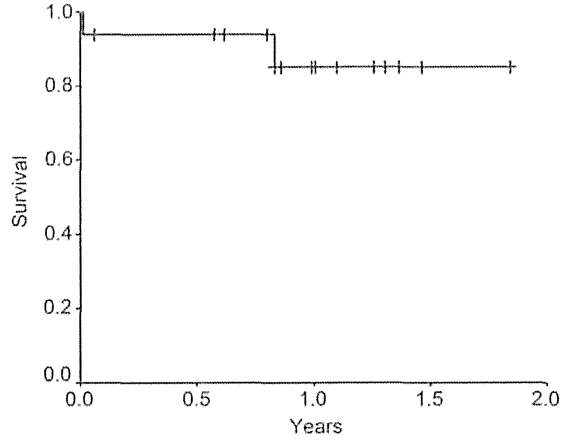

Figure 5: Two-year actuarial survival rate in the series. One patient died during initial hospitalization and another died 10 months postoperatively from chronic obstructive pulmonary disease.

observed. In our series, the mean preoperative values for the CCAs, ICAs and VAs were 454, 223 and 77 ml/min, respectively, and the calculated total cerebral blood flow was 601 ml/min. The postoperative values were 444, 230 and 84 ml/min, respectively, for the CCAs, ICAs and VAs and 629 ml/min for the calculated total cerebral blood flow. Thus, all the mean postoperative values in our study were consistent with the preoperative values, as well as with the values reported by Schöning *et al.*, although we did observe that blood flow volumes in the right CCA and right ICA were significantly greater than those in the left CCA and left ICA after the hybrid procedure. Because the diameter of the left CCA and left ICA is smaller than that of the prosthetic grafts we used (8 mm), the grafts could not increase flow in the vessel. However, the greater flow volume on the right side compensated for the lower volume on the left.

Preoperatively, the mean values for regional cerebral blood flow volume (without administration of acetazolamide) in the territories of the right and left ACA, MCA and PCA in our patients ranged from 37 to 41 ml/100 g/min. These values were slightly lower than the mean value of 45.4 ml/100 g/min observed by Ishii *et al.* [4] in healthy volunteers (mean age 63.5 years). Perhaps our patients had a lower regional flow volume because of their age. Our patient population was relatively old because the hybrid procedure was used primarily in those at high risk of complications from conventional surgery. Postoperative values for regional cerebral blood flow in our study were very similar to preoperative values.

SPECT studies using acetazolamide to assess regional cerebral perfusion showed that our patients had good cerebral vasoreactivity, even after distal hybrid repair. Remarkably, cerebral blood flow hyporeactivity to acetazolamide was not observed in any territory, either preoperatively or postoperatively. These findings indicate that both the right and left hemispheres of the brain had sufficient perfusion reserve both before and after aortic arch repair.

The limitations of our study include the small number of patients, its retrospective nature, and the lack of long-term follow-up. So far, none of our patients have had a late complication from their repair. However, data on the long-term safety of the procedure and the durability of the patency of the implanted bypass grafts and endovascular devices are not yet available, although extra-anatomic bypass grafting using an ePTFE prosthesis in carotid and subclavian reconstruction has previously been found to provide excellent patency rates [9, 10]. Moreover, use of the hybrid procedure in young, active patients requires specific investigation. We conclude, however, that our study provides good preliminary evidence that efficient regional cerebral blood flow and vasoreactivity are preserved in patients who undergo hybrid distal hemiarch repair for aortic arch disease.

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