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# Acute Aortic Dissection: Perspectives from the International Registry of Acute Aortic Dissection (IRAD)

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**Abstract** Acute aortic dissection is a rare but deadly disease first described over 200 years ago by the physician to the late King George II on necropsy. Over the ensuing 2 centuries, the understanding of the pathophysiology, presentation, diagnosis, treatment and follow-up has matured. In an effort to understand the contemporary treatment of this disease, the International Registry of Acute Aortic Dissection (IRAD) has enrolled over 2000 patients over the past 12 years. In this article we summarize the key lessons learned from this multi-national registry of patients presenting with acute aortic dissection.
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## Introduction

Acute aortic dissection was first described by Dr. Nicholls, physician to the late king George II on necropsy over 200 years ago. Since that time, acute aortic dissection (AAD) continues to be one of the most feared pain syndromes because of its high morbidity and mortality. Hirst and Kime published their seminal article in 1958 describing a 1–2% per hour mortality rate early after symptom onset from an ascending aortic dissection.[1] The speed of lethality and the mode of death which often involves severe physiologic derangements from complications such as pericardial tamponade, myocardial infarction, malperfusion syndromes to the brain, kidney, spinal cord and/or gut or frank exsanguination from aortic rupture has magnified the importance of early diagnosis and treatment which continues to be critical to survival.

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AAD poses a special challenge for physicians because of its relative rarity and its ability to mimic other more common conditions. For instance, the prevalence of coronary artery disease is 100—200 times more common then aortic dissection and it's incidence in the emergency room has been estimated to be 3 aortic dissections for every 1000 patients presenting with chest and/or back pain.[2–4] Additionally, estimating the true incidence of aortic dissection is a difficult undertaking. This stems from the number of aortic catastrophes that go undiagnosed and result in sudden death. Because many of these cases are in the elderly, autopsies are often deferred. Among patients on whom autopsy was performed, large series have shown the prevalence of aortic dissection ranges from 0.2% to 0.8%.[5,6]

With the high morbidity and mortality of AAD coupled with its relative low incidence, research in aortic dissection has largely been concentrated on single center registries enrolled over decades to allow for adequate numbers of patients for comparison and long-term follow-up. However, the treatment for aortic dissection is a rapidly moving field with evolving surgical techniques, anesthesia, cardiopulmonary support, ICU and follow-up care. The urgency to collect data on larger numbers of patients over a shorter period of time was necessary to effectively describe the clinical course, management, and outcomes of this aggressive disease.

## History of IRAD

Hoping to overcome the small numbers of patients enrolled at single centers over decades, three investigators convened at the American College of Cardiology symposium in 1995 to discuss combining their individual efforts to create a multi-center registry of aortic dissection. In 1996, the International Registry of Acute Aortic Dissection (IRAD) was established with the mission to better understand the presentation, diagnosis, management, and outcomes of patients presenting with acute aortic dissection in the modern era. By 2000, over 450 patients had been enrolled from 12 international aortic referral centers and its first paper was published.[7] Over the ensuing 8 years, IRAD has grown to include over 2000 patients from 26 sites and has now published over 33 papers to date.

In the present report, we will review what IRAD has learned from these 2000 patients regarding the clinical presentation, prognosis, diagnostic imaging, therapeutic approaches and follow-up in the management of AAD.

## Design

25 large referral centers in 12 countries are participating in this registry. All patients with AAD were enrolled beginning January 1st, 1996. Patients are identified at presentation or by searching hospital discharge diagnosis records and surgical and echocardiography laboratory databases. Diagnosis was based on history, imaging study findings, visualization at surgery, and/or post-mortem examination. Patients with aortic dissection secondary to trauma were excluded. A dataform of 290 variables, defined according to standard definitions, including demographics, history, physical findings, management, imaging studies, and outcomes was developed by IRAD investigators. Data were collected at presentation or by physician review of hospital records. Forms were then forwarded to the IRAD coordinating center at the University of Michigan and reviewed for internal consistency and face validity and then scanned into an Access database. External validation was performed during the inception phase through a random (5%) field selection and error audit. During this phase, 33% of patient report forms were re-reviewed for validation by each site.

