CLINICAL STUDY

Analysis of Short-Term Clinical Outcomes and Influencing Factors in Patients with Acute Type B Aortic Intramural Hematoma Treated with Optimal Medical Therapy

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Summary

This study aimed to investigate the short-term predictors of aortic-related adverse events in patients with acute type B aortic intramural hematoma (IMH) initially treated with optimized medical therapy.

A total of 157 patients with acute type B IMH were included in this study. These patients were divided into worsening group (n = 45) and stable group (n = 112) based on the incidence of aortic-related adverse events. The clinical data and imaging features of the two groups were compared. Multivariate logistic regression analysis of predictors of aortic-related adverse events in type B IMH was performed. Receiver operating characteristic (ROC) curve was applied to determine the optimal cutoff value for maximum descending aorta diameter (MDAD). Kaplan-Meier survival curve was used to analyze the incidence of aortic-related adverse events.

Worsening and stable groups were statistically significant in diuretics, abnormal D-dimer level, observation endpoint systolic blood pressure (SBP), MDAD, aortic atherosclerosis, ulcer-like projection (ULP), and thickness of hematoma ($P < 0.05$). Multivariate logistic regression showed that abnormal D-dimer level (OR = 12.464, P = 0.025), MDAD (OR = 1.113, P = 0.030), and ULP (OR = 5.849, P = 0.022) were powerful independent risk factors for predicting aortic-related adverse events in type B IMH, and observation endpoint SBP within 100-120 mmHg (OR = 0.225, P = 0.014) was a protective factor for predicting aortic-related adverse events in type B IMH. The cutoff value of MDAD was 35.2 mm.

Short-term imaging is recommended for type B IMH patients with abnormal D-dimer level, MDAD > 35.2 mm, and ULP. Blood pressure should also be strictly monitored and controlled during the acute phase of IMH.

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Key words: Aortic diseases, Aortic-related adverse events, Prognosis

Acute type B aortic intramural hematoma (IMH) is a type of acute aortic syndrome (AAS), accounting for about 10%-25% of AAS.[1)] IMH is divided into two types according to the Stanford classification. Type A IMH involves the ascending aorta with or without descending aorta involvement, accounting for about 30%-40%. Type B IMH does not involve the ascending aorta, usually originating far from the left subclavian artery ostium, but may involve the aortic arch, accounting for about 60%-70%. Acute type B IMH can progress to various types of aortic-related adverse events, including the risk of developing aortic dissection (AD), penetrating aortic ulcers (PAU), and aortic rupture.[2,3)] The early mortality rate of type A IMH is approximately 0%-8% through medical management; however, it may rise to 33%-80% when the medical management is unfavorable.[4)] Type B IMH has a rupture rate of 26% on admission and an in-hospital mortality rate of 6%-8%. About 44% of type B IMH treated with drugs rapidly progress.[5)] Computed tomography angiography (CTA) should be closely monitored during the diagnosis and treatment process to detect the tendency of IMH to AD, PAU, or aortic rupture, respectively. Corresponding treatment was given to improve the prognosis of patients. However, there are few studies on short-term clinical and imaging outcomes of IMH. This study aimed to observe clinical outcomes and imaging features of type B IMH patients who initially received optimized medical therapy (OMT) within 30 days and further explore the predictive factors of aortic-related adverse events to assist physicians in type B IMH risk assessment and clinical decision-making.

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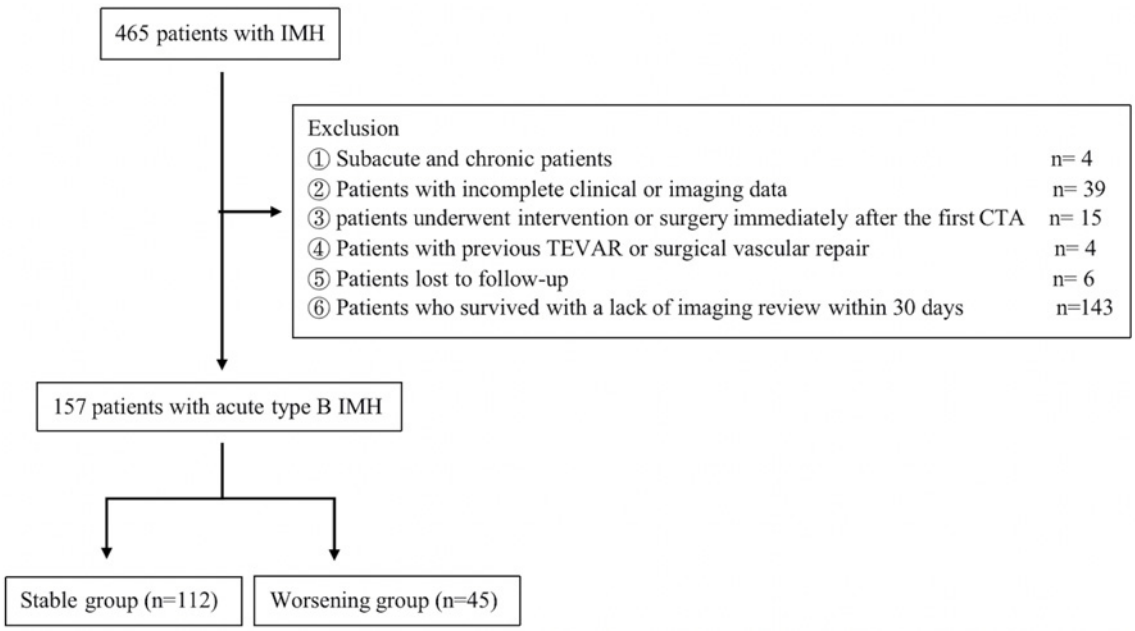

Figure 1. Intramural hematoma: flowchart of research. IMH indicates intramural hematoma; CTA, computed tomography angiography; and TEVAR, thoracic endovascular aortic repair.

