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Original Article

Influence of False Lumen Status on the Prognosis of Acute Type A Aortic Dissection without Urgent Surgical Treatment

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***Aim*: Recently, much attention has been focused on partial thrombosis of the false lumen in patients with acute aortic dissection. However, its effect on clinical outcomes in these patients, especially in case of acute type A aortic dissection, has not been clearly elucidated. This study evaluated the influence of the false lumen status, including partial thrombosis, on short-term clinical outcomes in acute type A aortic dissection patients without urgent surgical treatment.**

***Methods*: Sixty-two patients (29 males, mean age 73 ± 13 years) with acute type A aortic dissection who did not receive urgent surgical treatment at four hospitals were enrolled. Patients were divided into three groups based on the false lumen status on enhanced computed tomography image (complete thrombosis, $n=28$; partial thrombosis, $n=27$; patent, $n=7$). Patients with partial thrombosis were further divided into two groups (thrombus-dominant, $n=15$; flow-dominant, $n=12$).**

***Results*: The short-term mortality rate (in-hospital and 30-day) was significantly higher in patients with a patent false lumen, while no significant difference was seen between the other two groups. Patients with flow-dominant partial thrombosis had significantly higher short-term mortality rate than those with thrombus-dominant partial thrombosis (in-hospital, $p=0.001$ and 30-day, $p<0.001$).**

***Conclusions*: The short-term mortality rate in acute type A aortic dissection patients without urgent surgical treatment was lower in patients with partial thrombosis of the false lumen than in those with a patent false lumen. Furthermore, patients with flow-dominant partial thrombosis had higher mortality rate than those with thrombus-dominant partial thrombosis.**

Key words: Type A aortic dissection, False lumen status, Partial thrombosis

Introduction

A recent report showed that partial thrombosis of the false lumen is an independent predictor of long-term mortality in patients with acute type B aortic dissection[1]. Thereafter, much attention has been focused on partial thrombosis of the false lumen in patients with acute aortic dissection[2-8]. However, the issue about partial thrombosis of the false lumen has not been clearly elucidated. Furthermore, the extent of partial thrombosis has not been fully studied in these patients[6].

Type A dissection is associated with higher mortality, and often involves hemodynamic instability[9-11]. Therefore, research focused on type A dissection may contribute towards improving our understanding of the significance of false lumen status in patients with acute aortic dissection. However, urgent surgical repair is generally indicated for type A dissection[9], and data regarding false lumen status in type A dissection patients who do not undergo urgent surgical treatment are scarce.

Aim

The aim of this study was to evaluate the influence of the false lumen status, including partial thrombosis, on short-term clinical outcomes in acute

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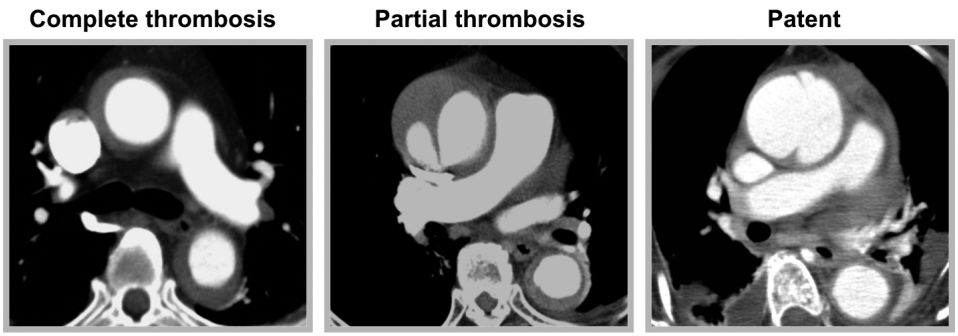

Fig. 1. Enhanced computed tomography images, which show complete thrombosis, partial thrombosis, and patent false lumen

type A aortic dissection patients without urgent surgical treatment.

Methods

Data of acute type A aortic dissection patients who were admitted and received initial medical treatment in four hospitals (Nagoya University Hospital, Yokkaichi Municipal Hospital, Toyota Memorial Hospital, and Handa City Hospital) between 2004 and 2013 were examined ($n=62$). Acute type A aortic dissection was defined as any non-traumatic dissection involving the ascending aorta and presenting within 14 days of the onset of symptoms. The diagnosis was confirmed by enhanced computed tomography (CT) immediately after emergency admission. Urgent surgical treatment was generally considered for all patients, and the final decision was based on various factors, including each patient's comorbidities and general condition. Initial medical treatment was defined as treatment not involving any surgical intervention during the first four days of admission. Blood pressure was controlled to maintain systolic blood pressure below 120 mm Hg immediately after admission, using continuous intravenous infusion and oral administration of antihypertensive drugs[12].

