Acute Intramural Hematoma of the Aorta
A Mystery in Evolution

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Background—The definition, prevalence, outcomes, and appropriate treatment strategies for acute intramural hematoma (IMH) continue to be debated.

Methods and Results—We studied 1010 patients with acute aortic syndromes who were enrolled in the International Registry of Aortic Dissection (IRAD) to delineate the prevalence, presentation, management, and outcomes of acute IMH by comparing these patients with those with classic aortic dissection (AD). Fifty-eight (5.7%) patients had IMH, and this cohort tended to be older (68.7 versus 61.7 years; $P<0.001$) and more likely to have distal aortic involvement (60.3% versus 35.3%; $P<0.001$) compared with 952 patients with AD. Patients with IMH described more severe initial pain than did those with AD but were less likely to have ischemic leg pain, pulse deficits, or aortic valve insufficiency; moreover, they required a longer time to diagnosis and more diagnostic tests. Overall mortality of IMH was similar to that of classic AD (20.7% versus 23.9%; $P=0.57$), as was mortality in patients with IMH of the descending aorta (8.3% versus 13.1%; $P=0.60$) and the ascending aorta (39.1% versus 29.9%; $P=0.34$) compared with AD. IMH limited to the aortic arch was seen in 7 patients, with no deaths, despite medical therapy in only 6 of the 7 individuals. Among the 51 patients whose initial diagnostic study showed IMH only, 8 (16%) progressed to AD on a serial imaging study.

Conclusions—The IRAD data demonstrate a 5.7% prevalence of IMH in patients with acute aortic syndromes. Like classic AD, IMH is a highly lethal condition when it involves the ascending aorta and surgical therapy should be considered, but this condition is less critical when limited to the arch or descending aorta. Fully 16% of patients have evidence of evolution to dissection on serial imaging. **(*Circulation*. 2005;111:1063-1070.)**

Key Words: aorta ■ hemorrhage ■ statistics ■ mortality

Acute aortic syndromes, a highly morbid set of conditions characterized by the sudden onset of thoracic pain, includes classic aortic dissection (AD) and intramural aortic hemorrhage with a variable clinical course.[1–3] Although there is consensus about the definition and treatment of classic AD,[1,4] the approach to acute intramural hematoma (IMH) of the aorta remains elusive.[5] Much of the controversy stems from an incomplete knowledge of its natural history.[6–9]

The International Registry of Aortic Dissection (IRAD) represents a unique multicenter, collaborative effort developed to elucidate the presentation, evaluation, management, and outcomes of patients with acute aortic syndromes.[2] Because of the registry's volume, (n>1000), IRAD represents a unique resource to explore controversies in acute aortic syndromes. In the present study, we explored the clinical presentation, management, and hospital outcomes of acute IMH.

Methods

IRAD Registry

The inception and structure of IRAD have been described previously.[2,10,11] In brief, 18 large referral centers in 6 countries agreed to participate in the ongoing registry, established in 1996. The main purpose of IRAD was to assess etiologic factors, modes of presentation, clinical features, treatment, and hospital outcomes of patients with acute AD. Beginning on January 1, 1996, consecutive patients with AD (both type A and type B) presenting to IRAD sites were enrolled. Patients were identified either prospectively at presentation or retrospectively by searching hospital discharge diagnosis records and/or surgery, pathology, and ultrasound databases. Diagnosis was suspected on the basis of the history and physical examination and was confirmed by imaging study, visualization at surgery, and/or postmortem examination.[2]

Patient Selection

Patients with acute aortic syndromes enrolled between January 1, 1996, and November 19, 2001, were analyzed and separated into those with "true IMH" and those with "classic AD." IMH was

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defined strictly as an aortic wall hematoma without a demonstrable intimal flap on imaging study and no radiologically apparent intimal tear, and acute AD was defined by visualization of an intimal flap separating 2 lumina; the acute stage was confined to the initial 14 days after symptom onset.[2] Although hemorrhage into the aortic media occurs in both disorders, an intimal tear with resultant false lumen is not present in IMH. Instead, hemorrhage occurs within the aortic wall due to either rupture of the vasa vasorum or, less commonly, an atherosclerotic, penetrating aortic ulcer.