Methods

Study population and enrollment criteria: This was a retrospective cohort study of consecutive patients with simple IMH diagnosed by CTA in the emergency and cardiovascular Department of the General Hospital of Northern Theater Command from April 2014 to July 2022. Patients who met the following criteria were included: (1) aged ≥ 18 years and (2) with simple acute type B IMH. The exclusion criteria were as follows: (1) subacute and chronic patients, (2) patients who underwent intervention or surgery immediately after the first imaging examination, (3) previous thoracic endovascular aortic repair (TEVAR) or surgical vascular repair, (4) patients with traumatic aortic injury, (5) patients with IMH combined with inherited diseases such as Marfan syndrome or connective tissue diseases, (6) patients with incomplete clinical or imaging data, and (7) patients lost to follow-up for 30 days (Figure 1). A total of 157 eligible type B IMH patients were included. According to the occurrence of aortic-related adverse events, the patients were divided into worsening group (n = 45) and stable group (n = 112). The Ethics Committee of the General Hospital of Northern Theater Command approved this study with an Ethics Batch Number Y(2022)151.

CTA measurement: All IMH were diagnosed by CTA + three-dimensional (3D) reconstruction examination of thoracic and abdominal aorta. The location and scope of aortic lesions were analyzed by at least two experienced clinicians, and the maximum ascending aorta diameter, maximum descending aorta diameter (MDAD), and maximum descending aorta hematoma thickness (MDHT) were measured.

Management and follow-up protocol: All patients received OMT including painkiller, anti-hypertension, heart rate control, and close monitoring. The primary treatment goals were to relieve pain and maintain the blood pressure (BP) at (100-120) mmHg/(70-80) mmHg (1 mmHg = 0.133 kPa) and heart rate (HR) at (60-70) beats/minute. CTA review was recommended for all patients at 7-14 days and 30 days after onset. Review of thoracic and abdominal aorta CTA + 3D reconstruction is required if the patient's condition deteriorates. Surgical or endovascular aortic repair can be performed for patients with aortic rupture tendency, AD, or PAU. The observation indicators included changes of MDHT, progression to AD, PAU, or pseudoaneurysm, newly developed pericardial and pleural effusion or increase of original pericardial and pleural effusion, uncontrolled BP and HR, clinical symptoms, and death.

Definitions: Acute IMH was defined as those with an interval between symptom onset and diagnosis of 0-14 days.[6] Observation endpoint BP refers to blood pressure measured at the time of aortic-related adverse events and before the end of the observation termination time. Abnormal D-dimer level was greater than 0.5 μg/mL. Aortic-related adverse events were defined as AAS complex events, which mainly included aortic-related death and progression to AD or PAU. AD[1] was defined as disruption of the medial layer provoked by intramural bleeding, resulting in the separation of the aortic wall layers and subsequent formation of true and false lumens with or without communication. PAU[3] was defined as an outpouching or crater-like protrusion in the aortic wall in the setting of intimal calcification and severe atherosclerotic disease and frequently accompanied by a medial hematoma around the protrusion. Ulcer-like projection (ULP),[7] also described as focal intimal disruption, was defined as a focal contrast material-filled pouch projecting outside of the opacified aorta lumen with a communicating orifice greater than 3

