Evaluation and Influence of Brachiocephalic Branch Re-entry in Patients With Type A Acute Aortic Dissection

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Background: Stanford type A acute aortic dissection (A-AAD) extends to the brachiocephalic branches in some patients. After ascending aortic replacement, a remaining re-entry tear in the distal brachiocephalic branches may act as an entry and result in a patent false lumen in the aortic arch. However, the effect of brachiocephalic branch re-entry concomitant with A-AAD remains unknown.

Methods and Results: Eighty-five patients with A-AAD who underwent ascending aortic replacement in which both preoperative and postoperative multiple-detector computed tomography (MDCT) scans could be evaluated were retrospectively studied. The presence of a patent false lumen in at least one of the brachiocephalic branches on preoperative MDCT was defined as brachiocephalic branch re-entry, and 41 patients (48%) had this. Postoperatively, 47 of 85 (55%) patients had a patent false lumen in the aortic arch. False lumen remained patent after operation in 34 out of the 41 (83%) patients with brachiocephalic branch re-entry, as compared to that in 13 of the 44 (30%) patients without such re-entry (P<0.001). Brachiocephalic branch re-entry was a significant risk factor for a late increase in the aortic arch diameter greater than 10 mm (P=0.047).

Conclusions: Brachiocephalic branch re-entry in patients with A-AAD is related to a patent false lumen in the aortic arch early after ascending aortic replacement and is a risk factor for late aortic arch enlargement.

Key Words: Aneurysm; Aorta; Dissection

Type A acute aortic dissection (A-AAD) remains to be a severe and complex disease because of its complications such as aortic rupture, aortic valve regurgitation, or malperfusion of vital organs. Although aortic dissection sometimes extends to brachiocephalic branches in patients with DeBakey type I aortic dissection, it is unclear how to treat these patients surgically. For instance, ascending aortic replacement, rather than total arch replacement, is performed in many cases with brachiocephalic branch dissection when initial entry is located at the ascending aorta. However, the effect of the presence of brachiocephalic branch dissection on the postoperative prognosis of A-AAD is greatly unknown.

The ascending aortic replacement in patients with a dissected branch in the brachiocephalic region often resulted in the remaining patent false lumen in the aortic arch postoperatively, despite the absence of anastomotic leakage. We assumed that the presence of re-entry in the distal portion of the brachiocephalic branches make a false lumen in the brachiocephalic branches patent, which then may cause a false lumen of the aortic arch patent after the ascending aortic replacement in patients with A-AAD.

A patent false lumen in the aortic arch is a well-known risk of late enlargement of the aortic arch.1 We therefore evaluated brachiocephalic branch re-entry associated with type A-AAD and examined the early and long-term effect of brachiocephalic branch re-entry on the aortic arch after ascending aortic replacement.

Methods

Study Group

We retrospectively studied 85 patients (49 men and 36 women; mean age, 62±12 years) who underwent ascending aortic replacement for A-AAD during the 9-year period from 2006 through to 2014, in whom multiple-detector computed tomography (MDCT) was performed preoperatively and postoperatively during hospitalization. Patients with an intramural hematoma or those 56 patients undergoing total arch replacement due to primary entry in the aortic arch were excluded. We also excluded 3 patients with primary entry at the proximal descending aorta who...
underwent ascending aortic replacement alone during the study period, because the aim of this study was to determine the influence of brachiocephalic branch re-entry after closure of primary entry.

This clinical study was approved by our institutional review committee, and informed consent regarding the principles outlined in the Declaration of Helsinki for participation in this study was obtained from each patient.

**Definition of Brachiocephalic Branch Re-entry**
The presence of a patent false lumen in at least 1 brachiocephalic branch, detected by preoperative MDCT as a double-barrel lumen at the supra-aortic arch slice, was defined as brachiocephalic branch re-entry. We eliminated cases with branch dissection ending near the branch orifice from the brachiocephalic branch re-entry.

