Long-Term Prognosis of Patients With Type B Aortic Intramural Hematoma

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Background—The long-term clinical course of patients with type B aortic intramural hematoma (IMH) and predictors for progression remains unknown. The difference of aortic pathology may have a different impact on clinical course compared with classic aortic dissection (AD). The purpose of this study was to investigate long-term clinical course and predictors of progression in patients with type B IMH.

Methods and Results—Clinical data were compared retrospectively between 53 patients with acute type B IMH (IMH group) and 57 patients with acute type B AD (AD group). All patients were treated initially with medical therapy. Two patients in IMH group and 14 patients in AD group underwent surgical repair because of aortic enlargement. The in-hospital mortality rate in IMH group was significantly lower than that in AD group (0% and 14%, P=0.006). Mean follow-up periods were 53±43 months, which revealed 3 and 5 late deaths, respectively. Eleven patients with IMH showed progression (development of aortic dissection or aortic enlargement) in follow-up imaging study. The actuarial survival rates in IMH group were 100%, 97%, and 97% at 1, 2, and 5 years, which were significantly higher than those in AD group (83%, 79%, and 79%) (P=0.009). Multivariate analysis identified age >70 years and new appearance of an ulcerlike projection as the strongest predictors of progression in patients with IMH.

Conclusions—Patients with type B IMH have better long-term prognosis than patients with AD. Older age and appearance of an ulcerlike projection are predictive for progression in patients with type B IMH. (Circulation. 2003;108[suppl II]:II-307-II-311.)

Key Words: aorta ■ follow-up studies ■ mortality ■ prognosis ■ survival

With the use of noninvasive imaging techniques, aortic intramural hematoma (IMH) has been recognized as a form of aortic dissection (AD), characterized primarily by aortic wall hematoma without demonstrable intimal flap, intimal tear and direct flow communication. IMH may cause a potentially catastrophic clinical events, including the occurrence of overt aortic dissection and the rupture of aorta.

Studies to date have suggested that patients with distal IMH involving the descending aorta (Stanford type B) have a favorable short-term prognosis. Song et al reported that absence of persistent flow communication in the false lumen resulted in a favorable remodeling process in IMH affecting distal descending aorta. The difference of aortic pathology may have a different impact on clinical course. However, it has been reported that even type B IMH could progress to overt dissection or aortic rupture. There is considerable controversy surrounding its prognosis and treatment and the long-term clinical course of patients with type B IMH remains unknown. In addition, predictors of progression in patients with type B IMH are not well investigated. The purpose of this study was to investigate long-term clinical course and predictors for progression in patients with type B IMH.

Methods

Patient Characteristics
From 1988 to 2000, 53 patients with acute type B IMH (IMH group) and 57 patients with acute type B AD (AD group) were admitted to our institutions within two days from the onset. The diagnosis was confirmed by clinical and diagnostic evaluations consisting of combinations of contrast-enhanced computed tomography (CT), magnetic resonance imaging (MRI), transesophageal echocardiography (TEE), and aortography. Patients with chronic AD or IMH were excluded. Typical double-channel aorta with dissecting membrane or intimal tear was an imaging criterion for diagnosis of AD. Regional thickening of the aortic wall >7 mm in a circular or crescent shape in TEE and a crescentic or circular high attenuation area along the aortic wall without enhancement after a contrast injection in the CT and MRI were considered diagnostic for IMH. Absence of dissection flap or intimal tear was also a prerequisite for diagnosis of IMH.

Treatment All patients were treated initially with medical therapy in both groups. Our initial therapeutic goal during the acute phase included...
the elimination of pain and the reduction of systolic blood pressure to 100 to 120 mm Hg. CT or TEE was repeated once a week during the acute stage. CT scans were then obtained twice or three times a year and at the onset of any new symptoms suggesting complications during the follow-up period. Patients who demonstrated aortic rupture or aortic enlargement (maximum diameter of the affected aorta ≥60 mm, or rapid enlargement of the affected aorta or ulcerlike lesion) during the follow-up period were referred for surgical repair and underwent urgent operation in both groups.

For all patients in both AD and IMH groups, several antihypertensive drugs such as calcium-channel antagonists, angiotensin-converting enzyme inhibitors, or beta blockers were administered orally during the course of hospitalization to achieve adequate blood pressure control.