This study was performed according to the guidelines of the Declaration of Helsinki and approved by the local Ethics Committee, which waived the requirement for written informed consent.

Imaging results were interpreted at each patient's hospital by experienced cardiologists and radiologists. On imaging, the status of the false lumen was classified as completely thrombosed if no flow was present, as partially thrombosed if both flow and thrombus were present, and as patent if flow was present in the absence of thrombus. Thus, all the patients were divided into three groups based on the status of the false lumen on initial CT image: patent, partial thrombosis, and complete thrombosis (**Fig. 1**). Furthermore, patients with partial thrombosis of the false lumen were divided into two groups, thrombus-dominant partial thrombosis if more than 50% of the false lumen was thrombosed of the total length of dissected aorta on visual inspection, and flow-dominant partial thrombosis in the remaining cases.

All patients were assessed for the occurrence of short-term clinical events, including all-cause death and late surgical treatment related to aortic dissection.

Data are presented as mean ± standard deviation. Categorical variables are expressed as count and percentages. Categorical data were compared using the χ^2 test or Fisher exact test. Continuous data were compared using an unpaired t test. Among the three groups, continuous data were compared using analysis of variance. Kaplan-Meier estimates were generated to describe outcome time-course. The log-rank test was used to compare differences. A p-value of <0.05 was considered statistically significant. All analyses were performed with the SPSS 18.0 software package (SPSS, Chicago, IL, USA).

Results

The mean age of the enrolled patients was 73 ± 13 years (**Table 1**). Majority of these patients (83.9%) had history of hypertension; only 1.6% had diabetes. Previous aortic dissection (12.9%) and aortic aneurysm (19.4%) were not uncommon.

Table 1 shows baseline characteristics of patients stratified according to the status of the false lumen, and major reasons for the initial medical treatment. On CT imaging, the false lumen was found to be completely thrombosed in 28 patients (45.2%), partially thrombosed in 27 (43.5%), and patent in 7 (11.3%). There were no significant differences in age, sex, clinical characteristics, and clinical presentations among the three groups.

Table 1. Patient characteristics

	All *n* = 62	Complete *n* = 28	Partial *n* = 27	Patent *n* = 7	*P*-value
Characteristic					
Age, years	73 ± 13	72 ± 11	72 ± 15	78 ± 8	0.49
Men	29 (46.8%)	11 (39.3%)	15 (55.6%)	3 (42.9%)	0.47
Hypertension	52 (83.9%)	27 (96.4%)	20 (74.1%)	5 (71.4%)	0.05
Dyslipidemia	16 (25.8%)	8 (28.6%)	8 (29.6%)	0 (0%)	0.25
Diabetes	1 (1.6%)	0 (0%)	0 (0%)	1 (14.3%)	0.02
Current smoker	13 (21%)	4 (14.3%)	8 (29.6%)	1 (14.3%)	0.34
Hemodialysis	2 (3.2%)	1 (3.6%)	1 (3.7%)	0 (0%)	0.88
Marfan syndrome	2 (3.2%)	0 (0%)	2 (7.4%)	0 (0%)	0.26
Previous aortic dissection	8 (12.9%)	2 (7.1%)	4 (14.8%)	2 (28.6%)	0.30
Previous aortic aneurysm	12 (19.4%)	4 (14.3%)	8 (29.6%)	0 (0%)	0.14
Previous cardiac surgery	4 (6.5%)	0 (0%)	4 (14.8%)	0 (0%)	0.06
Clinical presentation					
Chest/back pain	53 (85.5%)	26 (92.9%)	21 (77.8%)	6 (85.7%)	0.28
Abrupt onset of pain	45 (72.6%)	22 (78.6%)	20 (74.1%)	3 (42.9%)	0.16
Migration of pain	8 (12.9%)	3 (10.7%)	5 (18.5%)	0 (0%)	0.38
Hypotension	17 (27.4%)	7 (25.0%)	7 (25.9%)	3 (42.9%)	0.62
Any neurologic deficit	15 (24.2%)	4 (14.3%)	8 (29.6%)	3 (42.9%)	0.20
Aortic valve regurgitation	15 (24.2%)	6 (21.4%)	6 (22.2%)	3 (42.9%)	0.47
Widest diameter of ascending aorta, mm	49.0 ± 8.1	48.3 ± 8.7	48.4 ± 7.7	53.8 ± 6.3	0.25
Pericardial effusion	29 (46.8%)	13 (46.4%)	12 (44.4)	4 (57.1%)	0.83
Reason for nonoperative management					
Refusal of operation (dementia, frailty, high age)	23 (37.1%)	8 (28.6%)	12 (44.4%)	3 (42.9%)	
Delay in diagnosis	3 (4.8%)	1 (3.6%)	0 (0%)	2 (28.6%)	
Extensive comorbidity	8 (12.9%)	0 (0%)	6 (22.2%)	2 (28.6%)	
Encephalopathy			2	2	
Advanced cancer			1	0	
Prior thoracic surgery			3	0	
Thrombosis of the false lumen in ascending aorta	25 (40.3%)	18 (64.3%)	7 (25.9%)	0 (0%)	
Other	3 (4.8%)	1 (3.6%)	2 (7.4%)	0 (0%)	