**Operative Procedure**
We performed ascending aortic replacement with extracorporeal circulation accompanied by systemic cooling, temporary circulatory arrest, and selective cerebral perfusion. In general, the right axillary artery and right femoral artery were used for arterial perfusion. A small-diameter prosthetic graft was anastomosed to these vessels in an end-to-side fashion. The left axillary artery, left femoral artery, and ascending aorta served as alternative perfusion sites. We usually secure the arch vessels with rubber tape in a double-rolled fashion to fix catheters for cerebral perfusion with meticulous care so as not to make a new tear at the manipulated site in the dissected arch vessels. Temporary circulatory arrest was applied when the rectal temperature reached 25°C. During systemic circulatory arrest with selective cerebral perfusion by 3 balloon catheters, prosthetic anastomosis was performed with the open distal anastomosis technique. Polytetrafluoroethylene (Teflon; Meadox Medical Inc., Oakland, NJ, USA) felt strips were applied to both inside and outside of the aorta in a sandwich-like fashion, and sutured with 10–15 3-0 Ti-cron® mattress sutures to construct the aortic stump. Then, systemic perfusion was resumed via the side branch of the graft. The proximal aortic stump was constructed similarly to the distal side. Additionally, fibrin glue was applied in the false lumen of the proximal aorta to securely close the false lumen. Finally, we performed proximal prosthetic anastomosis and completed the reconstruction. Aortic root surgery was additionally performed when necessary.

**Evaluation of Postoperative MDCT Scans**
The status of the aortic arch was evaluated on postoperative MDCT and classified into the thrombosed false lumen or the patent false lumen. Patients with a patent false lumen in the aortic arch were then further classified according to the following groups: (1) patients with patent false lumen both in the brachiocephalic branch and aortic arch without distal anastomotic leakage (re-entry group); (2) patients with distal anastomotic leakage (leakage group); and (3) patients with both (combination group) (Figure 1). We defined distal anastomotic leakage as the presence of communication between the prosthesis lumen and the false lumen at a part of the distal anastomosis on postoperative MDCT scans.

**Postoperative Follow up**
A follow-up CT was performed annually after discharge. Contrast-enhanced CT was performed during the first several years after surgery, and a plain CT was performed subsequently when the patient’s condition remained stable. The risk factors for events, including aortic arch dilatation ≥10 mm in later period and at re-operation, were investigated.

**Statistical Analysis**
Continuous variables are expressed as the mean±standard deviation (SD). The statistical significance of differences between groups was evaluated using the unpaired t-test, Chi-squared test, and a 1-way analysis of variance with Bonferroni correction. The long-term survival was calculated according to the Kaplan-Meier method. Risk factors for late aortic dilatation were evaluated using the Cox proportional hazards regression analysis. The results of analyses are presented as hazard ratios (HR) with corresponding 95% confidence intervals (CI). All statistical analyses were performed using the R statistical package, version 2.13.0 (R Foundation for Statistical Computing, Vienna, Austria). P values of less than 0.05 were considered to indicate statistical significance.

**Results**

**Prevalence of Brachiocephalic Branch Re-entry and Patient Characteristics**
There were 41 patients (48%) who had brachiocephalic branch re-entry preoperatively. Nineteen patients had one branch re-entry, 12 patients had 2 re-entries, and 10 patients...
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Table 1. Preoperative Patient Characteristics