Data Collection

Data were acquired with the use of a standardized form that included fields for patient demographics, history, clinical presentation, physical findings, imaging study results, details of medical and surgical treatment, and outcomes. Completed data entry forms were forwarded by the participating IRAD sites to the coordinating center at the University of Michigan. Data forms were reviewed for internal validity and were scanned electronically into an Access database.

Clinical Events

Chart review was used to identify in-hospital clinical events and (in-hospital) death. Standard American College of Cardiology/American Heart Association definitions were used to document various in-hospital complications. Abrupt-onset pain was defined as sudden, severe pain in the chest, neck, or back, with maximum intensity at onset that brought the patient to medical attention. An ECG was noted as abnormal when it showed pathological Q waves, ST-segment deviation $\geq$2 mm, T-wave inversions, left bundle-branch block, or left ventricular hypertrophy.

Data Analysis

Presentation, evaluation, management, and outcomes among several cohorts in IRAD were compared between classic AD and patients without classic AD on initial imaging. IMH was considered when identified on the first or second imaging study and lack of any double lumen and/or intimal flap. Patients with true IMH were compared with those with classic AD with regard to presentation, physical findings, treatment, and outcomes.

Furthermore, the relationship between anatomic location of aortic involvement and outcome was analyzed for IMH of the ascending aorta and the aortic arch.[12,13] Finally, the diagnostic evolution was carefully tracked in patients whose initial imaging findings either showed IMH or were nondiagnostic. Evidence of progression allowed us to estimate the frequency and time course of IMH progression to AD.

Statistical Analysis

Summary statistics are presented as frequencies and percentages, mean$\pm$SD, or median and interquartile ranges. In all cases, missing data were not defaulted to negative, and denominators reflect only those cases reported. Nominal variables were compared by means of χ^2 tests and 2-sided Fisher exact tests when appropriate. Continuous univariate variables were tested by means of 2-sided Student t tests. By use of the Cochran-Armitage trend test, hospital mortality was related to the location of the central segment of IMH as seen on tomographic images.

Results

Among 1010 patients, 58 (5.7%) met the strict criterion of acute IMH. As shown in Table 1, patients with IMH tended to be older than those with classic AD ($P<0.001$), and the majority (60%) of IMHs were located in the descending aorta. Abrupt onset of severe chest or back pain was the most common presenting symptom for both IMH and AD (Table 2), and time from symptom onset to presentation was similar for IMH and classic AD. However, establishing the diagnosis of IMH required more time and a greater number of imaging tests then did classic AD (Table 3). As expected, aortic insufficiency was seen infrequently in IMH, and pulse deficits (and associated ischemic pain) were less common than in AD (Table 2).

Compared with patients with AD, patients with IMH were more likely to have a normal ECG (45.6% versus 29.8%; $P=0.012$), and no patient with an acute IMH had an acute myocardial infarction (Table 4). Patients with acute IMH were likely to have a smaller aortic diameter

TABLE 1. Demographics, Location, and History of Patients With AD and IMH*

Variable	Classic AD (n=952)	IMH (n=58)	P
Type			<0.001
A	616/952 (64.7)	23/58 (39.7)	
B	336/952 (35.3)	35/58 (60.3)	
Age, y (mean±SD)	61.7±14.3	68.7±10.4	<0.001
Sex			0.16
Female	294/952 (30.9)	23/58 (39.7)	
Male	658/952 (69.1)	35/58 (60.3)	
White	747/870 (85.9)	51/52 (98.1)	0.17
Hypertension	661/930 (71.1)	45/58 (77.6)	0.29
Marfan syndrome	50/927 (5.4)	0/58 (0.0)	0.11
Diabetes	42/916 (4.6)	3/56 (5.4)	0.74
Aortic valve disease	80/901 (8.9)	1/57 (1.8)	0.08
Bicuspid aortic valve (n=548)	16/521 (3.1)	1/27 (3.7)	0.58
Prior coronary artery bypass graft	51/895 (5.7)	3/56 (5.4)	>0.99

Values are n/N (%) or mean±SD.

*Missing data were not defaulted to negative, and denominators reflect only those cases reported.

