Analysis of predictive factors for progression of type B aortic intramural hematoma with computed tomography

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Purpose: **For patients with Stanford type B aortic intramural hematoma (IMH), medical treatment is usually selected. However, the outcomes of patients with type B IMH are not completely understood, and some cases can have fatal complications develop or surgical treatment necessitated. The purpose of this study was to investigate predictors of progression of the affected aorta in patients with type B IMH with initial computed tomography (CT) images.**
Methods: **Thirty-five patients with type B IMH were studied with serial CT images. Initially, medical therapy was selected for all patients. CT findings of the affected aorta were evaluated on admission and at follow-up. We divided the patients into two groups (progression group or regression group) on the basis of CT findings and investigated predictors of progression of the affected aorta with initial CT images.**
Results: **We defined 15 patients who showed increased maximum aortic diameter (n = 14), increased maximum aortic wall thickness (n = 3), progression to overt dissection (n = 4), or rupture of the aortic wall (n = 2) during the follow-up period as the *progression group*. The other 20 patients, who all showed decreased maximum aortic wall and aortic wall thickness, were defined as the *regression group*. In the maximum aortic diameter, an optimal cutoff value of 40 mm resulted in positive predictive and negative predictive values of 86.7% and 90.0%, respectively. Both a maximum aortic diameter of 40 mm or more ($P = .0011$) and a maximum aortic wall thickness of 10 mm or more ($P = .0009$) were shown to be significantly predictive of the progression with Cox regression analysis.**
Conclusion: **Maximum aortic diameter and maximum aortic wall thickness on initial CT images are predictive for progression of the affected aorta in patients with type B IMH. For type B IMH with a maximum aortic diameter of 40 mm or more or a maximum aortic wall thickness of 10 mm or more, careful follow-up studies must be required. (J Vasc Surg 2002;35:1179-83.)**

Recently, with noninvasive imaging techniques, such as computed tomography (CT), magnetic resonance (MR) imaging, and transesophageal echocardiography (TEE), aortic intramural hematoma (IMH) has been recognized and characterized primarily by aortic wall hematoma without intimal tear or penetrating ulceration.[1-7] Medical treatment usually is selected for patients with Stanford type B IMH.[2-6] However, the outcomes of patients with type B IMH are not completely understood, and some cases can have fatal complications develop or surgical treatment necessitated.[4,7-11]

Although verification of IMH can be achieved with a high degree of accuracy with MR imaging and TEE, CT has been used as the imaging method of first choice for the diagnosis and follow-up evaluation of IMH.[7,9,12] Previous studies have reported the maximum diameter of a dissected aorta during the acute phase as either a risk factor for survival or a predictor for aortic complications in patients with classic dissection and type A IMH.[7,13,14] However, few reports exist about the predictors for progression or regression in patients with type B IMH. In this study, we reviewed serial CT findings and the outcomes of patients with type B IMH. The purpose of this study was to investigate the predictors of progression of the affected aorta in patients with type B IMH with initial CT images.

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METHODS

Patients. The ethics committee at our hospitals approved this study. The study group consisted of 35 patients with Stanford type B IMH in two hospitals (Omura Municipal Hospital and National Nagasaki-Chuo Hospital) between 1984 and March 2001. All patients had sudden back or chest pain. Diagnoses of type B IMH were established with CT scan within 24 hours of the onset of pain with the following criteria: 1, a crescent-shaped area along the wall of the aorta with higher attenuation than blood at precontrast CT; 2, a noncontrast enhancement effect within the area seen on postcontrast CT; 3, no intimal flap in the aorta; and 4, no intimal tear or penetrating atherosclerotic ulcer.[1,7] In addition, the initial diagnosis of IMH was reconfirmed in all cases with TEE or MR imaging or both. The 24 men and 11 women in the study were between the ages of 43 and 86 years, with a mean age of 70.5 ± 11.5 years. Patients with Marfan syndrome and traumatic IMH were excluded from this study. Twenty-

nine of 35 patients had a history of hypertension. At admission, hypertension was present in all patients.