Table I. Baseline Characteristics

Variable	All patient (n = 157)	Stable group (n = 112)	Worsening group (n = 45)	P value
Age, years	62.55 ± 9.61	62.36 ± 10.07	63.02 ± 8.46	0.754
Male, n (%)	103 (65.6)	70 (62.5)	33 (73.7)	0.196
BMI, kg/m^2	25.09 ± 3.60	25.15 ± 3.76	24.94 ± 3.23	0.847
Drinking, n (%)	72 (45.9)	46 (41.1)	26 (57.8)	0.057
Smoking, n (%)	92 (58.6)	65 (58.0)	27 (60.0)	0.821
Medical history, n (%)				
Hypertension	118 (75.2)	83 (74.1)	35 (77.8)	0.630
Diabetes	7 (4.5)	7 (6.3)	0 (0.0)	0.193
Coronary artery disease	7 (4.5)	6 (5.4)	1 (2.2)	0.674
Cerebrovascular disease	15 (9.6)	8 (7.1)	7 (15.6)	0.105
Symptoms on admission, n (%)				
Chest or back pain	142 (90.4)	103 (92.0)	39 (86.7)	0.307
Abdominal pain	9 (5.7)	6 (5.4)	3 (6.7)	1.000
Low back pain	5 (3.2)	3 (2.7)	2 (4.4)	0.946
Pain of radiation	10 (6.4)	8 (7.1)	2 (4.4)	0.791
Medical, n (%)				
Antithrombotic drugs	10 (6.4)	4 (8.9)	6 (5.4)	0.413
Statins	23 (14.6)	10 (22.2)	13 (11.6)	0.089
Beta-blockers	93 (59.2)	64 (57.1)	29 (64.4)	0.400
Calcium antagonists	123 (78.3)	86 (76.8)	37 (82.2)	0.455
ACEI/ARB	44 (28.0)	35 (31.3)	9 (20.0)	0.156
Diuretics	3 (1.9)	0 (0.0)	3 (6.7)	0.022
Types of antihypertensive drugs ≥ 2	97 (61.8)	68 (60.7)	29 (64.4)	0.664
Laboratory examination				
CKMB, U/L	12.00 (9.00, 15.75)	12.40 (9.15, 16.00)	11.80 (8.80, 15.13)	0.428
TNT, μg/L	0.05 (0.01, 8.00)	0.03 (0.01, 7.00)	5.00 (0.01, 10.00)	0.049
ALT, U/L	17.32 (13.07, 23.83)	17.33 (12.68, 23.10)	17.08 (14.00, 27.54)	0.506
AST, U/L	20.21 (17.03, 23.74)	18.98 (16.69, 22.90)	21.43 (17.28, 25.81)	0.057
TG, mmol/L	1.42 (1.11, 2.07)	1.89 (1.18, 3.84)	1.31 (1.11, 1.89)	0.107
LDL, mmol/L	2.77 ± 0.88	2.83 ± 1.51	2.75 ± 0.60	0.882
WBC, 10^9 /L	11.13 ± 3.09	11.05 ± 3.03	11.32 ± 3.26	0.635
HG, g/L	135.91 ± 18.26	135.97 ± 17.53	135.79 ± 20.04	0.944
PLT, 10^9 /L	219.76 ± 78.52	221.19 ± 86.96	216.52 ± 55.64	0.750
CR, μmol/L	66.85 (52.05, 82.30)	65.60 (49.63, 80.97)	70.20 (57.73, 88.25)	0.068
CRP, mg/dL	7.80 (2.60, 21.60)	7.20 (2.60, 16.5)	9.90 (2.80, 31.23)	0.442
Abnormal D-dimer level, n (%)	108 (81.8)	69 (76.7)	39 (92.9)	0.025

Data are expressed as mean ± SD, median (quartile 1 to quartile 3), or n (%) . BMI indicates body mass index; ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blocker; CKMB, creatine phosphokinase myocardial band; TNT, troponin T; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TG, triglyceride; LDL, low-density lipoprotein; WBC, white blood cell; HG, hemoglobin; PLT, platelet count; CR, creatinine; and CRP, C-reactive protein.

Table II. Comparison of Blood Pressure and Heart Rate

Variable	All patient (n = 157)	Stable group (n = 112)	Worsening group (n = 45)	P value
Admission BP				
Systolic BP, mmHg	145.10 ± 28.67	148.06 ± 27.67	140.26 ± 28.79	0.198
Systolic BP within 100-140 mmHg, n (%)	47 (39.2)	31 (39.7)	16 (38.1)	0.860
Systolic BP within 100-120 mmHg, n (%)	14 (11.7)	10 (12.8)	4 (9.5)	0.812
Diastolic BP, mmHg	86.96 ± 16.18	87.51 ± 16.70	85.26 ± 15.19	0.469
Heart rate, BPM	84.82 ± 14.15	85.53 ± 13.64	83.51 ± 15.14	0.193
Observation endpoint BP				
Systolic BP, mmHg	127.22 ± 8.56	126.25 ± 8.20	129.92 ± 9.05	0.020
Systolic BP within 100-140 mmHg, n (%)	123 (87.2)	93 (89.4)	30 (81.1)	0.192
Systolic BP within 100-120 mmHg, n (%)	45 (31.9)	39 (37.5)	6 (16.2)	0.017
Diastolic BP, mmHg	78.88 ± 7.94	78.07 ± 8.03	81.08 ± 7.33	0.059
Heart rate, BPM	70.39 ± 6.87	69.88 ± 6.82	71.81 ± 6.91	0.151

Data are expressed as mean ± SD or n (%) . BP indicates blood pressure; and BPM, beats per minute.

Table III. CTA Characteristics

Variable	All patient (n = 157)	Stable group (n = 112)	Worsening group (n = 45)	P value
Onset to treatment, days	0.42 (0.21, 1.00)	0.44 (0.18, 1.00)	0.35 (0.23, 1.00)	0.655
Baseline CTA findings				
Pericardial effusion, n (%)	46 (29.3)	33 (29.5)	13 (28.9)	0.943
Pleural effusion, n (%)	3 (1.9)	1 (0.9)	2 (4.4)	0.198
Maximum ascending aorta, mm	43.06 ± 4.66	42.66 ± 4.92	44.05 ± 3.81	0.091
Maximum descending aorta, mm	34.04 ± 5.20	33.06 ± 5.11	36.45 ± 4.66	< 0.001
MDHT, mm	9.17 ± 3.21	8.96 ± 3.22	9.70 ± 3.17	0.195
Aortic atherosclerosis, n (%)	55 (35.0)	32 (28.6)	23 (51.1)	0.007
ULPs, n (%)	19 (12.1)	6 (5.4)	13 (28.9)	< 0.001
Segment numbers involved	2.36 ± 0.61	2.38 ± 0.63	2.33 ± 0.56	0.570
IMH involves diaphragm level, n (%)	141 (89.8)	99 (88.4)	42 (93.3)	0.355
IMH involves iliac artery, n (%)	14 (8.9)	8 (7.1)	6 (13.3)	0.218
Crescent hematoma, n (%)	88 (56.1)	64 (57.1)	24 (53.3)	0.664
Circular hematoma, n (%)	69 (43.9)	48 (42.9)	21 (46.7)	0.664
Follow-up CTA findings				
Newly developed pleural effusion, n (%)	16 (10.2)	10 (8.9)	6 (13.3)	0.409
Newly developed pericardial effusion, n (%)	3 (1.9)	1 (0.9)	2 (4.4)	0.198
Changes of MDHT, mm	−1.24 ± 3.10	−1.50 ± 2.92	−0.55 ± 3.47	0.012
Changes of MDAD, mm	−0.64 ± 5.04	−0.79 ± 5.03	−0.21 ± 5.09	0.693

