The International Registry of Acute Aortic Dissection (IRAD) was established in 1996, enrolling patients at large referral centres worldwide. It represents a unique opportunity to assess the current presentation, management and outcome of acute aortic syndrome (AAS). The IRAD is an observational registry with more than 1,500 patients enrolled at 21 tertiary centres in six countries. Collected data forms included more than 290 variables analysed by the co-ordinating centre at the University of Michigan. The IRAD registry provides new and valuable information regarding demographics, presenting symptoms and signs, diagnostic imaging, management and outcome of AAS.

Demographics and Risk Factors
The most common predisposing factor for AAS in the IRAD series was hypertension (72%). A history of atherosclerosis was present in 31% of patients and a history of cardiac surgery in 18%. In the total registry, 5 and 4% of cases of acute aortic dissection were thought to be related to Marfan’s syndrome and iatrogenic causes, respectively.

Analysis of young patients (<40 years of age) with dissection revealed that younger patients were more likely to have a history of hypertension (34%) or atherosclerosis (1%), but were less likely to have Marfan’s syndrome, bicuspid aortic valve and/or prior aortic surgery. Thirty-two per cent of patients with type A AAS were aged >70 years. Fewer elderly than younger patients were managed surgically (64 versus 86%; p<0.0001). In-hospital mortality was higher among older patients (43 versus 28%; p=0.006). Logistic regression analysis identified age >70 years as an independent predictor of hospital death for acute type A dissection.

Although less frequently affected by AAS (32%), women were significantly older and were diagnosed later than men. In-hospital complications of hypotension and tamponade occurred with greater frequency in women, resulting in higher in-hospital mortality compared with men (30 versus 21%; p=0.001). After adjustment for age and hypertension, mortality was higher among women than among men: type A dissection was associated with a higher surgical mortality of 32% compared with 22% in men.

Compared with those without Marfan syndrome, those with the syndrome (5%) were considerably younger (35±12 versus 64±13 years; p<0.001) and had a higher prevalence of type A aortic dissection (76 versus 62%; p=0.04), as well as a lower prevalence of intramural haematoma (2 versus 11%; p=0.03). Like other cardiovascular conditions, AAS exhibits significant circadian and seasonal/monthly variations. A significantly higher frequency of AAS occurred from 6.00am to 12.00pm compared with other time periods. On the other hand, the frequency of AAS was significantly higher during colder months, with a peak in January (p<0.001). However, seasonal/monthly variations were observed only among patients aged <70 years, those with type B AAD and those without hypertension or diabetes.

Clinical Presentation
The clinical manifestations of AAS are diverse and overlap, with a broad differential diagnosis requiring a high clinical index of suspicion to pursue and aggressively treat this disorder. Patients with aortic dissection typically present a cataclysmic onset and chest and/or back pain of a blunt, sometimes radiating nature. However, in contrast to classic teaching, ‘tearing’, ‘ripping’ or ‘migratory’ were not common descriptors of pain in IRAD. Chest pain was significantly more common in patients with type A than type B dissections (79 versus 63%), whereas both back pain (64 versus 47%) and abdominal pain (43 versus 22%) were significantly more common in type B dissection. Hypertension at the time of presentation was more frequent in type B than in type A dissection (70 versus 36%).

Syncope is a well-recognised symptom of acute aortic dissection, often indicating the development of dangerous complications, such as cardiac tamponade, obstruction of cerebral vessels or activation of cerebral receptors. Syncope was reported in 13% of patients in IRAD. These patients were more likely to die in the hospital (34 versus 23% of those without syncope) and were more likely to have cardiac tamponade, stroke, neurological deficits and a proximal dissection. Pulse deficits have also been studied in IRAD. A pulse deficit has been described in 30% of patients with an acute type A dissection compared with 21% of those with type B dissection. These patients have a higher rate of inhospital complications and mortality than those without a pulse deficit.

In another study from IRAD, the group of patients presenting with predominantly abdominal pain (5%) was analysed. These patients experienced higher mortality than those with more typical symptoms (10 versus 8%; p=0.02). This emphasises the atypical symptomatology in some patients and the possibility for acute aortic dissection to mimic other disorders such as stroke, myocardial infarction, vascular embolisation and abdominal pathology. Thus, diagnosis of this disease requires a high index of suspicion of an aortic dissection in patients with related risk factors.

