Usefulness of the Initial Noninvasive Imaging Study to Predict the Adverse Outcomes in the Medical Treatment of Acute Type A Aortic Intramural Hematoma

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Background—There have been contradictory reports about the outcomes of medically treated patients with type A aortic intramural hematoma (AIH), and it is not certain if the initial noninvasive imaging studies can provide any useful predictors for the adverse outcomes.

Methods and Results—Imaging studies and clinical outcomes of 25 consecutive patients with type A AIH who initially received medical treatment were analyzed retrospectively. Adverse outcomes (death, surgery, and development of dissection) occurred in 9 patients (group A), whereas the other 16 patients showed an uneventful course (group B). The hematoma thickness (14±4 versus 8±4 mm, P<0.005) and hematoma area (988±316 versus 555±352 mm², P<0.01) in the imaging study performed ≤48 hours after onset of initial symptoms were significantly larger in group A; maximal aortic diameter (53±6 versus 48±8 mm, P=0.10) and aortic cross-sectional area (2247±501 versus 1809±626 mm², P=0.09) were also somewhat larger in group A. The hematoma thickness was the only independent predictor for the adverse outcomes by stepwise multiple logistic regression analysis (odds ratio 1.41, 95% confidence interval 1.07 to 1.86, P<0.05). Hematoma thickness ≥11 mm predicted the adverse outcomes with sensitivity 89% and specificity 69%. No one with hemodynamically stable initial condition and the hematoma thickness <11 mm experienced the adverse outcomes.

Conclusion—Noninvasive imaging study provides important prognostic information in the medical treatment of acute type A AIH, and initial hematoma thickness seems to be the best index for predicting adverse clinical outcome. (Circulation. 2003;108[suppl II]:II-324-II-328.)

Key Words: aortic dissection • aortic intramural hematoma • imaging • prognosis

Acute type A aortic intramural hematoma (AIH) was initially considered as a precursor of aortic dissection (AD), and early surgical intervention was recommended due to very high mortality with medical treatment. However, there are some reports showing relatively benign clinical course with medical treatment and as substantial proportion of the patients showed complete resorption of the hematoma with medical treatment, aggressive medical treatment with timed surgery only in cases with complications was suggested as a rational strategy. Considering the fact that progression of AIH to overt AD is quite unpredictable, it would be very helpful to establish sensitive clinical predictors of the adverse outcomes with medical treatment. Therefore, we retrospectively analyzed imaging studies and clinical outcomes of patients with acute type A AIH to test if the initial noninvasive imaging studies can provide any useful predictors of the adverse outcomes.

Methods
From April 1993 to March 2001, routine clinical and diagnostic evaluation consisting of random combinations of contrast-enhanced radiograph computed tomography (CT), magnetic resonance imaging (MRI), and transesophageal echocardiography (TEE) identified 33 patients as having acute type A AIH in our institution (a part of these patients were included in our previous report). A definite crescentic or circular high attenuation area along the aortic wall without enhancement after contrast injection in CT and regional thickening of the aortic wall >7 mm in TEE without evidence of flow communication through intimal flap were considered diagnostic of AIH. Among 33 patients, 1 patient who did not perform CT in acute phase and another 1 patient who showed an ulcer-like projection into the hematoma space on the initial CT were excluded. Figure 1 summarizes the therapeutic strategy for the rest 31 patients with type A AIH. Until March of 1999, emergent surgery was recommended as a first choice of therapy, and 6 patients underwent surgery with operative mortality of 17% (1/6); however, the other 13 patients received initial medical treatment only as surgery was...
refused by the patients or was not feasible due to other combined medical illnesses such as malignancy, asthma and stroke. Hospital mortality of these patients was significantly lower than that of medically treated patients with typical proximal AD and some patients showed complete resorption of the hematoma. Therefore, from April of 1999, initial medical treatment with timed surgical intervention in cases with complications on follow-up imaging study has been recommended for 11 consecutive hemodynamically stable patients with acute proximal AIH; during this time, 1 patient was in shock at the initial presentation and died during preparation for emergent surgery within 24 hours after the symptom onset. As a whole, 25 patients received initial medical treatment, and these 25 patients (19 women) with mean age of 67 years (48 to 87 years) were the subjects of this study.