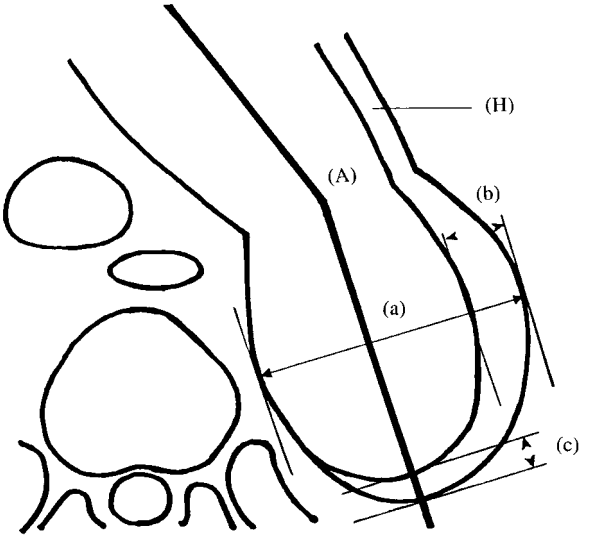
Initially, medical therapy was selected for all patients. In the acute phase, a calcium channel antagonist, nitrate, and β-blocker were administrated intravenously to reduce systolic blood pressure (100 to 120 mm Hg). In the chronic phase, several antihypertensive drugs, such as a calcium channel antagonist, angiotensin-converting enzyme inhibitors, or β-blocker, were administered orally to adequately control the blood pressure (<130 mm Hg). After discharge, all patients were followed at regular intervals and had well-controlled blood pressure (<130 mm Hg) during the follow-up period.

Follow-up computed tomography and analysis. Regular follow-up studies were performed every week during the first month and twice or three times a year after the second month. In patients with a new episode suggesting complications during the follow-up period, additional studies were performed. Without complications after 2 years from the onset, the patients had been excluded from regular CT follow-up series. The CT follow-up period after surgery also had been excluded from this study.

The follow-up CT studies were performed with nonenhanced and enhanced CT. Enhanced CT was done with a bolus injection of 100 mL of contrast material, generating axial images with contiguous 5 mm–thick sections from the top of the aortic arch to the abdominal aorta. *Aortic diameter* was defined as the diameter of the outer contour of the affected aorta. Measurements were taken on the basis of the accompanying calibrated scales in contrast-enhanced CT images. In the descending and abdominal aorta, the largest aortic diameter was measured in each slice. The aortic wall thickness also was measured from the intima to the adventitia in each slice.[7] Measurement methods of the aortic arch are shown in the Fig.[15] The maximum aortic diameter was the largest diameter of all aortic diameters. The maximum aortic wall thickness was the largest diameter of all aortic wall thickness.

From the 35 patients, we defined 15 patients who showed increased maximum aortic diameter, increased maximum aortic wall thickness, progression to overt dissection, or rupture of the aortic wall during the follow-up period as the *progression group*. The other 20 patients, who all showed decreased maximum aortic wall diameter and aortic wall thickness on the follow-up CT images, were defined as the *regression group*. The mean CT follow-up period was 15.71 ± 11.11 months (range, 10 days to 54 months). All 20 patients of the regression group had been followed for more than 6 months from the onset (mean, 13.40 ± 4.58 months). In this study, patients characteristics (age, gender, history of hypertension, diabetes mellitus, atherosclerotic diseases, hemodialysis, and smoking) also were evaluated.

Statistical analysis. All values are expressed as mean ± standard deviation. Univariate analysis was performed on all clinical and morphologic variables, with the χ^2 test or Fisher exact probability test used for categoric variables and the Student *t* test for continuous variables. Comparison of differences between admission and follow-up was done with the Student paired *t* test. The Cox proportional hazards model was used to identify predominant predictors for progression of the affected aorta in the patients with type B IMH thoughout the follow-up period with the use of stepwise multivariate analyses (entry and removal thresholds, 0.05 and 0.1, respectively). In all tests, a value of *P* less than .05 was considered significant. Data analysis was performed with the use of Stat-View J-4.5 for Macintosh (Abacus Concepts, Berkeley, Calif).