TABLE 2. Presenting Symptoms and Signs of Patients With AD and IMH*

Variable	Classic AD (n=952)	IMH (n=58)	P
History			
Chest pain	702/929 (75.6)	44/58 (75.9)	0.96
Back pain	494/911 (54.2)	37/58 (63.8)	0.16
Pain rated as worst ever	157/786 (20.0)	19/48 (39.6)	0.001
Abdominal pain	256/908 (28.2)	18/58 (31.0)	0.64
Pain migration	162/891 (18.2)	9/58 (15.5)	0.61
Leg pain	96/888 (10.8)	1/58 (1.7)	0.027
Abrupt onset	794/910 (87.3)	49/56 (87.5)	0.96
Physical exam			
Hypertensive	415/911 (45.6)	31/58 (53.4)	0.24
Hypotensive	103/914 (11.3)	4/58 (6.9)	0.30
Murmur of aortic regurgitation	304/872 (34.9)	7/57 (12.3)	<0.001
Pulse deficits	236/822 (28.7)	9/54 (16.7)	0.056
Ischemic lower extremity	80/900 (8.9)	2/56 (3.6)	0.22

Values are n/N (%).

*Missing data were not defaulted to negative, and denominators reflect only those cases reported.

TABLE 3. Time Delays in Presentation and Diagnosis of Patients With AD and IMH*

	Classic AD (n=952)	IMH (n=58)	P
Hours from symptom onset to presentation			0.58*
<4	458/663 (67.9)	28/45 (62.2)	0.43
4–24	118/663 (17.8)	8/45 (17.8)	>0.99
>24	95/663 (14.3)	9/45 (20)	0.30
Hours from symptom onset to diagnosis			0.04†
<4	206/732 (28.1)	7/49 (14.3)	0.04
4–24	292/732 (39.9)	19/49 (38.8)	0.88
>24	234/732 (32.0)	23/49 (46.9)	0.03

Values are n/N (%).

*Missing data were not defaulted to negative, and denominators reflect only those cases reported.

†Overall *P* value.

than were patients with classic AD and demonstrated fewer abnormalities on chest films (maximum average ascending aortic width, 4.39±1.12 cm versus 4.89±1.36 cm; $P=0.016$; Table 4).

Importantly, patients with IMH involving the ascending aorta were less likely to receive surgery compared with patients with AD (14 of 23 with IMH had surgery [60.9%] versus 508 of 616 [82.5%] with AD; $P=0.023$). In general, descending aortic IMH was managed without surgery in 31 of 35 (88.6%) cases (Table 5), including 2 patients who underwent endovascular stent grafting.

TABLE 4. Test Results of Patients With AD and IMH*

Variable	Classic AD (n=952)	IMH (n=58)	P
ECG findings			
Normal	271/908 (29.8)	26/57 (45.6)	0.012
Acute MI (new Q waves and/or ST-segment elevation)	42/848 (5.0)	0/55 (0.0)	0.10
Chest x-ray findings			
Normal	127/847 (15.0)	13/57 (22.8)	0.12
Widened mediastinum	523/846 (61.8)	28/55 (50.9)	0.11
Abnormal cardiac contour	197/824 (23.9)	8/55 (14.5)	0.11
Pleural effusion	148/820 (18.0)	8/56 (14.3)	0.48
Noninvasive imaging			
No. of imaging tests/patient (mean±SD)	1.84±0.75	2.05±0.71	0.032
Initial imaging			
CT scan	584/927 (63.0)	41/57 (71.9)	0.16
TEE scan	302/927 (31.7)	16/57 (27.6)	0.51
Widest ascending aortic diameter, cm (mean±SD)	4.89±1.36	4.39±1.12	0.016

Values are n/N (%) or mean±SD. ECG indicates electrocardiogram; MI, myocardial infarction; CT, computed tomography; and TEE, transesophageal echocardiography.

*Missing data were not defaulted to negative, and denominators reflect only those cases reported.

TABLE 5. Treatment of Patients With AD and IMH*

Variable	Classic AD	IMH	P
Overall	n=952	n=58	
Medical	342/952 (35.9)	38/58 (65.5)	<0.001
Surgical	570/952 (59.9)	18/58 (31.0)	<0.001
Percutaneous	40/952 (4.2)	2/58 (3.4)	>0.99
Ascending aorta	n=616	n=23	
Medical	105/616 (17.0)	9/23 (39.1)	0.012
Surgical	508/616 (82.5)	14/23 (60.9)	0.023
Percutaneous	3/616 (0.5)	0/23 (0.0)	>0.99
Descending aorta	n=336	n=35	
Medical	237/336 (70.5)	29/35 (82.9)	0.12
Surgical	62/336 (18.5)	4/35 (11.4)	0.30
Percutaneous	37/336 (11.0)	2/35 (5.7)	0.56

Values are n/N (%).