Table 2 shows baseline characteristics of patients with thrombus-dominant partial thrombosis and flow-dominant partial thrombosis. The patients with thrombus-dominant partial thrombosis tended to be older with higher rates of aortic regurgitation and pericardial effusion; however, no statistically significant differences were seen.

Fig. 2 shows Kaplan-Meier survival curves indicating freedom from all-cause death (2A), and all-cause death and late surgical treatment (2B) in patients stratified according to the status of the false lumen and compares the three groups (complete thrombosis, partial thrombosis, and patent). **Table 3** shows details of the in-hospital outcomes. Event-free rates were lowest in patients with a patent false lumen, while no significant differences were seen between patients with complete and partial thrombosis of the false lumen.

Fig. 3 shows Kaplan-Meier survival curves indicating freedom from all-cause death (3A), and all-cause death and late surgical treatment (3B) in patients with partial thrombosis of the false lumen and compares patients with flow-dominant partial thrombosis and thrombus-dominant partial thrombosis. **Table 3** shows the detail of in-hospital outcomes. Patients with flow-dominant partial thrombosis had significantly lower event-free rates than those with thrombus-dominant partial thrombosis.

Discussion

This study showed that the short-term mortality rate in acute type A aortic dissection patients without urgent surgical treatment was lower in patients with partial thrombosis of the false lumen than in those with a patent false lumen. Furthermore, in case of

Table 2. Patients characteristics (thrombus partial vs. flow partial)

	Thrombus dominant partial $n = 15$	Flow dominant partial $n = 12$	*P*-value
Age, y	75 ± 14	69 ± 16	0.33
Men	8 (53.3%)	7 (58.3%)	0.80
Hypertension	11 (73.3%)	9 (75.0%)	1.00
Dyslipidemia	7 (46.7%)	1 (8.3%)	0.04
Diabetes	0 (0%)	0 (0%)	
Current smoker	6 (40.0%)	2 (16.7%)	0.24
Aortic valve regurgitation	5 (33.3%)	1 (8.3%)	0.18
Widest diameter of ascending aorta, mm	48.8 ± 8.6	47.9 ± 6.8	0.77
Pericardial effusion	8 (53.3%)	4 (33.3%)	0.44
Ends filled with thrombus in false lumen			
Both ends	14 (93.3%)	3 (25%)	
Only proximal end	1 (6.7%)	6 (50%)	
Only distal end	0 (0%)	3 (25%)	