Measurement methods of aortic arch. We drew "central aortic line" perpendicular to aortic curvature *(A)*. Aortic diameter perpendicular to line was measured. Aortic diameter of outer contour of affected aorta is indicated *(a)*. At slice with largest aortic arch diameter, two individual aortic wall thicknesses from intima to adventitia are indicated with *(b)* and *(c)*. Larger diameter of two diameters was defined as aortic wall thickness of aortic arch. *H,* Intramural hematoma.

Table I. Clinical outcome of progression group of type B IMH

	Progression group (n = 15)
Increased maximum aortic diameter	14 (93.3%)
Increased maximum aortic wall thickness	3 (20.0%)
Progression to overt aortic dissection	4 (26.7%)
Rupture of aortic wall	2 (13.3%)
Surgical treatment	3 (20.0%)
Death	1 (6.7%)

RESULTS

Clinical outcome and computed tomographic findings. In the progression group (Table I), 14 of 15 patients showed increased maximum aortic diameter between 1 day and 24 months after the onset (mean, from 45.36 ± 12.35 mm to 55.21 ± 15.21 mm; $P < .0001$; progression rate,

Table II. Univariate correlation of patient characteristics with progression of type B IMH

	Progression group (n = 15)	*Regression group (n = 20)*	χ^2 *or t tests*	P *value*
Basic characteristics				
Age ≥ 70 years	9 (55.6%)	14 (70.0%)	0.38	.537
Male gender	9 (55.6%)	15 (75.0%)	0.895	.344
Hypertension	11 (73.3%)	18 (90.0%)	1.679	.195
Diabetes mellitus	1 (6.7%)	2 (10.0%)	0.122	.727
Atherosclerotic disease	4 (26.7%)	6 (30.0%)	0.047	.829
Hemodialysis	1 (6.7%)	1 (5.0%)	0.044	.8335
Smoking	6 (40.0%)	10 (50.0%)	0.345	.557
Initial computed tomography findings				
Maximum aortic diameter (mm)	45.00 ± 11.98	37.30 ± 6.92	2.396	.0224
Maximum aortic wall thickness (mm)	11.67 ± 4.37	7.40 ± 3.24	3.324	.0022
Involving aortic arch	14 (93.3%)	18 (90.0%)	0.122	.727
Pleural effusion	10 (66.7%)	17 (85.0%)	1.634	.201
Follow-up computed tomography findings				
ULP	4 (26.7%)	3 (6.0%)	0.729	.4301
Disappearance of IMH	3 (20.0%)	11 (55.0%)	6.022	.0261

Atherosclerotic diseases include atherosclerotic aneurysm, ischemic heart disease, and cerebrovascular disease.

Table III. Univariate and multivariate initial CT predictors of progression of type B IMH

			Univariate		*Multivariate*	
CT predictive factors	*Progression group (n = 15)*	*Regression group (n = 20)*	χ^2 *test*	P *value*	P *value*	*Hazard ratio*
Maximum aortic diameter ≥ 40 mm	13	2	20.572	<.0001	.0011	29.86
Maximum aortic wall thickness ≥ 10 mm	11	4	12.153	.0012	.0009	8.86

7.52 mm/y). In four of 15 patients, the affected aorta progressed to overt aortic dissection between 20 days and 36 months after the onset. Two patients underwent surgical repair (replacement of the ascending aorta and aortic arch) because of progression to type A overt aortic dissection 2 and 36 months after the onset, respectively. Two patients were undergoing observation.

In the other 11 patients, one patient died of aortic rupture 10 days after the onset. In one patient, surgery was performed because of aortic wall rupture 1 month after the onset. Nine patients were undergoing observation.

In 12 of 15 patients, IMH persisted during the follow-up period. Three of 15 patients showed increased maximum aortic wall thickness on final CT. Twelve of 15 patients showed decreased maximum aortic wall thickness. In four of 15 patients, an ulcer-like projection (ULP) newly appeared during the follow-up period. Two of four ULPs progressed to enlargement, and two ULPs progressed to overt aortic dissection.