*Missing data were not defaulted to negative, and denominators reflect only those cases reported.

The overall hospital mortality for IMH was similar to that of classic AD (20.7% versus 23.9%; $P=0.57$; Table 6). In particular, IMH of the ascending aorta carried an in-hospital mortality of 39.1%, nonsignificantly higher than that of AD, a condition more frequently treated surgically. Mortality for IMH involving the ascending aorta was 42.9% with surgical therapy and 33.3% with medical therapy, as opposed to a mortality rate of 24.2% with surgical therapy in classic AD involving the ascending aorta and 56.5% with medical therapy alone. Figure 1 demonstrates an association between increasing hospital mortality and the proximity of IMH to the aortic valve, irrespective of medical or surgical treatment (Table 7). Table 8 describes the cause of in-hospital death in patients with IMH, and Table 9 compares the severity of disease in IMH patients treated medically or with surgical therapy. In the overall IMH cohort, the incidence of hypotension, cardiac tamponade, ischemic spinal cord damage, and pericardial effusion was higher in the surgical group. In patients with type A IMH, only the incidence of pericardial effusion was significantly higher in the surgical group. In

TABLE 6. Hospital Outcomes of Patients With AD and IMH*

Variable	Classic AD (n=952)	IMH (n=58)	P
Overall hospital mortality	228/952 (23.9)	12/58 (20.7)	0.57
Type A			
Overall	184/616 (29.9)	9/23 (39.1)	0.34
Medical	61/108 (56.5)	3/9 (33.3)	0.30
Surgical	123/508 (24.2)	6/14 (42.9)	0.12
Type B			
Overall	44/336 (13.1)	3/35 (8.3)	0.60
Medical	26/274 (9.5)	3/31 (9.7)	>0.99
Surgical	18/62 (29.0)	0/4 (0.0)	0.57

Values are n/N (%).

*Missing data were not defaulted to negative, and denominators reflect only those cases reported.

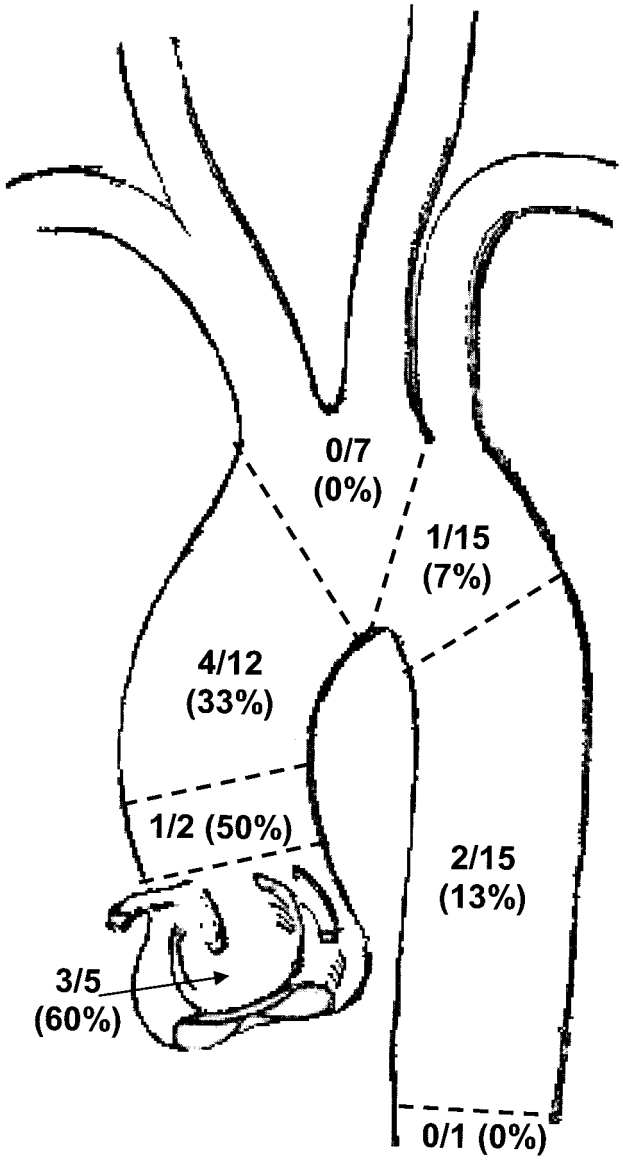

Figure 1. In-hospital mortality for IMH according to site of origin. IMH was defined after first imaging test failed to demonstrate IMH or dissection but second test confirmed IMH or first study showed IMH but no evidence of dissection. For 1 of the 58 patients described in text, presumed site of origin was not identified by investigator.

type B IMH, the incidence of hypotension and ischemic spinal cord damage was higher in the surgical group.