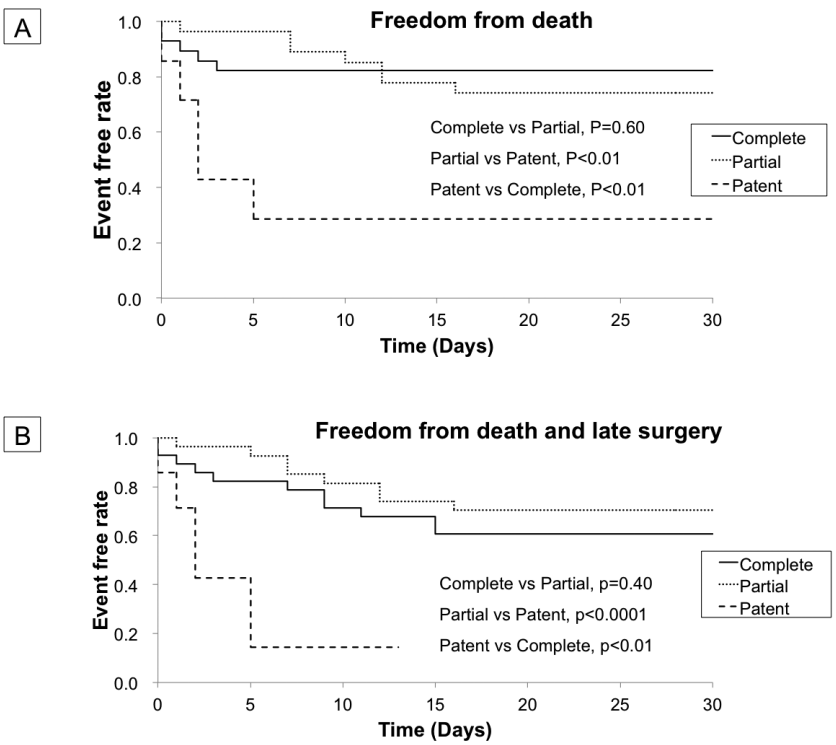

Fig. 2A. Kaplan-Meier survival curves stratified according to false lumen status (complete, partial, and patent)

The event free rate was higher in patients with partial thrombosis than patent false lumen. There was no significant difference between patients with partial thrombosis and complete thrombosis.

Fig. 2B. Kaplan-Meier survival curves indicating freedom from all cause death and late surgical treatment in all patients

The event free rate was higher in patients with partial thrombosis than patent false lumen. There was no significant difference between patients with partial thrombosis and complete thrombosis.

Table 3. In hospital outcomes

	All	Complete	Partial thrombosis				Patent
			All Partial	Thrombus-dominant	Flow-dominant	*P*-value*	
	n = 62	*n* = 28	*n* = 27	*n* = 15	*n* = 12		*n* = 7
Death	18 (29%)	6 (21.4%)	7 (25.9%)	0 (0%)	7 (58.3%)	0.001*	5 (71.4%)
Late surgical treatment	11 (17.7%)	7 (25%)	3 (11.1%)	1 (6.7%)	2 (16.7%)	0.57*	1 (14.3%)

*Thrombus-dominant partial thrombosis vs. Flow-dominant partial thrombosis

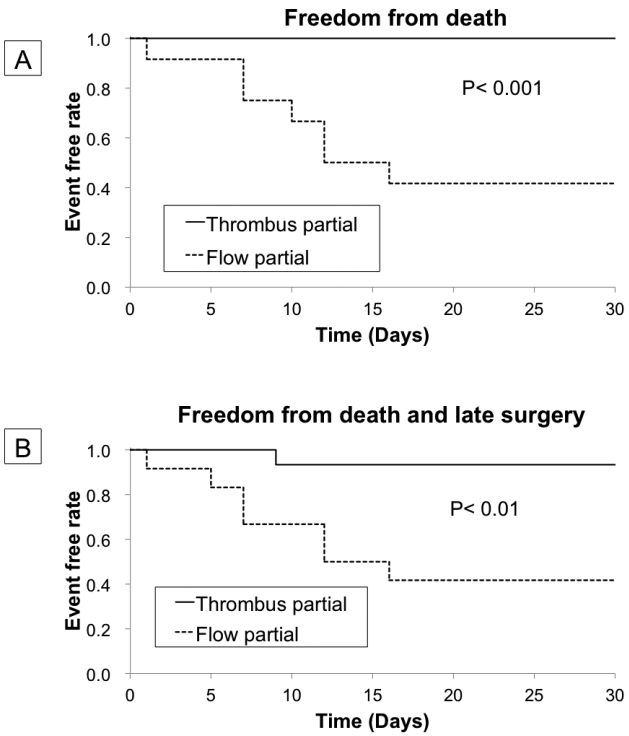

Fig. 3A. Kaplan-Meier survival curves in patients with partial thrombosis, and compared flow dominant partial thrombosis and thrombus dominant partial thrombosis

The event free rate was lower in patients with flow dominant partial thrombosis than thrombus dominant partial thrombosis.

Fig. 3B. Kaplan-Meier survival curves indicating freedom from all cause death and late surgical treatment in patients with partial thrombosis

The event free rate was lower in patients with flow dominant partial thrombosis than thrombus dominant partial thrombosis.

patients with partial thrombosis of the false lumen, those with flow-dominant partial thrombosis had higher mortality rate than those with thrombus-dominant partial thrombosis.

