Prediction of Progression or Regression of Type A Aortic Intramural Hematoma by Computed Tomography

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Background—It has been reported that early surgery should be required for patients with type A aortic intramural hematoma (IMH) because it tends to develop classic aortic dissection or rupture. However, the anatomic features of type A IMH that develops dissection or rupture are unknown. The purpose of this study was to investigate the predictors of progression or regression of type A IMH by computed tomography (CT).

Methods and Results—Twenty-two consecutive patients with type A IMH were studied by serial CT images. Aortic diameter and aortic wall thickness of the ascending aorta were estimated in CT images at 3 levels on admission and at follow-up (mean 37 days). We defined patients who showed increased maximum aortic wall thickness in the follow-up CT (n=9) or died of rupture (n=1) as the progression group (n=10). The other 12 patients, who all showed decreased maximum wall thickness, were categorized as the regression group. In the progression group, the maximum aortic diameter in the initial CT was significantly greater than that in the regression group (55±6 vs 47±3 mm, P=0.001). A Cox regression analysis revealed that the maximum aortic diameter was the strongest predictor for progression of type A IMH. We considered the optimal cutoff value to be 50 mm for the maximum aortic diameter to predict progression (positive predictive value 83%, negative predictive value 100%).

Conclusions—Maximum aortic diameter estimated by the initial CT images is predictive for progression of type A IMH.

(Key Words: aorta • follow-up studies • risk factors • tomography)

Aortic dissections typically originate from a primary intimal tear, separation of the aortic wall components, and propagation of blood between wall layers. Noninvasive imaging techniques such as computed tomography (CT), magnetic resonance (MR) imaging, and transesophageal echocardiography (TEE) have recently been used to identify a variant of aortic dissection, aortic intramural hematoma (IMH).1–11 Aortic IMH appears to be a separate entity, characterized primarily by aortic hematoma without demonstrable intimal flap or penetrating ulceration.12–16

Studies to date have suggested that aortic IMH carries morbidity and mortality rates that are similar to those of classic aortic dissection.3,6–9,11,17 The site of IMH is an important parameter to determine prognosis. It has been reported that early surgery should be required for patients with IMH in the ascending aorta (type A) because it tends to develop classic overt dissection or rupture, although most patients with type B IMH can receive medical treatment.3,6–9,11 However, previous studies showed that resolution of IMH during treatment of hypertension occurred even in the ascending aorta.1,11,18–21 The anatomic characteristics of the affected ascending aorta in type A IMH that develops overt dissection or aortic enlargement are still unknown.

CT is widely used as the imaging modality of first choice for the assessment of thoracic aortic disease and can be used even in clinically unstable patients. In addition, various diameters of the aorta can be measured easily in serial CT images. 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 enlargement in patients with aortic dissection.22,23 However, there are few data about the predictor for progression or regression in patients with type A IMH.24 The purpose of this study was to investigate the predictors of progression of type A IMH in a large series of patients with the use of serial CT images.

Methods

Patient Characteristics

The study group consisted of 22 consecutively evaluated patients with the diagnosis of acute type A IMH without an intimal tear and unrelated to penetrating atherosclerotic ulcer. Diagnoses were established prospectively with CT scan immediately after the emergent admission at 2 hospitals (Kobe General Hospital and Saiseikai
Kumamoto Hospital) from March 1991 to December 1997. There were 8 men and 14 women between the ages of 48 and 80 years, with a mean of 65 years. All 22 patients had sudden back or chest pain within 3 days before admission. Patients with Marfan’s syndrome and traumatic IMH were excluded from this study. In 8 patients, IMH involved the ascending aorta alone and in 14 patients IMH involved both the ascending and the descending aorta. The initial diagnosis of IMH was confirmed in all cases with TEE on admission. In all 22 patients, TEE showed a longitudinally oriented crescent area within the thoracic aortic wall. Doppler changes in this area indicate absence of flowing blood. 4,9,23–30 IMH was defined as maximal crescent or circular thickening of the aortic wall >7 mm.4 Absence of dissection flap, intimal tear, or penetrating atherosclerotic ulcer was a prerequisite for diagnosis of IMH.10

All patients were admitted to 2 hospitals, with a mean interval of 1±1 days from the episode of the onset. Hypertension was present in all patients.