A dedicated specific protocol of CT scans was used. All CT scans were obtained by helical scanning at 1-cm intervals with and without the rapid intravenous injection of 100 to 150 mL of contrast media at 2.5 to 3.0 mL/sec, and multidetector scanning has been used from 2000. The section thickness was 5 to 10 mm and scan delay was 25 to 30 seconds.

Using initial CT performed ≤48 hours after onset of initial symptoms, a representative aortic segment showing the maximal thickness of the hematoma was selected among the sections near the level of bifurcation of left and right pulmonary arteries for measurement of the maximal aortic diameter, hematoma thickness, aortic cross-sectional area, lumen area, and hematoma area using a computerized digitizer. All initial CT scans showed high attenuation hematoma in noncontrast scans, which finding was compatible with acute hematoma. Initial TEE of 24 patients was reviewed again to determine the presence of echo-free space, which was defined as crescentic or ovoid echo-lucent area within abnormally thickened aortic wall (Figure 2).13

Clinical and imaging follow-up data of the patients who received initial medical treatment were reviewed, and the clinical adverse outcomes with medical treatment were defined as death, aortic surgery, or development of AD in the ascending aorta. Development of AD was defined as appearance of typical ‘double-channel aorta’ with flow communication between true and false lumen through the intimal tear (Figure 3B, right). Remnant aortic wall thickness less than 3 mm was used as a criterion for complete resorption of AIH (Figure 3A, right).

Numerical values are expressed as mean ± SD. Statistical analysis of difference between groups was assessed by the Student unpaired t-test. The chi-square test and Fischer’s exact test were used to compare frequency ratios between groups. Multiple stepwise logistic regression analysis was used to identify independent predictors for the adverse outcomes. A receiver-operating characteristics (ROC) curve analysis was performed to determine the best cutoff value for predicting the adverse outcomes. Kaplan-Meier analysis was used to determine event-free survival rate, and the difference between groups was analyzed by log-rank test. A probability value <0.05 was considered statistically significant.

Results
Among the patients with initial medical management (n=25), there was one in-hospital mortality. This female patient was presented with shock and recovered with cardiopulmonary resuscitation. She was decided to undergo urgent surgery, but she finally died before the surgery was performed. The initial imaging studies demonstrated AIH involving only the ascending aorta with pleural and pericardial effusion. The initial maximal aortic diameter and hematoma thickness were 40 mm and 7 mm respectively.

In the other 24 patients with hemodynamically stable clinical presentation, no patient died during hospital admission, and clinical and imaging follow-up was possible in all patients with a mean duration of 9±12 months. AD developed in 7 patients 2±2 months after the symptom onset (17 days to 8 months), and 1 patient underwent surgery 25 days after the initial symptom onset due to the progressive increase of pleural and pericardial effusion. Among 7 patients with newly developed AD, 4 had an overt dissection involving the whole ascending aorta and 3 had a focal dissection in localized segment of the ascending aorta. Among 4 patients with overt AD, 2 patients underwent surgery; one refused surgery and surgery was contraindicated in the other one because of intractable asthma. Late death occurred in 1 patient because of cerebrovascular accident after surgery and another 1 in whom surgery was contraindicated.
As a whole, the adverse outcomes developed in 9 patients (9/25, 36%), and they were classified as group A. In the remaining 16 patients, any adverse outcomes did not occur during follow-up period of 12/11006-14 months, and they were classified as group B; among them, 13 patients (81%) exhibited complete resorption of the hematoma on follow-up imaging studies.

Table 1 summarizes the baseline clinical characteristics. The initial hematoma thickness and hematoma area in the imaging study performed 48 hours after onset of initial symptoms were significantly larger in group A. Although there was no statistical significance, the maximal aortic diameter and aortic cross-sectional area tended to be higher in group A. Prevalence of echo-free space on the initial TEE and other clinical characteristics were not significantly different between the 2 groups. Initial hematoma thickness was the only independent predictor for the adverse outcomes by stepwise multiple logistic regression analysis (odds ratio 1.41, 95% confidence interval 1.07 to 1.86, \( P < 0.05 \)).