Data are expressed as mean ± SD or n (%) . CTA indicates computed tomography angiography; MDHT, maximum descending aorta hematoma thickness; ULPs, ulcer-like projections; IMH, intramural hematoma; and MDAD, maximum descending aorta diameter.

mm. In this study, the aorta was divided into four segments according to 2014 ESC guidelines:[1] the ascending aorta (aortic sinotubular junction to proximal brachiocephalic trunk ostium), the transverse arch (brachiocephalic trunk ostium to the left subclavian artery ostium), descending thoracic aorta (distal ostium of the left subclavian artery to diaphragm level), and abdominal aorta (diaphragm level to the bifurcation of the iliac artery). If a hematoma involves one segment, it is recorded as 1, and if two segments are involved, it is recorded as 2, and so on. Aortic atherosclerosis was defined as marked calcification or irregular thickening of the aortic wall involving at least two segments. The diagnostic criterion for pericardial effusion is that the distance between the pericardium and the parietal pericardium is > 4 mm. A small amount of pericardial effusion refers to the distance of 5-14 mm (< 100 mL) during cardiac diastole. Medium volume of pericardial effusion refers to the distance of 14-24 mm (100-500 mL). A large number of pericardial effusion refer to the distance of ≥ 25 mm (> 500 mL). A small amount of pleural effusion is usually < 500 mL (effusion depth < 3 cm). A moderate pleural effusion refers to effusion volume between 500 and 1000 mL (the depth of the effusion is 3-5 cm). A large amount of pleural effusion refers to effusion volume greater than 1000 mL (effusion depth > 5 cm).[8]

Statistical analysis: Statistical analysis was performed with SPSS version 26.0 (SPSS, Chicago, Illinois). Continuous variables were reported as the mean ± SD or the median (quartile 1-quartile 3). Normally and non-normally distributed variables were compared using independent sample t-test and the Mann-Whitney U test, respectively. Categorical variables were expressed as frequencies and percentages and were compared using the χ^2 or Fisher's exact test. Receiver operating characteristic (ROC) curve was used to predict the risk of aortic-related adverse events. Unconditional logistic regression was used for multivariate analysis. The results were expressed by odds ratio (OR) and 95% confidence interval (CI). The Kaplan-Meier method was applied for the incidence of aortic-related adverse events, and the log-rank test was performed. All P values were two-sided with a P value < 0.05 considered statistically significant.

Result

Baseline characteristics and imaging features: Tables I, II show patient characteristics of the entire cohort (157 cases). There were statistically significant differences between the type B IMH worsening and stable groups in TNT (troponin T) [5.00 (0.01, 10.00) versus 0.03 (0.01, 7.00), P = 0.049], abnormal D-dimer level (92.9% versus 76.7%, P = 0.025), application of diuretics (6.7% versus 0, P = 0.022), and observation endpoint SBP [(129.92 ± 9.05) mmHg versus (126.25 ± 8.20) mmHg, P = 0.020]. Age, male, body mass index, drinking history, smoking history, medical history, symptoms on admission, other medications, and laboratory examination indicators were not statistically significant between the two groups (all P > 0.05).

Table III shows baseline and follow-up CTA findings. MDAD [(36.45 ± 4.66) mm versus (33.06 ± 5.11) mm, P < 0.001], aortic atherosclerosis (51.1% versus 28.6%, P = 0.007), ULP (28.9% versus 5.4%, P < 0.001), and changes of MDHT [(−0.55 ± 3.47) mm versus (−1.50 ± 2.92) mm, P = 0.012] in the type B IMH worsening and stable groups were statistically significant. There were no statistically significant differences between the time from onset to treatment, baseline pleural effusion, pericardial effusion, maximum ascending aorta diameter, MDHT,

Table IV. Logistic Regression Analysis of the Risk Factors of Intramural Hematoma Deterioration

Variable	Univariate analysis		Multivariate analysis	
	P value	HR (95% CI)	*P* value	HR (95% CI)
Drinking	0.059	1.963 (0.974-3.958)		
Statins	0.094	2.176 (0.876-5.406)		
TNT	0.679	0.999 (0.995-1.003)		
AST	0.248	1.021 (0.986-1.058)		
Abnormal D-dimer	0.034	3.957 (1.109-14.115)	0.021	14.060 (1.494-132.369)
Maximum ascending aorta	0.093	1.067 (0.989-1.152)		
Maximum descending aorta	< 0.001	1.143 (1.061-1.231)	0.030	1.113 (1.010-1.226)
Aortic atherosclerosis	0.008	2.614 (1.280-5.337)	0.708	1.200 (0.462-3.112)
ULPs	< 0.001	7.177 (2.524-20.407)	0.022	5.849 (1.284-26.640)
Changes of MDHT	0.092	1.116 (0.982-1.267)		
Observation endpoint SBP within 100-120 mmHg	0.021	0.323 (0.124-0.843)	0.014	0.225 (0.068-0.741)

