Keynote Lecture Series

Acute aortic syndrome

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Acute aortic syndrome (AAS) is a term used to describe a constellation of life-threatening aortic diseases that have similar presentation, but appear to have distinct demographic, clinical, pathological and survival characteristics. Many believe that the three major entities that comprise AAS: aortic dissection (AD), intramural hematoma (IMH) and penetrating aortic ulcer (PAU), make up a spectrum of aortic disease in which one entity may evolve into or coexist with another. Much of the confusion in accurately classifying an AAS is that they present with similar symptoms: typically acute onset of severe chest or back pain, and may have similar radiographic features, since the disease entities all involve injury or disruption of the medial layer of the aortic wall. The accurate diagnosis of an AAS is often made at operation. This manuscript will attempt to clarify the similarities and differences between AD, IMH and PAU of the ascending aorta and describe the challenges in distinguishing them from one another.

Keywords: Acute aortic syndrome (AAS); aortic dissection (AD); intramural hematoma (IMH); penetrating aortic ulcer (PAU)

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Introduction

Acute aortic syndrome (AAS) is a term used to describe a constellation of life-threatening aortic diseases that have similar presentation, but appear to have distinct demographic, clinical, pathological and survival characteristics (1). Many believe that the three major entities that comprise AAS: aortic dissection (AD), intramural hematoma (IMH) and penetrating aortic ulcer (PAU), make up a spectrum of aortic disease in which one entity may evolve into or coexist with another. Much of the confusion in accurately classifying an AAS is that they present with similar symptoms: typically acute onset of severe chest or back pain, and may have similar radiographic features, since the disease entities all involve injury or disruption of the medial layer of the aortic wall. The accurate diagnosis of an AAS is often made at operation. This manuscript will attempt to clarify the similarities and differences between AD, IMH and PAU of the ascending aorta and describe the challenges in distinguishing them from one another (*Video 1*).

Aortic dissection (AD)

Acute AD was first described by Morgagni in 1761 after the death of King George II of Great Britain (2). It is a highly lethal disease that has an incidence of 2.6 to 3.5 cases per 100,000 person-years (3). AD compromises the majority of AAS. A study from the International Registry of Acute Aortic Dissection (IRAD) revealed that two-thirds of the patients who present with AD are male, with an average age of 63 years, whereas women present with an average age of 67 years (4). Pathologically, AD is defined as a separation within the medial layer of the aortic wall caused by an intimal tear. As blood enters the medial layer, the division of the aortic wall can progress in either direction, antegrade or retrograde. The result is creation of true lumen and a false lumen in which higher mean pressure in the false lumen may cause dynamic or static compression and occlusion of the true lumen with resultant malperfusion of branches of the aorta and end-organ ischemia (5). The risk factors associated with AD include hypertension,

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atherosclerosis, prior cardiac surgery, known aneurysm and Marfan syndrome. Patients less than 40 years of age have risk factors that include Marfan syndrome, bicuspid aortic valve or prior surgery of the aorta (4,6). Dissection of the ascending aorta is two to three times more common than that of the descending aorta (6,7).

AD is classified according to the location and extent of involvement of the aorta. In the Stanford classification, a type A AD involves the ascending aorta and typically progresses distally to involve various extents of the arch and thoracoabdominal aorta. A Stanford type B AD involves the descending thoracic or thoracoabdominal aorta distal to the origin of the left subclavian artery (8). In the DeBakey classification of AD, a type I AD involves the ascending aorta, arch and descending thoracic aorta and may progress into the abdominal aorta. A DeBakey type II AD is confined to the ascending aorta. A DeBakey type IIIA AD involves the descending thoracic aorta distal to the left subclavian artery and proximal to the celiac artery. A DeBakey type IIIB dissection involves the thoracic and abdominal aorta distal to the left subclavian artery (9).