Treatment
Medical therapy was elected for all patients at the time of admission. We generally follow the blood pressure with an arterial line and monitor the ECG in the intensive care unit. Our initial therapeutic goal during the acute phase of IMH included the elimination of pain and the reduction of systolic blood pressure to 100 to 120 mm Hg. A calcium channel antagonist (nicardipine hydrochloride), nitrate (nitroglycerin), and β-blocker (propranolol) were administered intravenously to reduce blood pressure. Close clinical follow-up with transthoracic echocardiography (TTE), TEE, and CT was performed to minimize the risk of fatal complications. TTE was performed daily during the initial 5 days to monitor pericardial effusion and aortic regurgitation. Follow-up TEE was performed within 3 days after the admission. CT examination was generally performed at the first and third week after admission. Patients who demonstrated evidence of progression or dissection during the follow-up period were referred for surgical repair and underwent operation. Percardioctenesis was performed on admission in 4 patients with cardiac tamponade. These patients were treated medically after the pericardioctenesis.

Several antihypertensive drugs such as calcium channel antagonists, angiotensin-converting enzyme inhibitors, or β-blockers were administered orally during the course of hospitalization to achieve adequate blood pressure control (<120 mm Hg). After discharge, patients were followed up at regular intervals, and blood pressure was measured every 3 months with a standard bulk sphygmomanometer.

CT Analysis
IMH was defined by CT as a localized segmental and crescent high attenuation area along the aortic wall on noncontrast CT and relatively low attenuation area without enhancement on contrast-enhanced CT.1,31

The course of all 22 patients was followed up with CT examination. Twenty-one patients had the first routine follow-up CT examination within 3 weeks after the initial onset. In 3 patients, recurrence of chest pain or back pain or both resulted in repeat CT examination. Seventeen cases had another routine follow-up CT examination between 3 weeks and 3 months after the initial onset. All CT scans were obtained at 1-cm intervals from the aortic arch to the aortic bifurcation with and without the rapid intravenous bolus injection of 100 mL of contrast media. CT was performed with a model HSA-RP scanner (Kobe General Hospital) (GE Medical Systems) or TSX-0111A scanner (Saiseikai Kumamoto Hospital) (TOSHIBA). Ascending aortic images of CT were selected at 3 levels. The aorta at the level of the left or right main pulmonary artery was chosen as the median slice. The other 2 slices, which were superiorly and inferiorly adjacent to the median image, were also selected for evaluation. With the use of computerized planimetry, measurements were taken on the basis of the accompanying calibrated scales in the contrast-enhanced CT images. Major aortic diameter and minor aortic diameter, which were the longest and the shortest transverse of best-fit ellipses, the aortic wall thickness, and lumen diameter were measured in each of the slices (Figure 1). Maximum aortic diameter was defined as the largest diameter of all major and minor aortic diameters in all 3 slices. Wall thickness-to-lumen diameter ratio was calculated as the maximum wall thickness divided by the maximum aortic diameter.

To determine interobserver variability for these measurements, 20 studies were randomly selected and analyzed by 2 independent observers. To determine intraobserver variability, 20 studies were also repeated by the same observer. Interobserver and intraobserver variabilities for these measurements were 1.2% and 1.0%, respectively.

On the basis of the clinical outcome, the patients were divided into 2 groups: the progression group and the regression group. We defined patients who showed increased maximum aortic wall thickness in the follow-up CT images (n=9) or died of rupture (n=1) as the progression group (n=10). The other 12 patients, who all showed decreased maximum wall thickness in the follow-up CT images, were defined as the regression group.

Statistical Analysis
All values are expressed as mean±SD. Univariate analysis was performed on all clinical and morphological variables, with the χ² test used for categorical variables and the Student’s t test for continuous variables. Comparison of differences between admission and follow-up was done with Student’s paired t test. The Cox proportional hazards model was used to identify predominant predictors for progression of type A IMH throughout the follow-up period with the use of univariate and stepwise multivariate analyses (entry and removal thresholds, 0.05 and 0.1, respectively). In all tests, a value of P<0.05 was considered significant.

Results
Mean CT follow-up period was 37 days (range 7 to 113 days). There were no significant differences in CT follow-up period between the progression group and the regression group (27±19 vs 44±26 days, P=0.103). In the progression group, the maximum aortic wall thickness significantly increased in 9 patients from 14±5 to 21±7 mm (P=0.016), as shown in Table 1 and Figure 2, and 1 patient died of rupture of IMH. In this group, the maximum...
Aortic diameter also significantly increased from 55±6 to 63±9 mm (P=0.002). Six of these patients had overt aortic dissection. All patients in the progression group successfully underwent surgical repair after 40±32 days (mean±SD, range 7 to 94 days) from the onset except 1 patient, who declined operation and died.