TNT indicates troponin T; AST, aspartate aminotransferase; ULPs, ulcer-like projections; MDHT, maximum descending aorta hematoma thickness; SBP, systolic blood pressure; HR, hazard ratio; and CI, confidence interval.

number of involved segments of hematoma, IMH involves diaphragm level, IMH involves iliac artery, crescent hematoma, and circular hematoma, newly developed pleural and pericardial effusion at follow-up, and changes of MDAD between the two groups (all $P > 0.05$).

Logistic regression analysis for predicting early adverse aorta-related events: The variables with significant differences in clinical data and imaging features of the two groups ($P < 0.1$, the frequency of diuretic use in the stable group was 0, excluding univariate analysis) were analyzed by univariate logistic regression. Results showed that abnormal D-dimer level (OR = 3.957, 95% CI: 1.109-14.115, $P = 0.034$), MDAD (OR = 1.143, 95% CI: 1.061-1.231, $P < 0.001$), aortic atherosclerosis (OR = 2.614, 95% CI: 1.280-5.337, $P = 0.008$), ULP (OR = 7.177, 95% CI: 2.524-20.407, $P < 0.001$), and observation endpoint SBP within 100-120 mmHg (OR = 0.323, 95% CI: 0.124-0.843, $P = 0.021$) were predictors of aortic-related adverse events. Multivariate analysis was performed for variables with $P < 0.05$ in univariate analysis. Table VI shows the results of the univariable and multivariable logistic regression analysis for predictors of adverse aorta-related events. On multivariable analysis, abnormal D-dimer level (OR = 14.060, 95% CI: 1.494-132.369, $P = 0.021$), MDAD (OR = 1.113, 95% CI: 1.010-1.226, $P = 0.030$), and ULP (OR = 5.849, 95% CI: 1.284-26.640, $P = 0.022$) were the independent predictors of adverse aorta-related events in type B IMH patients, and observation endpoint SBP within 100-120 mmHg (OR = 0.225, 95% CI: 0.068-0.741, $P = 0.014$) was a protective factor for aortic-related adverse events. The ROC curve analysis revealed that the optimal cutoff value for the MDAD was 35.2 mm (sensitivity 68.9%, specificity 72.3%), with AUC of 0.704 (Figure 2).

Kaplan-Meier survival analysis based on factors influencing aortic-related adverse events: Kaplan-Meier curve of aortic-related adverse events was drawn according to MDAD, ULP, abnormal D-dimer level, and observation endpoint SBP within 100-120 mmHg, and log-rank test was performed. Figure 3 shows that Kaplan-Meier survival analysis showed a significant increase in aortic-related adverse events in MDAD > 35.2 mm, observation endpoint SBP > 120 mmHg or < 100 mmHg, with ULP, and abnormal D-dimer level, and the differences were statistically significant (all $P < 0.05$). In addition, the possibility of type B IMH progressed to PAU was increased when patients with MDAD > 35.2 mm, ULP and abnormal D-dimer level, and all the differences were statistically significant ($P < 0.05$). MDAD > 35.2 mm resulted in significantly higher aortic-related death, and the difference was statistically significant ($P < 0.05$).

Figure 4 shows that complete absorption of hematoma occurred in some patients during follow-up imaging, not only in the stable group but also in the worsening group. MDHT during the follow-up period was lower in the stable group than in baseline CTA, and the difference was statistically significant ($P < 0.001$), while the MDHT in the worsening group was not statistically significant ($P = 0.311$).

Treatment methods and clinical outcomes: The average decay time was 9.00 (7.50, 19.00) days after 45 patients received optimized drug therapy. Three patients died of aortic rupture, 8 developed AD, and 34 developed aortic penetrating ulcer. A total of 29 patients (64.4%) received TEVAR, and 13 (28.9%) with aortic penetrating ulcer refused TEVAR treatment. The mean follow-up time was 6.95 (4.25, 13.69) months. All patients survived after TEVAR, and two cases experienced ischemic stroke. Control images were taken from 17 patients. One patient developed a distal stent ulcer 1 month after TEVAR but not being treated. The remaining patients had no postoperative side effects. The stent apposition was good and the hematoma was absorbed. All patients who declined surgery survived, and one patient suffered a hemorrhagic stroke. During the image follow-up of six cases, one had ulcer progression and five had stable lesions.