Acute onset of severe chest or back pain is the most common symptom of acute AD occurring in 80% to 90% of patients. The classic description of tearing or ripping pain or proximal to distal migratory pain may not be present (4). Other symptoms include syncope, neurological deficit including stroke and paraplegia, acute congestive heart failure, myocardial ischemia, lower extremity ischemia, abdominal pain and shock (4,10). The classic physical finding of murmur of aortic insufficiency occurs only in 44%. A pulse deficit occurs only in 20–30% of patients with acute type A AD. Hypertension is present in only one-third with type A AD (4,6).

Complications of acute AD are related to malperfusion of aortic branches, incompetency of the aortic valve and rupture (11). Malperfusion of the coronary arteries in type A AD presents with myocardial ischemia and myocardial dysfunction of the affected coronary territories. Dissection into the aortic root may involve the commissures of the aortic valve causing poor leaflet coaptation leading to aortic insufficiency and signs of congestive failure. Pericardial effusion and tamponade from AD may present with hypotension and shock. Malperfusion of the brachiocephalic vessels results in cerebral ischemia, malperfusion of the visceral vessels results in mesenteric ischemia and malperfusion of the iliac and femoral vessels results in lower extremity ischemia. Paraplegia as a presenting symptom can be explained by malperfusion of the intercostal arteries arising from the descending thoracic aorta and/or the major collateral vessels that serve the spinal cord collateral network, namely the internal iliac and vertebral arteries (12). Malperfusion in type A AD has significantly greater mortality (31–44%) and complication rate even with additional surgical procedures to alleviate the malperfusion (13-15). Rupture of the dissected aorta is fortunately uncommon, but is an ominous complication with certain mortality unless swift surgical intervention is undertaken.

Imaging for AAS (and acute AD in particular) is critical to determine the type of AAS, elucidate the extent and location of the pathology and identify complications of the pathology. Multi-detector computed tomographic angiography (MD-CTA) is currently the diagnostic imaging modality of choice in an otherwise stable patient. It is highly sensitive and specific in determining the diagnosis of acute AD. Ideally, the MD-CTA should have arterial phase imaging, electrocardiographic-gating and include the entire aorta, iliac and femoral vessels. Other modalities such as transthoracic echocardiography (TTE) or transesophageal echocardiography (TEE) may be useful in the unstable patient who cannot tolerate transport to the radiological suite. Both TTE and TEE can provide important information such as aortic valve insufficiency, pericardial effusion, tamponade and regional wall motion abnormalities. However, both TTE and TEE have limited views of the aorta and cannot image the entire aorta. Magnetic resonance imaging and catheter angiography are seldom used as an initial radiological imaging study for acute AD (16).

Currently, there are no biomarkers that can provide a diagnosis of acute AD. The D-dimer, if elevated and greater than 500 μg/L, may provide insight into the severity and extensiveness of the AD, but cannot exclude the diagnosis of pulmonary embolism (17). Coronary angiography is generally not recommended as a diagnostic or adjunctive study for acute AD, however there is a significant minority of patients with acute coronary syndrome who are found to have acute AD at coronary angiography.

The treatment of acute AD is dependent upon the location of the involved aorta and the presence of complications of the AD. Medically managed acute type A AD has a mortality of 20% at one day, 30% at 2 days, 40% at 7 days and 50% at 30 days (4). Therefore, type A AD typically requires emergent surgical treatment which involves replacement of the ascending aorta, resection of intimal tears and aneurysmal aorta, and either restores competency to or replaces the aortic valve. A recent IRAD study, shows that 87–90% of acute type A AD are

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treated surgically with only 7–8% medically. The in-hospital surgical mortality for type A AD in IRAD remains approximately 20% over the past 20 years (6).