In the regression group, the maximum aortic wall thickness significantly decreased from 9±3 to 4±4 mm (P=0.001), as shown in Table 1 and Figure 3. In this group, maximum aortic diameter also significantly decreased from 47±3 to 44±4 mm (P=0.007). In 6 of these patients, IMH of the ascending aorta disappeared.

**Clinical Predictors of Progression of Type A IMH**

Table 2 shows the result of the univariate analysis of the clinical variables. Age, sex, diabetes mellitus, smoking, location of IMH, moderate aortic regurgitation, cardiac tamponade, pericardial effusion, and pleural effusion were not significant univariate predictors of progression.

**Aortic Dimensions in Initial CT and Predictors of Progression of Type A IMH**

Mean and maximum aortic dimensions in the initial CT images and predictors of progression of type A IMH are shown in Table 3. In the progression group, the maximum aortic diameter in initial CT images was significantly greater than that in the regression group (55±6 vs 47±3 mm, P=0.001). The maximum aortic wall thickness in the initial CT images was also significantly greater than that in the regression group (14±5 vs 9±3 mm, P=0.007). There were no significant differences in the maximum and mean lumen diameter between the 2 groups.

Within the initial CT variables, maximum aortic diameter (P=0.001), maximum aortic wall thickness (P=0.007), mean major aortic diameter (P=0.002), mean minor aortic diameter (P=0.003), and mean wall thickness (P=0.005) were found to be significantly correlated with progression of type A IMH. To determine the independent predictors for progression of type A IMH throughout the follow-up period, forward stepwise Cox regression analysis was performed. The only significant predictor of the progression group was found to be the maximum aortic diameter in initial CT images (P=0.0012). We calculated an optimal cutoff value of the maximum aortic diameter to predict progression by maximizing (100-% false-positive-% false-negative). With this criterion, an optimal cutoff value of 50 mm was found, resulting in positive predictive and negative values of 83% and 100%, respectively.

**Discussion**

In this study we evaluated serial CT images of type A IMH and demonstrated that the maximum aortic diameter of the ascending aorta in the initial CT images was predictive of progression or regression of type A IMH.

IMH was first described in 1920 as “dissection without intimal tear” and was considered a distinct entity at necropsy. The cause of IMH was believed to be rupture of the vasa vasorum in the aorta resulting in hematoma formation.32 The presence of aortic IMH can weaken the medial layer and potentially increase the likelihood of a classic aortic dissec-

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**Table 1. Changes in Ascending Aortic Dimensions**

<table>
<thead>
<tr>
<th>Metric</th>
<th>Progression Group</th>
<th>Regression Group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time from onset, d (mean±SD)</td>
<td>1±2</td>
<td>1±1</td>
<td></td>
</tr>
<tr>
<td>Mean major aortic diameter, mm</td>
<td>52±6</td>
<td>45±3</td>
<td>0.001</td>
</tr>
<tr>
<td>Mean minor aortic diameter, mm</td>
<td>50±5</td>
<td>44±3</td>
<td>0.006</td>
</tr>
<tr>
<td>Mean aortic wall thickness, mm</td>
<td>13±4</td>
<td>8±2</td>
<td>0.017</td>
</tr>
<tr>
<td>Mean lumen diameter, mm</td>
<td>40±6</td>
<td>37±3</td>
<td>0.386</td>
</tr>
<tr>
<td>Maximum aortic diameter, mm</td>
<td>55±6</td>
<td>47±3</td>
<td>0.002</td>
</tr>
<tr>
<td>Maximum aortic wall thickness, mm</td>
<td>14±5</td>
<td>9±3</td>
<td>0.016</td>
</tr>
<tr>
<td>Maximum lumen diameter, mm</td>
<td>42±6</td>
<td>38±3</td>
<td>0.245</td>
</tr>
</tbody>
</table>

**Figure 2.** Graphs depict maximum aortic wall thickness (left) and maximum aortic diameter (right) of the progression group in CT images on admission and at follow-up. Mean values±SD on admission and follow-up are shown in the solid lines with bars.