Insights from the International Registry of Acute Aortic Dissection – What Have We Learned?

a report by

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Hypertension

Diagnostic Strategies

Electrocardiogram
This test should be performed on all patients as it helps to differentiate pain from acute myocardial infarction, for which treatment may include anticoagulation, in contrast to aortic dissection, where this therapy would be contraindicated. A normal electrocardiogram (ECG) was seen in one-third of patients, and ECG showed non-specific ST- and T-wave changes in 42%, ischaemic changes in 15% and evidence of an acute myocardial infarction in 5% of patients with an ascending aortic dissection.

Chest X-ray
A routine chest X-ray is abnormal in 60–90% of cases with suspected aortic dissection. However, 12% of patients have a completely normal chest X-ray.1 Because of the limited sensitivity of this method, additional imaging studies are required in all patients.

Imaging Studies
During the IRAD period a shift was shown from an invasive (aortography) to a non-invasive diagnostic strategy for evaluating suspected thoracic aortic dissections. Most patients require multiple imaging studies to diagnose and characterise aortic dissection. In IRAD,10 the initial study was computed tomography (CT) in 61%, echocardiography in 33%, aortography in 4% and magnetic resonance imaging (MRI) in only 2%. The mean number of studies performed per patient was 1.8. In type A AAS, transoesophageal echocardiography was the most commonly used technique (79%), mainly in US sites. Imaging techniques revealed aortic regurgitation in 62%, pericardial effusion in 46% and coronary artery involvement in 14%. A proximal intimal tear was identified in the aortic root in 39% of patients, in the ascending aorta in 55% and in the aortic arch in 4%. For the diagnosis of acute aortic dissection, all four diagnostic tests (CT, transoesophageal echocardiography, MRI and aortography) demonstrate a high diagnostic sensitivity. However, the false-negative rate is still considerable, such that the diagnosis cannot be excluded confidently on the basis of a single test. Another imaging test is strongly recommended when the diagnosis is highly suspected clinically.10

IRAD contributed new imaging information that aids diagnostic accuracy. Maximum aortic diameters in acute type A dissection were <55mm in 59% of cases and <50mm in 40% of cases.11 Independent predictors of dissection at diameters <55mm were history of hypertension and age. Marfan’s syndrome patients were more likely to dissect at larger diameters (odds ratio [OR] 14.3). In-hospital mortality was not related to aortic size. Peri-aortic haematoma was present in 23% of cases (26% in type A and 19% in type B) and implied significantly greater mortality (33 versus 20%; p<0.001).12 A multivariate model demonstrated peri-aortic haematomas to be an independent predictor of mortality in patients with aortic dissections (OR 1.71).

Finally, a recent study showed that transoesophageal echocardiography provides prognostic information in type A AAS.13 Independent predictors of mortality were cardiac tamponade (OR 2.7), whereas dissection flap confined to the ascending aorta (OR 0.2) and false lumen thrombosis (OR 0.15) were protective. When only the surgically treated patients were considered, peri-aortic haematoma was an independent predictor of mortality.

Natural History and Prognosis

Type A Dissection
In-hospital mortality rate was 32.5% in type A dissection patients.14 In-hospital complications (neurological, myocardial or mesenteric ischaemia, kidney failure, hypotension, cardiac tamponade and limb ischaemia) were increased in patients who died compared with survivors (p<0.05 for all). Logistic regression identified the following presenting variables as predictors of death: age >70 years (OR 1.70), abrupt onset of chest pain (OR 2.50) hypotension/shock/tamponade (OR 2.97), kidney failure (OR 4.77), pulse deficit (OR 2.03) and abnormal ECG (OR 1.77); area under receiver operating curve 0.74. This analysis provides a useful and simple bedside risk prediction tool that could be used by physicians for determining the prognosis of patients with acute type A AAS.

Type B Dissection
Acute aortic dissection affecting the descending aorta is less lethal than type A dissection. Patients with uncomplicated type B dissection have a 30-day mortality of 10.5%.15 However, patients who develop ischaemic complications such as renal failure, visceral ischaemia or contained rupture often require urgent aortic repair, which carries a mortality of 20% by day two and 25% by day 30. Similar to type A dissection, advanced age, rupture, shock and malperfusion are important independent predictors of early mortality. A risk prediction model with control for age and gender showed hypotension/shock (OR 23.8), absence of chest/back pain on presentation (OR 3.5) and branch vessel involvement (OR 2.9) – collectively named ‘the deadly triad’ – to be independent predictors of in-hospital death.15 A subanalysis in elderly patients16 (>70 years) showed that hypotension/shock was more common and malperfusion of a visceral organ less frequent among the elderly cohort compared with the younger patients (16 versus 10%; p=0.07). A classification tree identified that elderly patients with hypotension/shock had the highest risk of death (56%). In the absence of this, any branch vessel involvement was associated with the highest mortality rate (29%), followed by the presence of peri-aortic haematoma (11%). In contrast, elderly patients without any of these three risk factors had an extremely low mortality rate (1.3%).