Figure 2 shows the progression of diagnosis in patients with suspected IMH. A total of 58 patients eventually met the criteria for diagnosis of IMH, and 8 of these subsequently developed classic AD on serial imaging. If diagnosis was based on initial imaging findings only, 7 of the 50 patients would have been missed. Eventually, 8 patients with an apparent IMH on initial imaging developed AD, and 7 patients with an uncertain diagnosis on initial imaging demonstrated evidence of IMH on a second study. Long-term follow-up at a mean duration of 1.6±1.2 years was available for 27 of the 46 patients with IMH. Although not statistically significant, patients with type A IMH had a trend toward higher mortality compared with patients with classic AD.

TABLE 7. Mortality in True IMH by Location and Management

	Management	
Location of Hematoma	Medical, n (%)	Surgical, n (%)
Root	1/1 (100.0)	2/4 (50.0)
Sinotubular junction	0/0 (. . .)	1/2 (50.0)
Ascending	2/5 (40.0)	3/8 (37.5)
Arch*	0/6 (0.0)	0/1 (0.0)
Left subclavian†	1/14 (7.1)	0/1 (0.0)
Descending	2/13 (15.4)	0/2 (0.0)
Abdominal	0/1 (0.0)	0/0 (. . .)

Values are n/N (%).

*Of the 7 arch dissections, 2 were labeled type A and 5 were labeled type B by the site investigator.

†One left subclavian dissection extended proximally and was coded as type A.

Discussion

Both the prevalence and natural history of acute IMH of the aorta remain difficult to determine.[13–15] IRAD provides a unique opportunity to examine IMH within the context of acute aortic syndromes. The prevalence of IMH among patients with nontraumatic acute aortic syndromes in IRAD is ≈6%. This figure is generally lower than that reported in other series (10% to 50%)[5,14–18] and thus lower than previously thought.[5,6,8,9] This may reflect the degree to which the diagnosis was considered among patients with abnormal but nondiagnostic initial imaging studies. Conversely, a low prevalence of IMH in the IRAD registry may also be explained by the fact that IRAD centers are tertiary referral centers, and IMH either may have gone undiagnosed in primary and secondary centers or was diagnosed but not referred by these centers. With eventual transfer to a tertiary IRAD center, once classic AD was diagnosed, it is possible that a number of patients may have already progressed from IMH to AD. These cases would not qualify in our report as IMH but would rather be diagnosed as classic AD. Given the dynamic evolution of IMH and the difficulty of early diagnosis, serial diagnostic imaging tests undoubtedly improve diagnostic performance.

IMH affected the descending aorta in 60% of cases, whereas classic AD affected the ascending aorta in nearly 65% of cases. Because IMH is generally a more localized

TABLE 8. Cause of Death in IMH Patients (n=12)

	Management	
Cause of Death	Medical	Surgical
Type A		
Neurological	0	1
Visceral ischemia	0	1
Acute rupture	2	0
Type B		
Nonspecified	1	4
Visceral ischemia	1	0
Acute rupture	2	0

TABLE 9. Comparison of Age, Disease Severity, and Comorbidities in IMH Patients Treated Surgically or Medically