Intramural hematoma (IMH)

IMH is defined as a hematoma within the medial layer of the aortic wall without the presence of intimal injury. It was first described by Krukenberg in 1920 at necropsy in which he found a "dissection without intimal tear" (18). The classical theory of pathogenesis of IMH is that of "rupture of the vasa vasorum" which results in bleeding within the media (19). This theory has not been validated scientifically (20). The distinction between IMH and AD is controversial, as some believe that all IMH are AD with thrombosis of the false lumen, and that an intimal tear is always present but not identified and therefore, IMH does not exist (21). Pathologically, there is a difference in the location of the cleavage plane within the aortic media of an IMH when compared to an AD. The outer media (toward the adventitia) of the IMH is thinner than that of AD (22). This difference may explain the higher risk of rupture and progression to AD for IMH (23-25). IMH more commonly involves the descending aorta whereas AD more commonly involves the ascending aorta (24,26,27). The mechanism by which an IMH is created is still not clearly elucidated.

To add to the controversy, surgical interrogation and higher resolution computed tomography (CT) imaging has discovered intimal defects in approximately 70% of initially diagnosed IMHs (28,29). This suggests that a majority of radiographically-appearing IMH are in fact AD with undetected intimal tears and thrombosis of the false lumen. These studies also suggest that our studies of IMH may not have "pure" data and that our knowledge of IMH is to be interpreted carefully.

The demographic of IMH is different than that of AD. Patients with IMH are older, more commonly present with aortic aneurysm and rarely occur in patients with Marfan syndrome (22,24,25,27). Females can have IMH more often than males in contradistinction to AD (23,27). Clinically, type A IMH is more often associated with pericardial tamponade and periaortic hematoma (23,24,27,29,30). And several studies have noted a higher risk of rupture than AD (26% *vs.* 8%) and/or progression to frank AD (23-25). There appears to be a greater prevalence of IMH in Chinese, Japanese and Koreans *vs.* Americans and Europeans (28–32% *vs.* 4–11%) (26,27,30-32). Additionally, there is a difference in efficacy of medical management of IMH in Japanese and Koreans, in which medical management has mortality rates less than that of AD treated surgically or otherwise (27,30). Interestingly, medical management of IMH in Chinese patients have similar outcomes to that of American and Europeans patients, high mortality (32%) and high risk of adverse outcomes (40%) (32). It is interesting to note that the outcome of medical management of acute type A AD does not differ between the Eastern and Western populations.

The entity called IMH is different from AD in terms of its pathologic, anatomic, demographic, ethnic and clinical characteristics, which adds to the confusion of the optimal treatment of type A IMH.

As with other AAS, the ideal imaging technique for IMH is rapidly acquired, high resolution, detailed and studies the entire thoracic and thoracoabdominal aorta. MD-CTA with intravenous contrast is should be the imaging study of choice for AAS. Radiographic features of a type A IMH shows a crescent-shaped thickening of the aortic wall, absence of intimal flap and absence of compression of the patent lumen. Periaortic hematoma is more common in IMH versus AD. There is a pericardial effusion in 60–70% of type A IMH, more common than in AD (22,24,26,27). TTE and TEE may not be diagnostic for IMH. The MD-CTA radiographic appearance of an IMH and an AD with complete thrombosis of the false lumen and no apparent intimal tear is identical.

The clinical presentation of IMH is similar to AD, however pain is often more common in IMH (22,24,26). Malperfusion and aortic valvular insufficiency is less common in IMH. As many as 10% of IMH may completely resolve, however 8–16% will evolve in to frank AD (23,24,26).

The medical treatment of type A IMH in Western countries has high mortality (33–40%) which has prompted an aggressive surgical strategy to avoid rupture and conversion to AD (24,25,30). Mortality for surgically treated IMH is similar to that of AD (24,25,27,30). In some Eastern countries, an initial medical approach to type A IMH has emerged with urgent surgery performed on patients with complications of the IMH. The in-hospital mortality of medical management in Song's study was 7.9%. There was no difference in mortality between the patients who did not have complicating features of the IMH and continued to have medical therapy and those who required surgery (6.1% *vs.* 8.8%). The overall hospital mortality of IMH was less than that of AD (27). The proportion of patients who eventually required urgent surgery was 32% in Song's study and similar to other reported series (27,31,33). Song and others identified

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aortic diameter (>50–55 mm) and thickness of the IMH (>10–16 mm) as risk factors for death, rupture and conversion to AD in patients who are medically treated (27,33).