With regard to type B aortic dissection, some studies have shown that patients with partial thrombosis of the false lumen have higher mortality[1] and aortic growth rate[2, 7] than those with a patent false lumen or complete thrombosis of the false lumen. On the other hand, another study demonstrated that the growth rate of the affected aorta among the three groups is highest in patients with a patent false lumen[8]. We have previously reported that the long-term mortality does not significantly differ among the

three groups[6]. Some reports refer to the partial thrombosis of the false lumen in type A aortic dissection. Larsen *et al.* showed that preoperative partial thrombosis of the false lumen in surgically treated type A aortic dissection is not an independent predictor of long-term outcomes[3]. Other reports showed partial thrombosis of the residual false lumen after surgical repair to be a significant independent predictor of aortic enlargement[4] and poor long-term survival[5]. Thus, at present, results regarding partial thrombosis of the false lumen are conflicting.

As previously reported[6], it is important to study the extent of partial thrombosis in patients with acute aortic dissection. In this context, we consider the proportion of the thrombosed lumen to the false lumen as one of the main parameters. Although Tsai *et al.* mentioned that the formation of partial thrombosis may occlude distal tears and impede outflow[1], the effects of a 90% thrombosed false lumen might be different from those of a 10% thrombosed false lumen. However, previous studies could not reveal these differences in respect of partial thrombosis because of small sample sizes.

In this study, the patients with partial thrombosis of the false lumen did not have worse clinical outcomes than those with a patent false lumen. Furthermore, we delved into the issue of extent of partial thrombosis. Patients with partial thrombosis of the false lumen were divided into two groups based on the proportion of the thrombosed lumen to the false lumen. Patients with flow-dominant partial thrombosis had significantly higher short-term mortality rate than those with thrombus-dominant partial thrombosis. Although it may be a little premature, the results of this study suggest the extent of thrombosed false lumen can be used as risk stratification, and would lead to revealing of the diversity of partial thrombosis.

This study has a number of limitations. First, sample size was relatively small. Second, imaging techniques might have varied across the hospitals contributing to possible misclassification of the false lumen status. Third, the proportion of the thrombus in the false lumen was assessed only by visual inspection when classified into thrombus-dominant or flow-dominant partial thrombosis. Fourth, non-operative management was decided by the attending team of each hospital over the study period, and the reasons were varied, which might bias the results. Fifth, this study involved only non-surgical candidates and we did not compare our results against those who underwent urgent surgery, and therefore cannot comment on whether initial medical treatment is a valid option. Sixth, our data did not contain the data of laboratory examinations including D-dimer. However, at present, there are only few studies on the status of the false lumen in patients with type A aortic dissection and especially the extent of partial thrombosis in these patients. Thus, it would be beneficial to accumulate data on this issue.

Conclusion

Patients with partial thrombosis of the false lumen did not have worse short-term clinical outcomes than those with complete thrombosis of the false lumen or a patent false lumen in case of type A aortic dissection patients without urgent surgical treatment. Furthermore, the extent of partial thrombosis might influence clinical outcomes in these patients.

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Conflict of Interest

Dr. Ishii has received lecture fees from Astellas, Daiichi-Sankyo and Otsuka. Dr. Murohara has received lecture fees from Bayer, Daiichi Sankyo, Dainippon Sumitomo, Kowa, MSD, Mitsubishi Tanabe, Nippon Boehringer Ingelheim, Novartis, Pfizer Japan, Sanofi-Aventis, and Takeda. Dr. Usui has received lecture fees from Japan Blood Products Organization, and Terumo. Dr. Komori has received lecture fees from Sanofi-Aventis, Otuka, Daiichi Sankyo. Dr. Murohara has received unrestricted research grant for Department of Cardiology, Nagoya University Graduate School of Medicine, from Astellas, Daiichi Sankyo, Dainippon Sumitomo, Kowa, MSD, Mitsubishi Tanabe, Nippon Boehringer Ingelheim, Novartis, Otsuka, Pfizer Japan, Sanofi-Aventis, Takeda, and Teijin. Dr. Usui has receive unrestricted research grant for Department of Cardiac Surgery, Nagoya University Graduate School of Medicine, from Terumo, Medtronic, Edwards, Japan Lifeline, Senko Medical Instrument, and St. Jude Medical Japan. Dr. Komori has received unrestricted research grant for Department of Vascular Surgery, Nagoya University Graduate School of Medicine, from Sanofi-Aventis, Otsuka, Daiichi Sankyo, Eisai, and Gore Japan.

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Review

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