The remodeling or healing process was assessed by comparing the initial and follow-up imaging studies in IMH group. Progression was defined as development of aortic dissection (development with typical "double-channel aorta" with intimal flap), increased hematoma thickness or aortic enlargement. On the other hand, regression was defined as decreased hematoma thickness or disappearance of abnormal wall thickening. Aortic enlargement with decreased hematoma thickness was regarded as progression. An ulcerlike projection (ULP; ulcerlike lesion) was defined as a localized blood-filled pouch protruding into the thrombosed lumen of the aorta.\textsuperscript{13} It showed the same degree of contrast enhancement as the aortic lumen on postcontrast CT scans.

Ten variables were tested separately for prediction of progression (Table 4). We assessed age at the time of initial diagnosis, sex, presence of chronic hypertension, presence of diabetes mellitus, smoking history and previous cerebrovascular disease. The maximum aortic diameter and aortic wall thickness were measured at the site of IMH appearance on initial CT images. Involvement of abdominal aorta was also assessed on initial CT images. Finally, new appearance of ULP was evaluated on CT images in the acute stage.

**Statistical Analysis**

All values are expressed as mean ± 1 SD except for survival rates. Survival analysis was performed with Kaplan-Meier analysis and differences in survival between groups were examined with the log-rank test. Variability of survival rate was expressed as ± 1 SEM. Univariate analysis was performed on categorical variables with the chi-square analysis or Fisher’s exact test and unpaired Student’s t-test for continuous variables. Cox proportional-hazards model was used to identify predominant predictors for progression of type B IMH throughout follow-up period using stepwise multivariate analyses (entry and removal thresholds, 0.05 and 0.1, respectively). A probability value <0.05 was considered statistically significant.

**Results**

Table 1 summarizes the clinical features of all patients. The prevalence of hypertension, diabetes mellitus, hyperlipidemia, history of smoking, cerebrovascular disease, ischemic heart disease, and hemodialysis did not show any significant difference between two groups. However, involvement of abdominal aorta was significantly more frequent in AD group than in IMH group ($P=0.0004$). As for complications, the incidence of renal ischemia and leg ischemia were significantly higher in AD group than in IMH group.

In AD group, 14 patients underwent emergent or urgent surgical repair 35±28 days after the onset (graft replacement of descending aorta). On the other hand, 2 patients underwent urgent surgical repair 6 and 65 days after the onset because of impending rupture or aortic enlargement in IMH. Graft replacement of descending aorta was performed with complete resection of the IMH in one patient. In the other patient, the IMH involving the arch and the descending aorta was partially resected and graft replacement of total arch and proximal descending aorta was performed under selective cerebral perfusion. Actuarial freedom estimates from aortic operation in IMH group were 98±2%, 96±3%, and 96±3% at 1, 6, and 12 months, which were significantly higher than those in AD group (89±4%, 73±6%, and 73±6%, respectively) ($P=0.001$). There were 4 operative deaths: 0 (0%) in IMH group and 4 (29%) in AD group ($P=0.999$). The causes

Figure 1. Complete resolution of hematoma in a patient with type B aortic intramural hematoma. Initial computed tomography showed characteristic crescent wall thickening in the descending aorta (A, B). One year after the onset, follow-up study showed complete resolution of hematoma (C, D).

Figure 2. Progression to overt aortic dissection in a patient with type B aortic intramural hematoma. Initial computed tomography showed characteristic crescent wall thickening in the descending aorta (A). One month after the onset, follow-up study revealed development of localized aortic dissection (B).
of death were: complications of uncontrollable bleeding in 1, and multiorgan failure in 3.

There were no early deaths in IMH group and 8 deaths in AD group: of these, 4 patients died after surgery, 1 patient died of rupture and 3 patients died of malperfusion-related complications. The overall in-hospital mortality rate of the patients in IMH group was 0%, which was significantly lower than that of patients in AD group (14%, \( P = 0.006 \)). Table 2 shows the follow-up periods for both groups and the cause of late deaths. There were 3 late death in IMH group and 5 late deaths in AD group (\( P = 0.476 \)). In IMH group, 2 patients died of cancer and 1 patient died of pneumonia. The actuarial survival rates in IMH group were 100%, 97 ± 3%, and 97 ± 3% at 1, 2, and 5 years (Figure 3), which were significantly higher than those in AD group (83 ± 5%, 79 ± 6%, and 79 ± 6%, respectively) (\( P = 0.009 \)).