It appears that there is a difference in the disease process and behavior of IMH in regards to ethnicity. The proportion of AAS that is diagnosed as IMH is larger in Asians *vs.* Americans and Europeans (31). Some Asians (Japanese and Koreans) can be managed initially without surgery and surgery is reserved for those who develop complications of the IMH with very good outcomes (27,33). However, in North Americans, Europeans and Chinese, the mortality of medical management is prohibitively high and emergent or urgent surgical intervention is recommended (24,25,30,32).

Penetrating aortic ulcer (PAU)

PAU is a term initially described by Shennan in 1934 to and further defined by Stanson in 1986 to describe an ulcer-like lesion that erodes through the internal elastic lamina of the aortic wall and can allow hematoma formation within the media (34,35). PAUs account for 2–7% of AAS (36) and may be the least understood of the triad. PAUs are intimately associated with atherosclerosis of the aorta (35). The vast majority is located in the descending thoracic aorta (85–95%) and is much less common in the ascending aorta and arch (36-41). There is an association of PAU with the term "IMH" since there can be concomitant hematoma within the media which may portend a higher risk of aortic complication (41). However, by definition, the hematoma associated with a PAU cannot be an IMH since there is violation of the intima. Furthermore, the term "ulcer-like projection" or ULP is another term used in conjunction with "IMH" to describe a PAU with medial thrombosis. PAUs can proceed to frank AD, but are thought to be the lead point in less than 5% of all AD (34,40).

Patients with PAUs are older (aged in their 70s) and have risk factors that are associated with atherosclerosis including hypertension, hyperlipidemia, coronary artery disease, tobacco abuse and infrarenal abdominal aortic aneurysms (37-39,41). The symptomatic PAUs present similarly to other AAS with pain. The risk of rupture of a type A PAU may be as high as 33% to 40% (23,37). Asymptomatic ascending and arch PAUs do not appear to follow the same benign natural history as asymptomatic descending or thoracoabdominal PAUs (23,37,39,41).

Radiographic imaging of PAUs reveal an ulcer-like lesion that penetrates the aortic wall to varying degrees causing hematoma formation within the media, pseudoaneurysm or rupture as it penetrates through the adventitia. PAU with medial thrombosis confers a higher risk profile, however PAUs without medial thrombosis are more common in the ascending aorta (41).

The treatment of type A PAU is surgical owing to its natural history and predilection for rupture. Even asymptomatic ascending or arch PAUs should be managed operatively. Graft replacement of the ascending aorta is the standard treatment of a PAU of the ascending aorta. Transverse arch PAUs can be managed by open graft replacement or endovascular techniques often with brachiocephalic vessel debranching.

Conclusions

AAS of the ascending aorta is a highly lethal triad of aortic diseases. AD is the most common and still carries a significant mortality even when surgically treated. The medical management of type A AD is reserved for those who would not survive the operation. AD presenting with visceral or cerebral malperfusion carries a high mortality, however should not discourage immediate operative repair. IMH is an entity that is not well understood mechanistically and is difficult to correctly identify preoperatively. Many radiographic IMHs are AD with thrombosis of the false lumen. However, IMH appears to be a distinct entity with different demographics, clinical characteristics and optimal treatment strategies that may have an ethnic or genetic basis. PAUs of the ascending aorta are uncommon, but are thought to follow a malignant clinical course even when asymptomatic.

The treatment of type A AAS is surgical. However, there is compelling evidence to suggest that type A IMH in Korean and Japanese patients is best managed medically with surgical intervention reserved for those who develop complications. Over 30% of Japanese and Korean patients treated medically will eventually require surgery.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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