Discussion

IMH, a unique entity within the spectrum of AAS, has received more attention due to its similar mortality risk to AD. Previous studies have been very limited and controversial on factors related to IMH progression and predictors of adverse events. It is known that factors such as long-term hypertension, atherosclerosis, and smoking[9] may lead to changes in the structure of the vascular me-

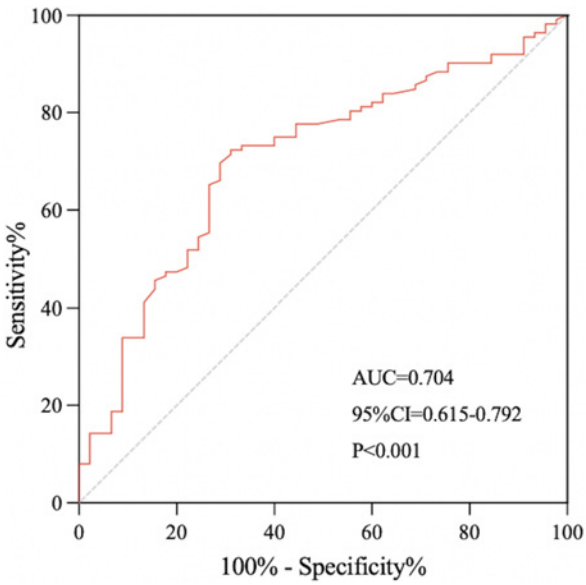

Figure 2. Receiver operating characteristic curve analysis for prediction of aortic-related adverse events based on maximum descending aorta diameter.

dia, decreased vascular elasticity, and hardened and brittle lumens, thereby leading to the formation of IMH. From the traditional view, IMH originates from the ruptured vasa vasorum in the medial wall layers, which is characterized by no intimal tear and no direct blood flow connection between the true and false lumens. However, studies using multidetector CT as a diagnostic imaging mode have shown that intimal tears can be detected at an early stage.[3] Moreover, the intimal rupture also provided a more reasonable explanation for the transformation of IMH into PAU, AD, and even aortic rupture. The development of IMH is hardly predictable. As the disease progresses, IMH may regress or be completely absorbed[10] or may progress to typical AD, rupture, or aneurysm expansion.[11] Whether medical treatment with a wait-and-see approach can be used in patients with type B IMH depends on the risk of adverse events during follow-up. The previous study showed[7] that most aortic-related adverse events occurred in the first month after the diagnosis of IMH, which was also confirmed by Li, *et al*.[2] Therefore, our study analyzed the short-term clinical outcomes and imaging characteristics of type B IMH patients and detected high-risk patients with IMH deterioration at an early stage. Patients will have a better prognosis attributed to timely intervention.

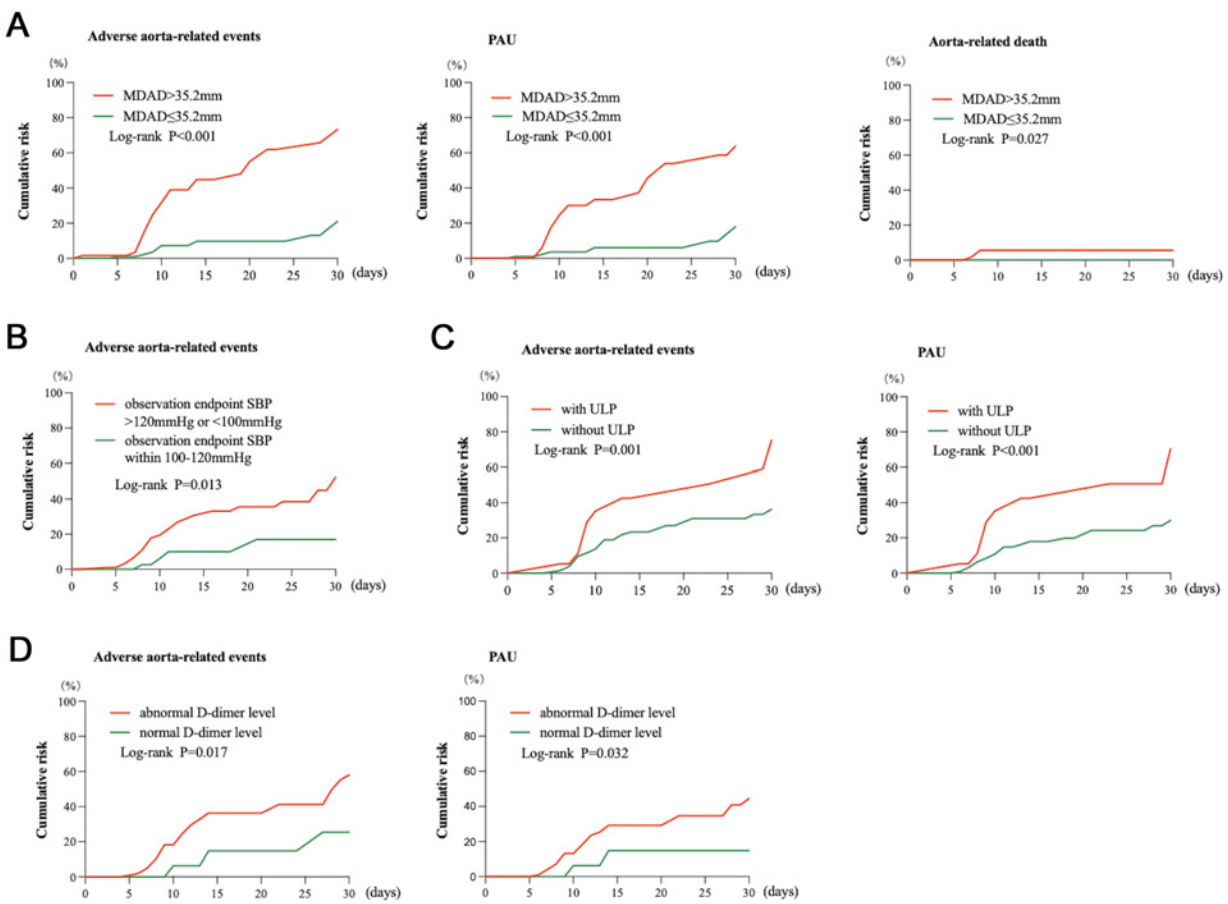

Figure 3. Kaplan-Meier survival curve. **A:** MDAD indicates maximum descending aorta diameter. **B:** Observation endpoint SBP indicates observation endpoint systolic blood pressure. **C:** ULP indicates ulcer-like projection. **D:** D-dimer level.