**Figure 3.** Graphs depict maximum aortic wall thickness (left) and maximum aortic diameter (right) of the regression group in CT images on admission and at follow-up. Mean values±SD on admission and follow up are shown in the solid lines with bars.
It has been reported that type A IMH should require early surgery because it tends to develop classic overt dissection or rupture. However, the clinical data available so far are too limited to draw any conclusion. The previous studies reported that a formal distinction between type A and type B IMH might be justified with respect to both prognosis and treatment, and the site of IMH was an important parameter for determining prognosis. In the study by Robbins et al, all 3 patients with type A IMH ultimately underwent surgery. In the study by Mohr-Kahaly et al, 2 of 3 patients with type A IMH developed communicating dissection or outward rupture. However, in the study by Vilacosta et al, 3 of 8 patients with type A IMH showed favorable response to medical treatment. Similar clinical data were demonstrated in the previous reports. In addition, Sueyoshi et al reported that 7 of 13 patients with type A IMH had been doing well without surgical intervention. Their results were similar to our results. In our study, IMH regressed or disappeared in 12 (55%) of 22 patients, whereas 10 (45%) of 22 patients with type A IMH showed progression. All patients with progression of type A IMH showed enlargement of the affected aorta, and 6 of these patients had classic aortic dissection. The differences in frequencies of progression of type A IMH between the previous early studies and our study may result from differences in medical treatment or the imaging techniques used to establish the diagnosis of IMH. The patients in our investigation had close surveillance, including initial intensive care unit monitoring, aggressive blood pressure control, and frequent serial follow-up imaging studies. Furthermore, absence of dissection was documented in our study with TEE in all patients. Thus it is unclear whether those patients in the previous early studies are directly comparable to the patients that we have reported.

In the current study, a Cox regression analysis revealed that the maximum aortic diameter in the initial CT images was the only significant predictor of progression of type A IMH. Furthermore, with a cutoff value of 50 mm in the maximum aortic diameter, the positive and negative predictive values for progression of IMH were 83% and 100%, respectively. This suggests that patients with type A IMH can be treated medically without surgery when the ascending aortic diameter is <50 mm and that surgical repair may be necessary when the ascending aortic diameter is ≥50 mm. This finding is in concordance with the previous study by Ide et al, who reported that transition to a classic dissection was found exclusively in patients with a markedly dilated ascending aorta.

### Table 2. Correlation of Clinical Characteristics With Progression of Type A IMH

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Progression Group (n=10)</th>
<th>Regression Group (n=12)</th>
<th>χ² or t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>65±11</td>
<td>63±11</td>
<td>0.535</td>
<td>0.599</td>
</tr>
<tr>
<td>Sex, male/female</td>
<td>4/6</td>
<td>4/8</td>
<td>0.015</td>
<td>0.903</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>10 (100)</td>
<td>12 (100)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>1 (10)</td>
<td>3 (25)</td>
<td>0.125</td>
<td>0.724</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>2 (20)</td>
<td>6 (50)</td>
<td>1.023</td>
<td>0.312</td>
</tr>
<tr>
<td>Location of aortic abnormality, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Involving the aortic arch</td>
<td>6 (60)</td>
<td>10 (83)</td>
<td>0.552</td>
<td>0.458</td>
</tr>
<tr>
<td>Involving the descending aorta</td>
<td>5 (50)</td>
<td>9 (75)</td>
<td>0.591</td>
<td>0.442</td>
</tr>
<tr>
<td>Complications, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic regurgitation (&gt;moderate)</td>
<td>2 (20)</td>
<td>0 (0)</td>
<td>0.775</td>
<td>0.379</td>
</tr>
<tr>
<td>Cardiac tamponade</td>
<td>2 (20)</td>
<td>2 (17)</td>
<td>0.125</td>
<td>0.724</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>4 (40)</td>
<td>5 (42)</td>
<td>0.127</td>
<td>0.722</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>8 (80)</td>
<td>10 (83)</td>
<td>0.125</td>
<td>0.724</td>
</tr>
</tbody>
</table>