	Medical (n=40)	Surgery (n=18)	*P*
All IMH patients			
Age, y (mean±SD)	68.2±10.2	69.9±11.1	0.57
Myocardial ischemia	1/35 (2.9)	0/18 (0)	0.99
Mesenteric ischemia/infarction	1/35 (2.9)	1/18 (5.6)	0.99
Acute renal failure	2/35 (5.7)	0/18 (0)	0.54
Extension of dissection	2/35 (5.7)	1/18 (5.6)	0.99
Hypotension	3/35 (8.6)	7/18 (38.9)	0.02
Pericardial effusion	5/39 (12.8)	12/18 (66.7)	<0.001
Cardiac tamponade	0/35 (0)	5/18 (27.8)	0.003
Ischemic peripheral neuropathy	0/38 (0)	1/17 (5.9)	0.31
Ischemic spinal cord damage	0/38 (0)	3/17 (17.6)	0.03
Ischemic lower extremity	1/39 (2.6)	1/17 (5.9)	0.52
Coma/altered consciousness	2/39 (5.1)	1/17 (5.9)	0.99
Heart failure	2/38 (5.3)	1/17 (5.9)	0.99
Type A IMH patients (n=23)	n=9	n=14	
Age, y (mean±SD)	68.0±8.3	69.0±12.0	0.83
Myocardial ischemia	0/8 (0)	0/14 (0)	...
Mesenteric ischemia/infarction	1/8 (12.5)	0/14 (0)	0.36
Acute renal failure	0/8 (0)	0/14 (0)	...
Extension of dissection	2/8 (25)	0/14 (0)	0.12
Hypotension	2/8 (25)	4/14 (28.6)	0.99
Pericardial effusion	3/9 (33.3)	12/14 (85.7)	0.02
Cardiac tamponade	0/8 (0)	5/14 (35.7)	0.12
Ischemic peripheral neuropathy	0/9 (0)	1/13 (7.7)	0.99
Ischemic spinal cord damage	0/9 (0)	1/13 (7.7)	0.99
Ischemic lower extremity	0/9 (0)	1/13 (7.7)	0.99
Coma/altered consciousness	0/9 (0)	1/13 (7.7)	0.99
Heart failure	1/9 (11.1)	1/13 (7.7)	0.99
Type B IMH patients (n=35)	n=31	n=4	
Age, y (mean±SD)	68.3±10.8	73.0±7.3	0.41
Myocardial ischemia	1/27 (3.7)	0/4 (0)	0.99
Mesenteric ischemia /infarction	0/27 (0)	1/4 (25)	0.12
Acute renal failure	2/27 (7.4)	0/4 (0)	0.99
Extension of dissection	0/27 (0)	1/4 (25)	0.13
Hypotension	1/27 (3.7)	3/4 (75)	0.003
Pericardial effusion	2/30 (6.7)	0 (0)	0.99
Cardiac tamponade	0/27 (0)	0/4 (0)	...
Ischemic peripheral neuropathy	0/29 (0)	0/4 (0)	...
Ischemic spinal cord damage	0/29 (0)	2/4 (50)	0.01
Ischemic lower extremity	1/30 (3.3)	0/4 (0)	0.99
Coma/altered consciousness	2/30 (6.7)	0/4 (0)	0.99
Heart failure	1/29 (3.4)	0/4 (0)	0.99

Values are n/N (%) or mean±SD.

process, at least initially, it is less frequently associated with aortic valve insufficiency, pulse deficits, acute myocardial infarction, and aneurysmal dilation of the aorta. Nevertheless, despite limited aortic involvement, the overall mortality

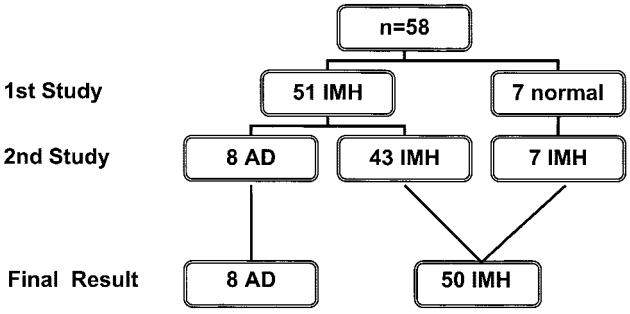

Figure 2. Evolution in diagnosis of IMH in IRAD. This figure illustrates challenge of diagnosing acute IMH as patients progress through multiple imaging tests. In IRAD, 51 patients had diagnosis of IMH without signs of classic AD after first imaging test (left half of figure). Of these 51, 8 patients (or 16%) demonstrated signs of classic AD on second testing, whereas 43 showed IMH only on second, and in some instances, on third or even fourth imaging studies. Right half of figure identifies 7 patients for whom diagnosis of acute aortic syndrome was strongly suspected, but initial imaging test showed neither classic AD nor findings of IMH and second testing revealed IMH. Not shown are patients whose initial imaging was nondiagnostic, but second imaging study showed classic AD.

remained high (20.7%). Although we do not have supporting data, it is possible that the high mortality may be related to rupture in medically managed, proximal IMH.