| Preoperative patient characteristics | All patients (n=85) | Brachiocephalic branch re-entry presence (n=41) | Brachiocephalic branch re-entry absence (n=44) | P value |
|-------------------------------------|---------------------|-----------------------------------------------|-----------------------------------------------|---------|
| Age (years) mean±SD                 | 62±12               | 61±12                                         | 63±11                                         | 0.44    |
| Proportion of males                 | 49 (58)             | 29 (71)                                       | 20 (46)                                       | 0.03    |
| Family history of aortic dissection | 1 (1)               | 1 (2)                                         | 0 (0)                                         | 0.48    |
| Diabetes mellitus                   | 7 (8)               | 2 (5)                                         | 5 (11)                                        | 0.44    |
| Hypertension                        | 62 (73)             | 25 (61)                                       | 37 (84)                                       | 0.03    |
| Coronary artery disease             | 3 (4)               | 0 (0)                                         | 3 (7)                                         | 0.24    |
| Chronic kidney disease              | 6 (7)               | 2 (5)                                         | 4 (9)                                         | 0.68    |
| Connective tissue disease           | 3 (4)               | 2 (5)                                         | 1 (2)                                         | 0.60    |
| Aortitis                            | 3 (4)               | 1 (2)                                         | 2 (5)                                         | 1       |
| Other collagen disease              | 2 (2)               | 1 (2)                                         | 1 (2)                                         | 1       |
| Cerebral malperfusion               | 10 (12)             | 7 (17)                                        | 3 (7)                                         | 0.19    |

Data are presented as n (%), unless otherwise stated.

Table 2. Proportion of Cases With a Patent False Lumen at the Aortic Arch After Ascending Aortic Replacement

| Classification of the causes     | All patients (n=85) | Brachiocephalic branch re-entry presence (n=41) | Brachiocephalic branch re-entry absence (n=44) | P value |
|----------------------------------|---------------------|-----------------------------------------------|-----------------------------------------------|---------|
| Brachiocephalic branch re-entry  | 47 (55%)            | 34 (83%)                                      | 13 (30%)                                      | <0.0001 |
| Distal anastomotic leakage       | 13                  | 0                                             | 13                                            |         |
| Combination                       | 14                  | 14                                            | 0                                             |         |

Data are presented as n (%), unless otherwise stated.

had 3 re-entries. The patients were classified into 2 groups according to the presence or absence of re-entry, and their demographic characteristics are shown in Table 1. The prevalence of hypertension (61% vs. 84%, P=0.03) and sex (males 71% vs. 46%, P=0.03) differed significantly between these 2 groups. However, there was no difference in age (P=0.44).

Relationship Between a Postoperative Patent False Lumen in the Aortic Arch and Brachiocephalic Branch Re-entry

After surgery, 47 patients (55%) had a patent false lumen in the aortic arch; 20 were classified into the re-entry group, 13 into the leakage group, and 14 into the combination group (Table 2), while false lumen was thrombosed in the remaining 38 patients (thrombosed false lumen). Thirty-four patients (83%) out of 41 patients with brachiocephalic branch re-entry preoperatively had a patent false lumen in the aortic arch postoperatively, and they were allocated into the re-entry group or combination group but not to the distal anastomotic leakage group. While only 13 patients (30%) out of 44 patients without brachiocephalic branch re-entry had a patent false lumen in the aortic arch postoperatively, all of them were allocated to the distal anastomotic leakage group. The incident rate of postoperative patent false lumen in the aortic arch was significantly higher in the patients with brachiocephalic branch re-entry than in the patients without brachiocephalic branch re-entry (83% vs. 30%; P<0.0001, Table 2).

Long-Term Follow up

Three patients (3.5%) died in hospital. Among the 82 patients who were discharged, 73 (89%) were able to be follow up completely. The mean follow-up period was 46±26 (6–103) months. Four patients died due to non-aortic-related events (geromarasmus 1, lung cancer 1, urethral cancer 1, and cerebral infarction 1) during the follow up. Two patients (1 in the leakage group and 1 in the combination group) required reoperation and underwent total arch replacement in later years. The overall survival rate of the 85 patients at 5 years was 91%.