In the regression group, nine of 20 patients showed persistent IMH during the follow-up period. In three of 15 patients, a ULP newly appeared during the follow-up period. All three ULPs disappeared or remained unchanged during the follow-up period.

Correlation of patient characteristics and computed tomographic findings. Table II shows that basic characteristics, such as age, gender, history of hypertension, diabetes mellitus, atherosclerotic diseases (including atherosclerotic aneurysm, ischemic heart disease, and cerebrovascular disease), hemodialysis, and smoking were not significant univariate predictors of progression. In the progression group, the maximum aortic diameter on initial CT was significantly greater than that in the regression group (45.00 ± 11.98 mm [range, 31 to 82 mm] versus 37.30 ± 6.92 mm [range, 29 to 61 mm]; $P = .0224$). The maximum aortic wall thickness on initial CT was significantly greater than that in the regression group (11.67 ± 4.37 mm [range, 5 to 20 mm] versus 7.40 ± 3.24 mm [range, 2 to 15 mm]; $P = .0022$). No significant differences were found in the location of IMH or pleural effusion on initial CT. Also, no significant difference was found in the appearance of ULPs on follow-up CT. However, a significant difference was found in the disappearance of IMH on follow-up CT ($P = .0261$).

Predictors of progression in type B aortic intramural hematoma on initial computed tomography. We calculated the optimal cutoff value of the maximum aortic diameter and the maximum aortic wall thickness to predict progression with maximizing (100 − % false-positive − % false-negative). Positive predictive values (true positive/[true positive + false positive]) and negative predictive values (true negative/[true negative + false negative]) were calculated. In the maximum aortic diameter, an optimal cutoff value of 40 mm was found, resulting in positive predictive and negative predictive values of 86.7% and 90.0%, respectively (a maximum aortic diameter of 40 mm;

13 of 15 patients with progression versus two of 20 patients with regression). In the maximum aortic wall thickness, an optimal cutoff value of 10 mm was found, resulting in positive predictive and negative predictive values of 78.6% and 81.0%, respectively (a maximum aortic wall thickness of 10 mm; 11 of 15 patients with progression versus four of 20 patients with regression). With use of univariate analysis, a maximum aortic diameter of 40 mm or more ($P < .0001$) and a maximum aortic wall thickness of 10 mm or more ($P = .0012$) were found to be significantly correlated with progression (Table III). For determination of the independent predictors on initial CT for progression throughout the entire follow-up period, forward stepwise Cox regression analysis was performed. Both a maximum aortic diameter of 40 mm or more ($P = .0011$) and a maximum aortic wall thickness of 10 mm or more ($P = .0009$) were shown to be significantly predictive of progression with the use of multivariate Cox regression analysis. The hazard ratio for the presence of maximum aortic diameter 40 mm or more was 29.86 times higher than that for less than 40 mm, and the hazard ratio for the presence of a maximum aortic wall thickness 10 mm or more was 8.86 times higher than that for less than 10 mm (Table III).

DISCUSSION

IMH was first described in 1920 as "dissection without intimal tear."[16] The cause of IMH was believed to be rupture of the vasa vasorum in the aorta resulting in hematoma formation.[5,7] IMH and overt aortic dissection may represent a continuum of the same disease, and progression of an IMH with rupture into the lumen may be one mechanism for aortic dissection.[1-11] However, the exact mechanism of IMH formation remains to be investigated. In some cases, it may result from early complete thrombosis of both a false lumen and intimal disruption in classic dissection that originates from an intimal tear.[9] Some reports suggested that small intimal disruption may be overlooked even at surgery and autopsy.[12,17] Thus, differentiation of "true" IMH from "false" IMH with imaging alone is impossible. In this study, diagnoses of IMH were made with imaging methods, but further studies are needed to establish the disease entity of IMH.