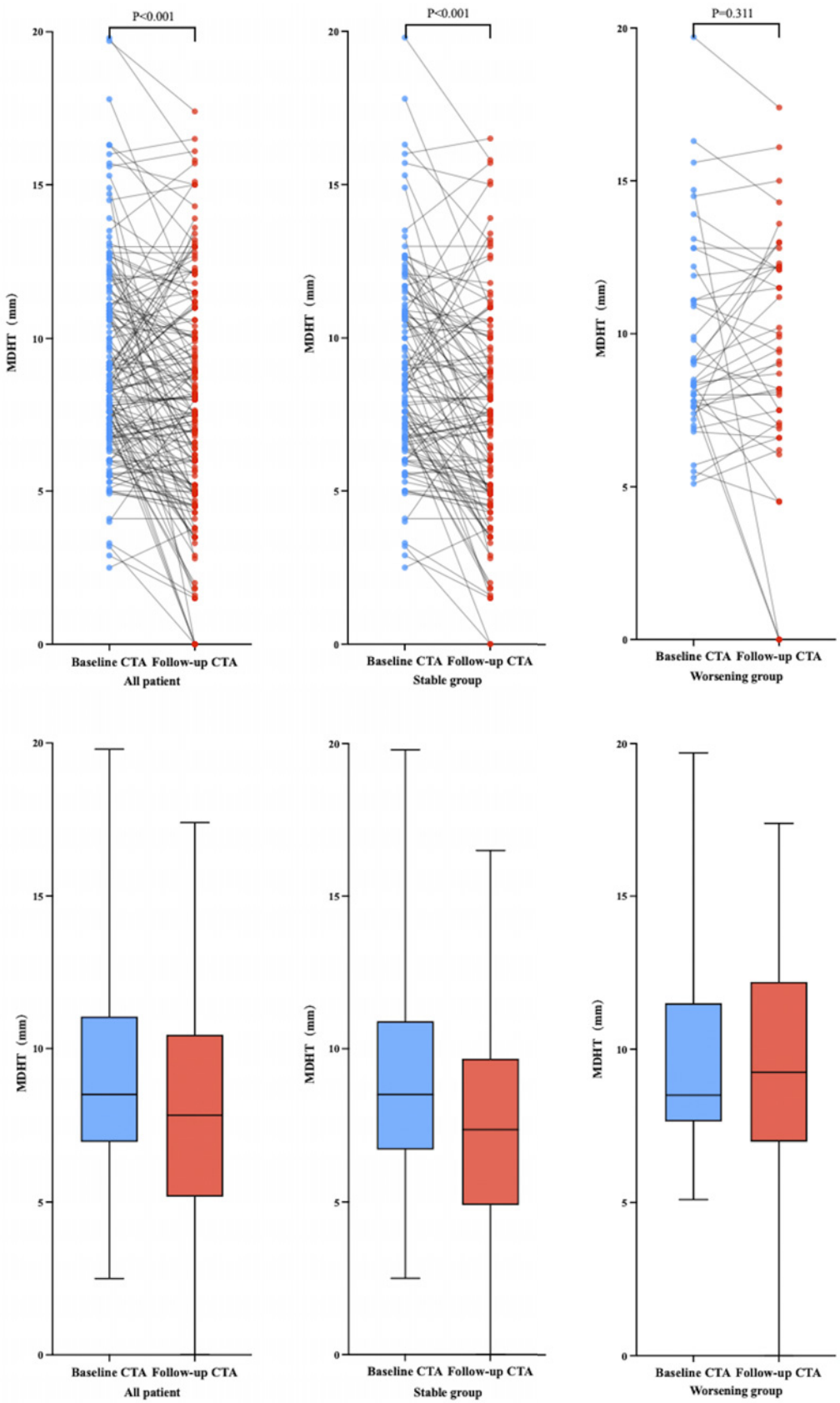

Figure 4. Hematoma thickness in different periods between the two groups.

Aortic IMH is considered a precursor of dissection. IMH patients will tear the intimal of the aorta due to a sudden increase in BP, and the blood will flow between the muscular layer and the endothelium of the aorta, causing severe pain, which is manifested as tearing pain, and the degree of pain is related to BP. Therefore, the first principle of IMH treatment is to control BP. In most studies, intravenous or oral anti-hypertensive drugs were used to maintain the SBP within 100-120 mmHg during hospitalization,[12,13] while sedation and analgesia, anti-pulse rate, close monitoring, defecation, and other related treatments were carried out. However, few studies have focused on anti-hypertension after hospital discharge. We provided targeted publicity and education to each IMH patient upon admission. In addition, imaging features and clinical data including BP were regularly followed up after discharge. High-quality CTA review enables timely detection of aortic deterioration, and patients benefit from regular follow-up and timely guidance on their BP control. In this study, multivariate analysis showed that observation endpoint SBP within 100-120 mmHg was a protective factor for aortic-related adverse events, and the incidence of aortic-related adverse events was significantly higher for SBP of > 120 mmHg or < 100 mmHg than for SBP within 100-120 mmHg. Therefore, in addition to imaging follow-up, strict BP management during follow-up is also very important.