In IMH group, follow-up imaging study could be obtained in 47 patients. Table 3 shows the results of follow-up imaging studies. Thirty-six patients showed regression of IMH. The remaining 11 patients showed progression of IMH. ULPs were newly identified during the hospital course in 16 (34%) of the 47 patients with IMH. In 9 (56%) of the 16 patients with new development of ULP, projections progressed to aortic enlargement or overt dissection. Whereas, projections disappeared in 4 patients and remained unchanged in 3 patients.

Table 4 and 5 show the results of univariate and multivariable analysis for predictors of progression in patients with type B IMH. Age > 70 years, new appearance of ULP, and aortic diameter were the significant predictors with the use of univariate analysis. With the use of multivariate Cox regression analysis, the strongest predictors of progression in patients with type B IMH were age > 70 years and new appearance of ULP.

### Discussion

The main findings of this study was as follows: (1) Patients with type B IMH have different clinical features and better long-term prognosis than patients with type B AD. (2) New
appearance of ULP and age >70 years were predictive of progression in patients with type B IMH.

Robbins et al\(^2\) first reported that patients with IMH involving the descending thoracic aorta could probably be treated conservatively but require antihypertensive therapy and serial aortic imaging surveillance. Vilacosta et al\(^14\) reported that one patient with type B IMH died from aortic rupture, whereas the remaining 6 patients did well during follow-up. Similar clinical data were demonstrated in the previous reports. Shimizu et al\(^8\) reported that in-hospital mortality in patients with type B IMH was 5%. Song et al\(^10\) reported that in-hospital mortality was 1% and the 3-year survival rate was 87% in patients with type B IMH. Their results were similar to our results. However, Tittle et al\(^9\) reported that 3 of 8 patients with IMH involving descending aorta had aortic rupture at admission and 2 patients underwent operation due to aortic enlargement. Considerable controversy surrounding its prognosis and treatment has been existed. In this study, in-hospital mortality rate in patients with IMH was 0% and actuarial 5-year survival rate was 97% with initial medical therapy. Considering both low in-hospital mortality and good long-term prognosis, it seems likely that supportive medical therapy with frequent follow-up imaging studies and timed surgical repair may be a reasonable option as the initial treatment in patients with type B IMH.

In previous clinical studies on patients with classic AD, persistent flow communication in the false lumen has been reported as one of the important variables determining long-term morbidity and mortality.\(^15\) Song et al\(^11\) reported that disappearance of abnormal wall thickening with complete restoration of the aorta occurred in 70% patients with IMH, which was significantly more frequent than in AD group. Thus, they concluded that absence of persistent flow communication in the false lumen resulted in a favorable remodeling process in IMH affecting distal descending aorta. In this study, 26 patients with IMH showed disappearance of hematoma in the descending aorta and none of these patients died in the follow-up periods. In addition, no patient died in IMH group, whereas 6 patients died in AD group because of aortic rupture or post-operative complication for aortic enlargement. Therefore, it seems likely that the higher survival rate in IMH group may be related to the absence of persistent flow communication.

In the current study, the incidence of complications including leg and renal ischemia was significantly higher in AD group than IMH group. Tittle et al\(^9\) reported that there were no instances of early or late branch organ occlusion related to the aortic process in any patients in their study. We previously reported that the incidence of stroke was significantly lower in patients with type A IMH than type A AD.\(^16\) Therefore, the difference of aortic pathology in patients with IMH may have a different impact on the incidence of serious complications compared with classic AD.

It has been reported that IMH with ULP or penetrating atherosclerotic ulcer (PAU) was associated with a progressive disease course.\(^13,17\) Sueyoshi et al\(^13\) reported that 12 of 17 projections progressed to complications such as enlargement (n=10) or progression to overt dissection. Ganaha et al\(^17\) reported that IMH with PAU was significantly associated with a progressive disease course and concluded it was important to make a clear distinction between IMH with and without PAU. Their results were consistent with our results. In this study, 16 ULPs were newly identified during the follow-up period and 9 projections progressed to complications such as enlargement or progression to overt dissection. In addition, multivariate analysis identified new appearance of an ULP as one of the strongest predictors of progression in patients with type B IMH in this study. Therefore, close follow-up imaging study must be necessary for type B IMH patients with an ULP.