The aortic arch diameter increased by 5.9±7.7 mm in patients with a patent false lumen, which is significantly bigger than that in the patients who had a thrombosed false lumen (0.7±6.0 mm, P=0.0021). In addition, the increase in the aortic arch diameter during follow up differed significantly according to the presence or absence of brachiocephalic branch re-entry (7.8±7.1 mm vs. 0.9±6.3 mm in the non-brachiocephalic branch re-entry group; P<0.0001). The changes in the aortic arch diameter among the patients with a thrombosed false lumen and those in the re-entry group, the leakage group, and the combination group are shown in Figure 2. There were significant differences among the 4 groups (P=0.0008) and significant differences in the changes in diameter were also noted among the thrombosed group, re-entry group, and combination group (thrombosed group vs. re-entry group P=0.01, thrombosed group vs. combination group P=0.007). An aortic event (enlargement of the aortic arch ≥10 mm and re-operation) occurred in 9 cases with brachiocephalic branch re-entry and 3 cases without during the follow-up period. The cumulative event incidence in patients with brachiocephalic branch re-entry is shown in Figure 3.

Risk Factors for Aortic Arch Dilatation

Risk factors for aortic arch dilatation ≥10 mm in later period were investigated. A univariate analysis showed
that younger age and brachiocephalic branch re-entry were significant risk factors. Only the existence of brachiocephalic branch re-entry remained as a significant risk factor in the multivariate analysis (HR: 4.01, 95% CI: 1.02–15.81, P=0.047, Table 3).

Discussion

Surgery is the best treatment of choice for patients with A-AAD,3 and its outcomes have recently improved.2,4,5 Better surgical outcomes are attributed to improvements in the preoperative CT diagnosis, development of extracorporeal circulation, prosthetic graft quality, and the acquisition of new operative techniques for procedures such as stump reconstruction and graft anastomosis.2,4,6 In recent years, the main objectives of surgery have been broadened from perioperative mortality to long-term prognosis including aortic events in later period.7 Although some studies have recommended total arch repair at the initial surgery because of apprehension of future aortic dilatation or other late aortic events,8,11 a recent meta-analysis showed that proximal aortic repair in patients with A-AAD may result in lower early mortality than extensive aortic repair.12 In addition, redo aortic surgery can be performed in all segments of the aorta with good outcomes.13,14 At our institution, we have performed ascending aortic replacement in patients who had a major entry in the ascending aorta and total arch replacement in those who had a major entry in the aortic arch,15 because we consider entry-site resection to be the most important goal of surgical treatment for A-AAD. Indeed, ascending aortic replacement for A-AAD has been performed in many Japanese hospitals.16

Although ascending aortic replacement has been performed in patients who had a primary entry in the ascending aorta, a patent false lumen in the aortic arch remained in many cases postoperatively. A patent false lumen is known to increase a risk for late aortic enlargement.1 Distal anastomotic leakage has been noted to be one of the main causes for patent false lumen in the aortic arch,17 thus resulting in late aortic dilatation.17,18 Potential causes of distal anastomotic leakage include the technique used for stump construction or anastomosis. Although other techniques, in addition to our method, have been reported to lead to robust aortic stump construction,19,20 it is almost inevitable to prevent distal anastomotic leakage completely.

CT is a useful modality for diagnosing A-AAD,21 and the

| Table 3. Risk Factors for a Late Increase in Arch Diameter of ≥10mm |
|-----------------------------|-----------------------------|
| **Univariate analysis** | **Multivariate analysis** |
| **P value** | **HR (95% CI)** | **P value** | **HR (95% CI)** |
| Brachiocephalic branch re-entry | 0.01 | 5.58 (1.51–20.63) | 0.047 | 4.01 (1.02–15.81) |
| Aortic arch diameter just after surgery | 0.09 | 0.91 (0.81–1.02) | 0.62 | 0.96 (0.81–1.13) |
| Age | 0.004 | 0.93 (0.88–0.98) | 0.18 | 0.96 (0.90–1.02) |
| Sex | 0.76 | 0.83 (0.27–2.65) | 0.86 | 1.15 (0.25–5.41) |
| Distal anastomotic leakage | 0.12 | 2.47 (0.79–7.67) | 0.37 | 1.79 (0.50–6.39) |