### Table 3. Univariate and Multivariate CT predictors of Progression of Type A IMH

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Progression Group</th>
<th>Regression Group</th>
<th>t</th>
<th>P</th>
<th>Odds Ratio</th>
<th>95% Confidence Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean major aortic diameter, mm</td>
<td>52±6</td>
<td>45±3</td>
<td>3.570</td>
<td>0.002</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean minor aortic diameter, mm</td>
<td>50±5</td>
<td>44±3</td>
<td>3.403</td>
<td>0.003</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean aortic wall thickness, mm</td>
<td>13±4</td>
<td>8±2</td>
<td>3.204</td>
<td>0.005</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean lumen diameter, mm</td>
<td>40±6</td>
<td>37±3</td>
<td>1.393</td>
<td>0.179</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximum aortic diameter, mm</td>
<td>55±6</td>
<td>47±3</td>
<td>3.965</td>
<td>0.001</td>
<td>0.0012</td>
<td>1.205</td>
</tr>
<tr>
<td>Maximum aortic wall thickness, mm</td>
<td>14±5</td>
<td>9±3</td>
<td>2.990</td>
<td>0.007</td>
<td>1.076</td>
<td>1.349</td>
</tr>
<tr>
<td>Maximum lumen diameter, mm</td>
<td>42±6</td>
<td>38±3</td>
<td>1.689</td>
<td>0.107</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wall thickness/lumen diameter</td>
<td>0.37±0.20</td>
<td>0.25±0.08</td>
<td>2.019</td>
<td>0.057</td>
<td></td>
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</table>
aorta of >50 mm in diameter. However, their finding, based on relatively small numbers of type A IMH patients, was not strong enough to offer a distinct prediction of progression or regression of type A IMH.

Previous studies suggested that hematoma formation within the media of the aortic wall caused a structural weakness of the media, and both structural weakness of the media and mechanical stress might cause fusiform aneurysm or classic aortic dissection with an intimal flap. With respect to aortic enlargement, there are a few studies addressing the prediction of aortic enlargement throughout the entire follow-up period in classic aortic type B dissection. Masuda et al referred to maximum diameter of the dissected aorta during the acute phase as a risk factor for survival during the chronic phase. Kato et al reported that aortic enlargement in chronic type B dissection can be predicted by using 2 factors obtained at the onset of dissection: maximum diameter of the dissected aorta and location of the primary entry site. They suggested that the enlargement of type B dissection was closely correlated with wall stress on the dissected aorta. However, there are anatomic differences between type A IMH and classic type B dissection, and wall stress is related to aortic lumen diameter in IMH. Considering the results that there were no significant differences in the maximum and mean lumen diameters between the progression group and the regression group in this study, some other factors such as distensibility may play an important role in progression or regression of type A IMH.

It is difficult to clarify the mechanism of progression or regression of type A IMH because of difficulty in detecting pathological changes in hematoma with the use of CT and TEE. Other imaging modalities, such as MR imaging, may have a possibility to detect pathological changes. MR imaging not only visualizes blood sequestration but also allows assessment of the age of the hematoma based on the formation of methemoglobin. Nienaber et al reported that subacute IMH revealed a high signal intensity on both T1- and T2- weighted images caused by methemoglobin formation. Murray et al reported that MR images of patients who had early subacute complications showed signal intensity changes of hematoma that were consistent with recurrent bleeding. Although MR imaging of acutely ill patients can be problematic because of life-support and monitoring equipment, close serial follow-up of IMH with MR imaging may be useful to clarify what happens to the hematoma.

Surprisingly, our results do not suggest an increased risk associated with pericardial effusion or cardiac tamponade. In the setting of classic aortic dissection, cardiac tamponade is the most common cause of death. Isselbacher et al reported that cardiac tamponade was associated with an early mortality rate of 60%. They also suggested that pericardiocentesis in treating cardiac tamponade might be harmful rather than beneficial. However, few data are available for the treatment of cardiac tamponade in type A IMH. In this study, 4 patients underwent successful pericardiocentesis with neither death nor progression of type A IMH immediately after the pericardiocentesis. Although the number of patients in this study is small, our results raise the possibility that pericardiocentesis is not necessarily harmful for type A IMH patients with cardiac tamponade.

There are several potential limitations in our study. First, pathological confirmation of IMH was not available in all cases. Although diagnosis was supported with other imaging modalities, it is possible that small intimal tears could have been missed with all imaging modalities. Second, we did not take into account the variations of normal aortic dimensions. The age-related normal values for the aortic dimensions may have to be taken into account. Third, 4 patients received medical therapy after the pericardiocentesis. Although no death occurred, the numbers of patients who underwent pericardiocentesis in this study were small enough, and most physicians and surgeons would recommend surgery in such patients. Considering no operative death in the surgical group in this study, surgery in patients with cardiac tamponade may be a safer route to follow.

Conclusions

Progression of type A IMH can be predicted by the maximum aortic diameter of the affected ascending aorta. Further studies involving larger numbers of patients in a multicenter setting may be needed to establish therapeutic strategy of type A IMH. Nevertheless, this study might provide a new direction for the continued discussion of treatment of patients with acute type A IMH.

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References

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