In this study, our indications for surgical intervention for AD or IMH were (1) maximum diameter of the affected aorta $\geq 60\ mm$, (2) rapid enlargement of the affected aorta, (3) rapid enlargement of ulcerlike lesion and (4) rupture of the affected aorta. Previous studies have recommended that operation should be performed for patients with AD when the aortic diameter $>55\ mm$.\(^15,18,19\) In terms of surgical indications for IMH, Cambria\(^20\) recommended that early intervention should be considered when the descending aortic diameter approaches the 6 cm range in patients with IMH. Our indications were similar to those in the previous reports and seem to be reasonable. However, surgical indications for the high-risk patients with type B IMH are still unclear. Further investigations may be needed to establish therapeutic strategy of high-risk type B IMH.

Endovascular treatment with a stent-graft has been recently considered as a less invasive alternative to surgical graft replacement for patients with aortic dissection.\(^21,22\) Ganaha et al\(^17\) reported that they treated 6 patients with type B IMH with PAU by endovascular methods and that a stent-graft success-

<p>| TABLE 4. Univariate Analysis of Predictors of Progression of Type B IMH |</p>
<table>
<thead>
<tr>
<th>Progression (n=11)</th>
<th>Regression (n=36)</th>
<th>P</th>
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<tbody>
<tr>
<td>Age, years</td>
<td>75±6</td>
<td>65±10</td>
</tr>
<tr>
<td>Male</td>
<td>8 (73%)</td>
<td>22 (61%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>9 (82%)</td>
<td>36 (100%)</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>1 (9%)</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>History of smoking</td>
<td>4 (36%)</td>
<td>18 (50%)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>1 (9%)</td>
<td>2 (6%)</td>
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<tr>
<th>CT findings</th>
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<tbody>
<tr>
<td>Maximum aortic diameter on initial CT images (mm)</td>
<td>42±8</td>
<td>37±5</td>
<td>0.025</td>
</tr>
<tr>
<td>Maximum aortic wall thickness on initial CT images (mm)</td>
<td>12±3</td>
<td>10±4</td>
<td>0.287</td>
</tr>
<tr>
<td>Involvement of abdominal aorta</td>
<td>7 (64%)</td>
<td>26 (72%)</td>
<td>0.710</td>
</tr>
<tr>
<td>New appearance of ulcerlike projection</td>
<td>9 (82%)</td>
<td>2 (19%)</td>
<td>0.0003</td>
</tr>
</tbody>
</table>

CT = computed tomography.

| TABLE 5. Multivariate Analysis of Predictors of Progression of Type B IMH |
|------------------|-----------------|---|
| Age >70 years    | 37.43 | 0.010 |
| New appearance of ulcerlike projection | 22.16 | 0.009 |
fully covered the PAU in all patients. In this study, no patients were treated with endovascular methods. Considering a progressive disease course of IMH with an ULP or PAU, early intervention with this minimally invasive endovascular approach may have considerable advantages in these patients compared with medical treatment or conventional surgical repair.

In this study, multivariate analysis identified age >70 years as one of the strongest predictors of progression in patients with type B IMH. Previous studies reported that elastic properties of the aorta decrease with age.23,24 Although the exact mechanisms of progression in patients with IMH remains unclear, decreased distensibility of descending aorta may play an important role in the disease process in patients with IMH.12,25

One limitation of this study was relatively small sample number for multivariate analysis. The results of multivariate analysis must be taken with caution. Further studies involving larger numbers of patients in a multicenter setting may be needed.

Conclusions

Patients with type B IMH have better long-term prognosis than patients with type B AD. Low incidence of complication and high rates of disappearance of hematoma indicates that the absence of a direct-flow communication through an intimal tear in IMH is a good prognostic finding. On the other hand, new appearance of an ULP and older age were identified as the strongest predictors of progression of type B IMH.

References

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