The area under the curve on ROC curve of initial hematoma thickness (0.85) was larger than that of the maximal aortic diameter (0.73) for predicting development of adverse events (Figure 4). The sensitivity and specificity of hematoma thickness \( \geq 11 \) mm to predict the adverse outcomes were 89% (8/13) and 92% (11/12) respectively. No one with the initial thickness \(< 11 \) mm experienced the adverse outcomes, except 1 patient who was initially in shock. The initial maximal aortic diameter \( \geq 48 \) mm had the same predictive values as initial hematoma thickness (Table 2). The event-free survival rate at 12 months was significantly higher in the patients with initial hematoma thickness \( < 11 \) mm than those with the thickness \( \geq 11 \) mm (92±8 versus 32±14%, \( P < 0.05 \)) (Figure 5A); patients with the maximal aortic diameter \( < 48 \) mm showed significantly lower event-free survival rate (Figure 5B).

**Discussion**

In this study, we have confirmed that the initial noninvasive imaging study can provide very important prognostic information in medically treated patients with acute type A AIH and initial hematoma thickness is the best predictor of the adverse outcomes with medical treatment. As in type B

| TABLE 1. Comparisons of Baseline Characteristics and Initial Measurements Between the Patients With Adverse Outcomes (Group A) and Those Without (Group B) |
|----------------------------------|------------------|------------------|----------|
| Age (years)                      | Group A (N=9)    | Group B (N=16)   | \( P \)  |
|                                 | 68±11            | 66±10            | 0.72     |
| Sex (male/female)               | 1/8              | 5/11             | 0.36     |
| Hypertension                    | 8 (89%)          | 12 (75%)         | 0.62     |
| Diabetes mellitus               | 1 (11%)          | 1 (6%)           | 1.0      |
| Smoking                         | 2 (22%)          | 8 (50%)          | 0.17     |
| DeBakey type (I/II)             | 6/3              | 15/1             | 0.12     |
| Pleural effusion                | 6 (67%)          | 12 (75%)         | 0.67     |
| Pericardial effusion            | 7 (78%)          | 12 (75%)         | 1.0      |
| Cardiac tamponade               | 0 (0%)           | 2 (13%)          | 0.52     |
| Aortic regurgitation=moderate    | 1 (13%)          | 1 (7%)           | 0.67     |
| Maximal aortic diameter (mm)    | 53±6             | 48±8             | 0.10     |
| Hematoma thickness (mm)         | 14±4             | 8±4              | <0.005   |
| Aortic cross-sectional area (mm²)| 2247±501         | 1809±626         | 0.09     |
| Lumen area (mm²)                | 1259±371         | 1254±438         | 0.97     |
| Hematoma area (mm²)             | 988±316          | 555±352          | <0.01    |
| Echo-free space                 | 5/8 (63%)        | 7/16 (44%)       | 0.67     |

As a whole, the adverse outcomes developed in 9 patients (9/25, 36%), and they were classified as group A. In the remaining 16 patients, any adverse outcomes did not occur during follow-up period of 12±14 months, and they were classified as group B; among them, 13 patients (81%) exhibited complete resorption of the hematoma on follow-up imaging studies.

**TABLE 2. Diagnostic Accuracy of the Initial Hematoma Thickness and Maximal Aortic Diameter to Predict the Adverse Outcomes in Medically Treated Patients With Type A Aortic Intramural Hematoma**

<table>
<thead>
<tr>
<th>Adverse Outcomes (+)</th>
<th>Adverse Outcomes (−)</th>
</tr>
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<tbody>
<tr>
<td>(n=9)</td>
<td>(n=16)</td>
</tr>
<tr>
<td>Hematoma thickness( \geq 11 ) mm</td>
<td>8 (89%)</td>
</tr>
<tr>
<td>Hematoma thickness(&lt; 11 ) mm</td>
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<tr>
<td>Aortic diameter( \geq 48 ) mm</td>
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<td>1 (11%)</td>
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Hematoma thickness\( \geq 11 \) mm; sensitivity (89%), specificity (69%); Aortic diameter\( \geq 48 \) mm; sensitivity (89%), specificity (69%).
AIH,º presence of echo-free space in the hematoma of ascending aorta on initial TEE was not the predictor of the adverse outcomes. Although this was a retrospective observational study, this information might be useful in deciding the treatment strategy for each patient.