CI, confidence interval; HR, hazard ratio.
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recent development of MDCT has allowed detailed evaluations to determine whether the brachiocephalic branches are involved in a dissection.22 When a brachiocephalic branch is dissected, the branch has a double-barrel lumen, and there has to be a re-entry on the distal side of the branch, although the re-entry often cannot be detected because it is outside of the CT scan range. Patients who have a DeBakey type I aortic dissection usually have several secondary tears in the descending aorta or near the visceral aortic branches; however, such tears have a minimal effect on the patency of the aortic arch false lumen. Postoperative three-dimensional CT in the early phase often shows that blood is supplied to the false lumen through brachiocephalic branch re-entry. This blood flow then returns to the false lumen at the aortic arch and continues to the descending aorta or connects with the distal anastomotic leakage. Therefore, brachiocephalic branch re-entry is thought to be a main gate to the arch false lumen.

Recently, Uchino et al reported that brachiocephalic artery dissection is a risk factor for a patent false lumen at the aortic arch after hemiarch replacement, although they did not describe their definition of brachiocephalic branch dissection. In this study, we revealed that the remainder of the re-entry site at the brachiocephalic branches is also one of the important factors of patent false lumen at the aortic arch after ascending aortic replacement. To the best of our knowledge, this is the first study to investigate brachiocephalic branch re-entry and its effects.

Because of very few re-do cases and no aorta-related deaths in late phase in our study, we decided to use the length of the dilatation of the aneurysm as an aortic event. Previous studies have shown that a chronic dissected aortic arch aneurysm with a patent false lumen after ascending aortic replacement enlarged approximately 1 mm per year on average.19 Our experience of 5 mm dilatation with a mean interval of 46 months during the follow-up period is compatible to these results. We then considered that enlargement of the aortic arch greater than or equal to 10 mm is out of the ordinary, and we set 10 mm of dilatation as the cut-off value. As a result, the existence of brachiocephalic branch re-entry was deemed a risk factor for aneurysm dilatation ≥10 mm.

As previously mentioned, many hospitals, including our facility, have performed ascending aortic replacement in patients who have A-AAD via a primary entry at the ascending aorta. We therefore recommend performing aortic arch replacement at initial surgery in patients who have A-AAD concomitant with brachiocephalic branch re-entry, except for in the cases where patients have very high risks such as advanced age, the presence of malperfusion of vital organs, or severe coagulopathy. Availability of new hemostatic agents, which can be applied even during heparinization, may reduce the risk of bleeding at the anastomotic sites during the aortic arch replacement procedure, and may improve the operative results.

Study Limitations

There are some limitations associated with this study. The major limitations of this study include the low number of patients and the relatively short follow-up period. The main reason for these limitations was due to availability of preoperative MDCT scans, which was introduced recently in our hospital. Another important limitation is the retrospective nature of the study, and the relatively low complete follow-up rate of ~90% due to acceptance of patients from distant areas. And another limitation is the lack of graphical evidence of brachiocephalic branch re-entry itself in some patients due to usual limited scanned areas of the chest-abdomen-pelvis CTs. To confirm the details of the branch dissection or brachiocephalic branch re-entry itself, a neck-chest-abdomen-pelvis CT is mandatory at the first examination.

Conclusion

The preoperative presence of a brachiocephalic branch re-entry in patients with A-AAD was related to a patent false lumen in the aortic arch early after ascending aortic replacement and is a risk factor for late aortic arch enlargement. Aortic arch replacement should therefore be considered for patients who have A-AAD with brachiocephalic branch re-entry, depending to their systemic conditions.

Acknowledgments

The authors gratefully acknowledge the contribution of Prof. Takeharu Yamanaka, Department of Biostatistics, Yokohama City University, in aiding in our statistical analyses. There were no funding sources for this study.

Grants

None.

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