Multivariate analysis in this study showed that MDAD of baseline CTA was a significant independent predictor, and the optimal cutoff value of MDAD was 35.2 mm. Patients with MDAD > 35.2 mm had a higher risk of aortic-related adverse events. Many previous studies[2,7,14,15] had also confirmed that the greater the aortic diameter, the higher the risk of adverse events. In addition, studies have suggested that IMH thickness and changes in IMH thickness can be used as independent predictors of IMH disease progression.[2] In our study, the regression degree of MDHT was lower in the worsening group than in the stable group; however, there was no significant difference in the MDHT of baseline CTA between the two groups. Such research result had been proved to be reasonable in other studies.[10] This may be related to the vascular rupture when IMH evolved into AD or PAU, resulting in no active blood flow in the vascular and the regression of hematoma.

ULP has been recognized as an independent predictor of adverse events in IMH patients, whether it appears in the first examination or follow-up examination,[2,10] suggesting that small intimal rupture plays an important role in the development of IMH. Kitai, *et al*.[16] described 38 patients with IMH, 23.7% of whom had intimal defects. Nineteen patients (12.1%) had ULP at baseline CTA because we initially excluded patients with IMH and PAU. Such screening eliminates the influence of PAU on prognosis, thus strictly controlling the indications of initial OMT of type B IMH and providing the best medical treatment for AAS patients in our center. The incidence of ULP in baseline CTA was significantly higher in the worsening group than in stable group, indicating that patients with ULP were at higher risk of aortic-related adverse events than those without ULP, which was also supported in a study by Moral, *et al*.[11] Although the definition of intimal rupture, timing of initial diagnosis, and imaging protocols vary across studies, the diagnosis of intimal rupture has important clinical significance in the management of type B IMH.

Previous studies have not been very clear about the relationship between pleural effusions and IMH complications. Some studies showed that new-onset pleural effusion was an independent predictor of aortic-related adverse events in IMH and the presence of pleural effusion was taken as one of the indicators to judge the rupture or imminent rupture of the aortic wall.[2,5] In our study, baseline and new-onset pleural effusion during the follow-up period were not associated with aortic-related adverse events, and there was no significant increase in patients with baseline pleural effusion during follow-up CTA, which may be related to the shorter interval between onset and medical treatment. The average median time from onset to presentation was 0.42 days, while the initial CT scan of Li, *et al.*[2] was completed within 2 days.

Gorla, *et al*. showed that the elevated D-dimer level was an independent risk factor for in-hospital mortality in IMH patients,[17] but other studies showed that the level of D-dimer in IMH patients was mostly normal.[18,19] Therefore, whether D-dimer levels are elevated in IMH patients remains a debate. D-dimer is a plasma soluble fibrin degradation product, and its increase reflects the activation of the coagulation and fibrinolytic system and indirectly reflects the activity of thrombosis.[20] Nazerian, *et al*.[21] showed that the sensitivity and specificity of D-dimer in the diagnosis of AAS were 96.7% and 64%, respectively. Our study found that 108 patients (81.8%) had D-dimer levels higher than the threshold, which was consistent with the conclusion of Zhang, *et al*.[22] that the D-dimer levels were higher than the normal value by 86.0%. This further supports the conclusion that D-dimer levels are increased in IMH patients. The potential reason may be that IMH may activate the coagulation and fibrinolytic system while nourishing the arterial rupture. In the study by Zhang, *et al.*, D-dimer level was moderately correlated with IMH length, hematoma cross-sectional area, and volume index, suggesting that D-dimer level can reflect the extent of lesion involvement and hematoma hemorrhage volume to a certain extent. D-dimer levels were significantly higher in the deteriorated group than in the stable group in our study, and the risk of aortic-related adverse events was higher in patients with elevated D-dimer levels than those with normal D-dimer levels. Therefore, although IMH is a rare type of AAS, D-dimer can be used as a laboratory screening indicator in IMH patients prior to CTA examination to facilitate the initial assessment of patient.

Study limitations: This study has some limitations. Firstly, as any single-center registry study, we analyzed the data retrospectively, not as a randomized study, and selection bias cannot be ruled out. Secondly, approximately one-third of patients lost short-term imaging follow-up, which was mainly due to patients being transferred back to the referral facility for medical treatment and follow-up. In addition, the diagnosis of IMH was confirmed by radiology, and there may be an invisible intimal

tear that can only be detected during surgery. However, the patients of our study did not require surgical exploration, so pathological specimens of intimal defect could not be obtained, which may cause certain impact on the results of our study. Finally, the other limitation of this study is that since sample size is limited, the results of the survey would not be generalized.

Conclusion

Abnormal D-dimer level, MDAD, and ULP were independent risk factors for predicting aortic-related adverse events in type B IMH, and observation endpoint SBP within 100-120 mmHg was a protective factor for aortic-related adverse events in type B IMH. MDAD > 35.2 mm had a better predictive effect on aortic-related adverse events in type B IMH.

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Disclosure

Conflicts of interest: The authors declare no conflicts of interest.

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