As with classic AD, the mortality rate of IMH involving the ascending aorta is a particular cause for concern, with 9 of 12 deaths seen in this cohort corroborating previous reports.[5,6] Previous observational reports favor surgery as the treatment of choice for ascending IMH, at least in white patients. However, the high mortality rate in both medically and surgically treated patients may be explained by delayed surgical management and may reflect a selection bias of the sickest patients for surgery. The relatively low mortality rate reported in Asian IMH patients may be due to a genetic factor or the fact that more limited IMHs were diagnosed and included in their series, because the percentage of IMH in Asia in suspected AD is much higher than in our study.[8,13,15,18] Hypothetically, it is possible that those receiving surgery may represent patients in whom initial watchful waiting was complicated by the development of classic AD with complications, although we do not have data to support this. Because the mortality of acute IMH involving the ascending aorta remains high (Figure 1) and nearly 16% of patients who had IMH on an initial imaging study had developed frank AD by the second imaging test (Figure 2), the IRAD data continue to favor consideration for timely surgical approach to such patients. This approach is supported by other reports that have suggested that IMH may progress to classic AD in as many as 28% to 47% of patients and may carry a risk of aortic rupture in 20% to 45% of cases.[4] Regression may occur but is less common and is not predictable in proximal IMH involving the ascending aorta.[16] On the other hand, acute IMH involving the descending aorta had an in-hospital mortality risk of <10%, similar to that seen with descending or type B AD (Table 6). The initial medical treatment for this condition appears justified.[14]

Acute IMH confined to the arch remains a controversial subject. In our series there were 7 such patients, and we observed no mortality in this small cohort, even though 6 of the 7 were managed medically. Currently, aggressive medical treatment alone, with a target heart rate <60 bpm and blood pressure <120/80 mm Hg and at least 1 additional initial imaging study followed by later serial imaging to exclude frank AD or early aneurysmal expansion, appears to be a reasonable strategy for management of such patients. Studies of larger numbers of patients and/or clinical trials will be needed to further delineate the optimal treatment and imaging sequence for this group of patients, although the current recommendations for medical therapy are supported by IRAD results.

Several prior studies, most of them single center and with small sample sizes, have evaluated the clinical features, management, and outcomes of patients with IMH. Song et al[19] studied 24 patients with IMH and suggested that the absence of continuous flow communication may explain a more favorable clinical course of IMH than for AD and that medical treatment with frequent imaging follow-up and timed elective surgery in cases with complications may be a rational option for patients with proximal IMH. In a larger series of 124 patients with IMH, Song et al[18] demonstrated that patients with aortic IMH had a high rate of resorption with medical treatment regardless of the affected site. Tittle et al[20] studied 19 patients with IMH and stated that because of the high early rupture rate, the frequency of radiographic worsening, and the documented occurrence of late rupture, surgical replacement of the aorta for these unstable vascular lesions was indicated, so long as the patient's comorbidities did not preclude surgical intervention. Ganaha et al[21] suggested that IMH caused by a penetrating ulcer was significantly associated with a progressive disease course, whereas IMH without a penetrating ulcer typically had a stable course, especially when limited to the descending thoracic aorta. von Kodolitsch et al[16] studied 66 patients with IMH and demonstrated that regardless of aortic diameter, IMH of the ascending aorta (type A) is at high risk for early progression, and thus, surgical repair should be performed without delay. Moizumi et al[22] studied 33 patients with type A IMH and suggested that 70% of type A IMHs could be managed expectantly and that >50% could be treated medically alone. Evangelista et al[23] monitored 50 patients with IMH clinically and by imaging techniques at 3, 6, and 12 months and annually thereafter and demonstrated that the most frequent long-term evolution of IMH is aortic aneurysm or pseudoaneurysm. In their analysis of 68 patients with IMH, Evangelista et al[17] demonstrated ascending aortic involvement as a significant predictor of early mortality. Complete regression without changes in aorta size is observed in one third of cases, and progression to classic AD is less common. A normal aortic diameter in the acute phase is the best predictor of IMH regression without complications, and the absence of echolucent areas and atherosclerotic, ulcerated plaque are associated with evolution to aortic aneurysm.[23] Motoyoshi et al[24] studied 36 patients with IMH and suggested that urgent surgical repair was not necessary for all type A IMH patients to achieve favorable surgical outcome with careful imaging follow-up. Moizumi et al[25] reported long-term outcomes for 95 cases of type A and type B IMH, showed that adverse events occur equally in both types of IMH of the aorta, and recommended close follow-up for at least 5 years because most IMHs of aorta-related events occur during this period.