In type B IMH, the natural history and prognosis are not completely understood, and few reports exist about the predictors for progression or regression in patients with type B IMH. Usually, patients with classic type B aortic dissection are treated with antiimpulse therapy during the acute phase because the mortality rate with this treatment is reported to be equal to or slightly better than that for surgical treatment during the acute phase.[13,18,19] Surgical treatment should be selected if the aortic diameter becomes enlarged or if the aorta ruptures during the chronic phase; careful observation is necessary. In patients with type B IMH, medical treatment is usually selected,[2-6] and careful observation is necessary but very difficult.

Our results indicate that progression of type B IMH can be predicted by two independent factors: maximum aortic diameter and maximum aortic wall thickness of the affected aorta. With respect to aortic enlargement, a few studies address the prediction of aortic enlargement throughout the entire follow-up period in classic aortic type B dissection. Masuda et al[13] reported that the maximum diameter of the dissected aorta during the acute phase is a risk factor for survival during the chronic phase. Kato et al[14] reported that aortic enlargement in chronic type B dissection can be predicted with two factors obtained at the onset of dissection: the maximum diameter of the dissected aorta and the location of the primary entry site. They suggested that the enlargement of type B dissection is closely correlated with wall stress on the dissected aorta. In IMH, however, wall stress is related to the aortic flow lumen diameter. In type A IMH, Kaji et al[7] reported that the maximum aortic diameter is predictive for progression on initial CT, and they suggested that some other factors, such as distensibility, may play an important role in the progression or regression of IMH. In type B IMH, we also consider that distensibility may play an important role in progression or regression. According to our results, in the maximum aortic diameter, an optimal cutoff value of 40 mm is found, resulting in positive predictive and negative predictive values of 86.7% and 90.0%, respectively. In type A IMH, Kaji et al[7] considered the optimal cutoff value to be 50 mm for the maximum aortic diameter to predict progression on initial CT. Because a difference is seen in normal aortic diameter between the ascending aorta and the other parts of the aorta, our cutoff value of 40 mm for the maximum aortic diameter to predict progression may be appropriate.

Our results showed that the maximum aortic wall thickness of the affected aorta can predict progression of type B on initial CT. Acute IMH may be incompletely thrombosed and unstable, and small blood flow from the vasa vasorum may remain. We hypothesize that the thickness of IMH reflects instability of the false lumen and the aortic wall is exposed to stress from both true and false lumen like a classic dissection during the acute phase. Moreover, malnutrition of the aortic wall caused by stagnating or standing blood flow of the false lumen may damage the affected wall during both the acute and chronic phases.

Although the purpose of this study was to investigate predictors of progression with initial CT images, our results showed that a significant difference in disappearance of IMH on follow-up CT is seen. Nishigami et al[10] investigated how IMHs (including type A and B) change serially during a follow-up period with TEE. Their results showed that the cardiovascular event-free rate in disappearance of IMH is lower than that in persistent IMH. Their results and our results reveal that persistence of IMH can be a risk factor of progression during the follow-up period.

In this study, 14 of 15 patients showed increased maximum aortic diameter between 1 day and 24 months after the onset. In four of 15 patients, the affected aorta progressed to overt aortic dissection between 20 days and 36 months after the onset. These results suggest that type B IMH can progress not only during the acute phase but also during the chronic phase. A previous report suggested that aneurysm of the affected aorta with IMH can develop as a

late complication and grow faster than atherosclerotic aneurysm.[9] In IMH, both structural weakness and mechanical stress can cause aneurysm formation.[7,9] These effects may be conspicuous and continuous during the chronic phase. Therefore, our results suggest that a long-term follow-up study is also needed for type B IMH with a maximum aortic diameter of 40 mm or more or maximum aortic wall thickness of 10 mm or more.

CONCLUSION

This study shows that progression of the affected aorta in patients with type B IMH can be predicted with the maximum aortic diameter and maximum aortic wall thickness on initial CT. For type B IMH with a maximum aortic diameter of 40 mm or more or a maximum aortic wall thickness of 10 mm or more, careful follow-up studies must be necessitated.

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Please see related commentary by Dr Richard P. Cambria on pages 1295-6.