Variants

Intramural Haematoma
Although the clinical manifestations of intramural haematoma are similar to those of acute aortic dissection, the former tends to be more of a segmental process; therefore, radiation of pain, pulse deficits and aortic valve insufficiency are less common.17 The natural history of acute IMH continues to be debated. In patients with symptoms consistent with acute aortic dissection, acute IMH accounts for 5–20% of cases; in IRAD it accounted for 5.7% of AAS. This cohort tended to be older (69 versus 62 years of age; p=0.001) and more likely to have distal aortic involvement (60 versus 35%; p=0.0001). Overall mortality was similar to that of classic dissection (21 versus 24%). The analysis demonstrated an association between increasing hospital mortality and the proximity of IMH to the aortic valve, regardless of medical or surgical treatment.

Treatment
One of the important contributions of IRAD is to show the current management and outcome of AAS. Type A acute aortic dissection was treated surgically in 81.7% of cases.18 The reasons for medical treatment...
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  - 2009 — Milan, June 12–16
  - 2010 — Oslo, June 18–22
  - 2011 — Milan, June 17–21
  - 2012 — London, April 26–30
  - 2013 — Milan, June 14–18
  - 2014 — Athens (as a joint ISH/ESH meeting)
  - 2015 — Milan

- **2007 ESH/ESC Guidelines on management of hypertension**
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- **Working Groups**
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Important dates
- Deadline for submission of abstracts: January 15, 2009
- Deadline for early registration: March 31, 2009
- Deadline for pre-registration: May 11, 2009
- Hotel reservation: May 29, 2009

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Hypertension

in the remaining patients were advanced age, severe co-morbid illness or refusal of any surgical intervention. The ascending aorta was replaced in 92% of patients, the partial arch in 23.2% and the complete arch in 12%. The aortic valve was replaced in 23% of cases. A composite aortic valve graft was used in 14% of cases. The mortality in surgically treated patients was 25%. In unstable patients it was 31.4% compared with 16.7% in stable patients. A model with intraoperative haemodynamic and surgical variables showed that intraoperative hypotension, a right ventricle dysfunction at surgery and the need to perform coronary revascularisation were predictors of surgical death. 19

At present, endovascular interventions or surgical repair have no proven superiority over medical treatment in stable patients with type B AAS. In the IRAD series, 73% of patients were managed medically. In-hospital mortality for these patients was 10%. 15 Twelve per cent of acute type B aortic dissections were managed with endovascular therapy; this was similar to the number of patients treated with surgery (15%). Mortality in patients treated surgically was 29%. 20 Factors associated with increased surgical mortality based on univariate analysis were pre-operative coma or altered consciousness, partial thrombosis of the false lumen, evidence of peri-aortic haematomata on diagnostic imaging, descending aortic diameter >60mm, right ventricle dysfunction at surgery and shorter time from the onset of symptoms to surgery. The two independent predictors of surgical mortality were age >70 years (OR 4.3) and pre-operative shock/hypotension (OR 6.1).

Long-term Follow-up

In patients with type A AAS who survive to hospital discharge, predictors of follow-up all reflect patient history variables as opposed to in-hospital parameters or in-hospital complications, which may be explained by the successful in-hospital treatment of the acute dissection. 21 Survival for patients treated with surgery was 91% at three years and 69% without surgery. Predictors of mortality were a history of atherosclerosis and previous cardiac surgery (OR 2.1 and 2.5, respectively, as independent surgical variables). Involvement of the aortic arch was addressed in a recent study. 24 It was found that 25% of patients with AAS type B had involvement of the aortic arch on cross-sectional imaging. Of these, the arch was the site of the intimal tear in at least 37%. Aortic arch involvement in patients presenting with AAS type B did not appear to increase the risk of either in-hospital or follow-up mortality.

Conclusions

Much has been learned about the risk factors, clinical presentation, diagnosis and management of acute aortic dissection from the IRAD registry. However, despite recent advances in diagnostic and therapeutic techniques, mortality in acute aortic syndromes remains high. This observation might reflect both a logistic problem and the inadequacy of the surgical approach in the attempt to treat patients in extreme conditions. IRAD data highlight the notion that a stable clinical status in acute proximal dissection heralds a positive surgical outcome. Although the time interval between symptom onset and surgical intervention remains a major factor in terms of mortality, cardiologists should improve diagnostic pathways and vascular staging in AAS and set up referral networks together with allocation systems.