AIH has been described as a precursor of overt AD; however, there are few data about the clinical predictor for the development of AD in type A AIH. Nishigami et al reported that persistence of AIH more than 1 month after the symptom onset and the maximum aortic diameter >45 mm were risk factors associated with development of AD.º However, their data have some limitations for being applied to the patients with type A AIH, as they included both type A and B AIH and only small numbers of patients with type A AIH (n=8) were included in their series of 44 patients. Kaji et al reported that initial maximal aortic diameter ≥50 mm was useful for predicting progression of the hematoma with negative predictive value of 100% in patients with type A AIH.º Although maximal aortic diameter was also important factor determining the event-free survival in our study, the initial hematoma thickness was somewhat better in predicting the adverse outcomes. Difference in the study protocols may explain the different conclusions. In Kaji’s study, the ‘progression’ was defined as increased maximum aortic wall thickness in the follow-up CT images (n=8) and death due to rupture (n=1). Instead of predictors for the ‘progression’ in the follow-up image study, we investigated the predictors for the clinical adverse outcomes including development of AD, surgery and death, which are harder event than simple increase of maximum wall thickness and would have more clinical implications.

Recently Ganaha et al demonstrated that AIH with penetrating atherosclerotic ulcer was associated with a progressive disease course.¹⁴ However, as they mentioned, penetrating atherosclerotic ulcer are mainly located in the descending aorta, and it can be rarely found in the ascending aorta, which implies that this finding may not be a useful predictor in type A AIH. Although there was no typical atherosclerotic ulcer in the ascending aorta in our series of patients, 2 patients who showed ulcer-like projection on the follow-up imaging studies finally developed focal AD later. The clinical significance of such an ulcer-like projection needs to be investigated with further studies.

The mechanism of progression or resorption of AIH is still elusive. As Kaji’s report, in our study, maximal aortic diameter could be used as a good prognostic index. The best cutoff values were quite similar between Kaji’s and our report. It is well known that aortic diameter is an important determinant of aortic wall stress and there are some investigations showing strong association between the maximal aortic diameter and progressive enlargement of the aorta in patients with typical AD.¹⁵,¹⁶ However, simple increase of aortic wall stress related with increased aortic diameter cannot explain the mechanism of progression in AIH, as the inner aortic luminal diameter or area, a real determinant of aortic wall stress related with increased aortic diameter and progressive enlargement of the aorta in patients with type AD.¹⁵,¹⁶

Our study has some limitations. The best cutoff value of the initial hematoma thickness for patients with type A AIH was 11 mm in our study, but it was not tested for patients with type B AIH. As the affected site of AIH is the most important parameter determining the prognosis in patients with acute aortic syndrome, different clinical factors can exert more powerful impact on the prognosis in patients with acute aortic syndrome. Eventually, all patients with type A AIH who had aortic rupture was very low according to the recent Kaji’s report,¹¹ this catastrophic clinical event seems to occur relatively frequently in the western countries.¹⁸ Longer follow-up observation of more patients is needed to assess the real impact of the initial hematoma thickness or the maximal aortic diameter on the natural history of proximal AIH. In our series, we also observed that focal AD developed late after 8 months in 1 patient, although other 6 patients showed AD within 3 months after the symptom onset. In group B, we’ve
failed to demonstrate complete resorption of the hematoma in 3 patients (19%); imaging follow-up period of 2 patients were less than 2 months and that of the other 1 patient was 18 months. Although they were clinically stable, it is evident that 2 month is not long enough to rule out the possibility of development of adverse outcomes.

Although our data showed that the initial noninvasive imaging study can provide useful indices to identify patients at high risk during medical treatment of type A AIH, other clinical variables are also important predictors, as was reported in patients with acute type A AD.17 In our series of type A AIH, the hematoma thickness of one patient who was in shock at the initial presentation and expired before emergent surgery was only 7 mm (less than 11 mm), and we believe that hemodynamic stability at the initial presentation should take priority in determining the initial treatment strategy over initial hematoma thickness on various imaging studies. Based on our data, emergent surgery should be the only treatment option for hemodynamically unstable patients with acute type A AIH. This is important as there is a report showing higher incidence of aortic rupture on hospital admission in patients with AIH compared with those with typical AD.18 For hemodynamically stable patients, the initial hematoma thickness measured by non-invasive imaging studies can provide very useful prognostic information; if hematoma thickness was <11 mm, successful medical treatment might be anticipated because the sensitivity and negative predictive value in predicting the adverse outcomes for these selected patients were both 100%. However, as the chance of adverse outcomes increases dramatically in case of hematoma thickness ≥11 mm, even in the initially stable patients, close monitoring is absolutely necessary with consideration of surgical intervention. Further study is still needed for determination of the optimal timing of surgery in these selected patients.

References
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