TABLE 10. Long-Term Follow-Up of IMH Patients Compared With Patients With Classic AD

	IMH (n=27)*	Classic AD (n=418)	*P*
All IMH patients			
Death	7 (25.9)	66 (15.8)	0.18
New aneurysm or dissection	2 (7.4)	36 (8.6)	>0.99
New aortic insufficiency	0 (0.0)	13 (3.1)	>0.99
Acute hospitalization	2 (7.4)	44 (10.5)	>0.99
Type A only	n=8	n=256	
Death	3 (37.5)	33 (12.9)	0.08
New aneurysm or dissection	2 (25.0)	19 (7.4)	0.13
New aortic insufficiency	0 (0.0)	9 (3.5)	>0.99
Acute hospitalization	1 (12.5)	26 (10.2)	0.58
Type B only	n=19	n=162	
Death	4 (21.1)	33 (20.4)	>0.99
New aneurysm or dissection	0 (0.0)	17 (10.5)	0.22
New aortic insufficiency	0 (0.0)	4 (2.5)	>0.99
Acute hospitalization	1 (5.3)	18 (11.1)	0.70

Values are n (%).

*Of the 58 patients with IMH, 12 died in the hospital. Of the remaining 46 patients, long-term follow-up (1.6±1.2 years) was available in 27 patients.

Although these studies have helped elucidate the natural history and management of patients with IMH, they have been limited by the single-center nature of the analysis and relatively small sample sizes. Novel features of our analysis include the multicenter nature of the study, a strict imaging definition of IMH, and the ability to compare clinical outcomes with surgical and medical therapy across multiple centers. We provide a closer approximation of the true prevalence of IMH, an understanding of the relationship between anatomic location of aortic involvement and clinical outcome, and an estimation of the frequency and time course of IMH progression to classic AD.

Limitations

Because most clinical information in IRAD was obtained by chart review, the database is subject to referral and ascertainment bias common to retrospective registry analysis. Imaging and ECG interpretations were reported at each center, were considered diagnostic, and were not analyzed by a separate core laboratory. Because IRAD hospitals are tertiary referral centers, some IMHs may have escaped diagnosis at primary evaluation, resulting in transfer of only the more complicated cases of IMH or after progression to classic AD. Furthermore, the delay in IMH patients' arrival at IRAD centers may imply evolution of some of these cases to classic AD.

Although there is potential for some overlap in one or more of the articles from the individual registry centers, the

strength of this report lies in the cases obtained from 18 different centers that used a strict definition of IMH, wherein IMH was considered "true" when it was reported on the first or second image and there was no evidence of dissection, double lumen, and intimal flap. The single-center series by Evangelista et al[17] included a 10-year time period from January 1990 to December 2000 and thus, covered a different time frame from that of IRAD (January 1996 to November 2001). The Nienaber series[5] included 5 centers in Germany and Italy, only 2 of which provide data to IRAD. Therefore, although there is potential for minimal overlap, the cohort studied in this analysis is quite different from that of any previously published studies. Finally, conclusions drawn from the follow-up data must be made with great caution, because it is conceivable that many of the 40% of patients lost to follow-up may have died.

Conclusions

Acute IMH accounts for at least 6% of nontraumatic acute aortic syndromes. Involvement of the ascending aorta carries substantial mortality, and urgent or emergent operative intervention may be appropriate, whereas arch and descending IMH are less likely to be associated with an adverse outcome and a nonsurgical approach may be appropriate. However, it must be noted that mortality was high with both medical and surgical therapy in type A IMH in this series. Nearly 16% of patients who appear to have IMH on initial imaging show signs of progression to classic AD on a subsequent imaging study. We believe that a nonsurgical approach for patients with no complications and IMH limited to the arch or descending aorta is justified, especially when one or two diagnostic imaging studies have excluded involvement of the ascending aorta. The 26% mortality rate of patients with IMH surviving hospitalization at 1 year is a cause for concern and underscores the importance of appropriate longitudinal follow-up of these high-risk patients. We recommend follow-up imaging and examination at 1, 3, 6, 9, and 12 months after discharge and annually thereafter, similar to that for patients with classic AD.

Appendix

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