Yearly follow-up data were obtained for 5 years after discharge with standardized forms. Collected data included variables on clinical, imaging, and mortality data. When applicable, missing data on mortality were obtained through the Social Security Death Index. At each enrolling hospital, study investigators worked with their ethics or institutional review board to obtain appropriate approval to participate. Full details of the IRAD structure and methods have been previously published.[7]

## Epidemiology

With our first publication in 2000, we reported on the first 450 patients enrolled in the registry. Two-thirds of the

**Table 1** Demographics and history of patients with acute aortic dissection

| Variable | $n$[a](%) | Type A, $n$(%) ($N = 289$) | Type B, $n$(%) ($N = 175$) | $P$, type A versus B |
|---|---|---|---|---|
| Demographics | | | | |
| Age, mean (SD), y | 63.1 (14.0) | 61.2 (14.1) | 66.3 (13.2) | <0.001 |
| Male | 303 (65.3) | 182 (63.0) | 121 (69.1) | 0.18 |
| Patient history | | | | |
| Marfan syndrome | 22/449 (4.9) | 19 (6.7) | 3 (1.8) | 0.02 |
| Hypertension | 326/452 (72.1) | 194 (69.3) | 132 (76.7) | 0.08 |
| Atherosclerosis | 140/452 (31.0) | 69 (24.4) | 71 (42) | <0.001 |
| Prior aortic dissection | 29/453 (6.4) | 11 (3.9) | 18 (10.6) | 0.005 |
| Prior aortic aneurysm | 73/453 (16.1) | 35 (12.4) | 4 (2.3) | 0.006 |
| Diabetes | 23/451 (5.1) | 12 (4.3) | 11 (6.6) | 0.29 |
| Prior cardiac surgery | 83 (17.9) | 46 (15.9) | 37 (21.2) | 0.16 |

$N = 464$.
Reproduced with permission from *JAMA*.[7]
[a] Denominator of reported responses is given if different than stated in column heading.

**Table 2** Prior cocaine use in IRAD

| Variable | No history of cocaine ($n = 916$) | Cocaine before dissection ($n = 5$) | *P* |
|---|---|---|---|
| Type A | 575 (62.8) | 1 (20) | 0.068 |
| Type B | 341 (37.2) | 4 (80) | |
| Age, years | 62.4 ± 13.8 | 44.4 ± 3.9 | <0.001 |
| Black race | 17 (2.0) | 4 (80) | <0.001 |
| Prior hypertension | 658 (72.3) | 5 (100) | 0.330 |
| Marfan's syndrome | 48 (4.3) | 0 (0) | ••• |
| Presentation hypertensive | 408 (46.2) | 4 (80) | 0.189 |
| Myocardial ischemia | 76 (8.8) | 1 (25) | 0.311 |
| Myocardial infarction | 43 (5.0) | 0 (0) | ••• |
| Mortality | 211 (23) | 2 (40) | 0.328 |

Values are number of patients (%) or mean ± SD. Reproduced with permission from *Circulation*.[9]

patients were male with a mean age of 63.1 years old (95% confidence interval, 61.8—64.4 years).[7] Type A dissection was more common accounting for 61.2% of the cases (Table 1). A history of cardiac surgery was present in 17.9% of patients, 31.0% have known atherosclerosis and the most common risk condition for aortic dissection was systemic hypertension (72.1%). Other risk conditions such as Marfan syndrome and iatrogenic dissections were infrequent, occurring in 4.9% and 4.3% respectively.

Other risk factors such as cocaine use have also been explored in IRAD. Hsue and colleagues reported that 14/38 (37%) of patients admitted to their inner-city hospital over 20 years reported using cocaine in the minutes or hours proceeding their presentation.[8] IRAD had enrolled 921 cases of AAD at that time of which only 5 (0.5%) were associated with cocaine use.[9] This discrepancy in numbers likely represents the heterogeneity of patient groups in different cities as well as the different likelihood of being asked questions regarding illicit drug use and the documentation in the medical record. However, aspects of the IRAD experience did confirm some of the observations of Hsue *et al*. When complications of cocaine use do strike the aorta, it usually does so in the descending aorta and generally afflicts predominantly young, black, hypertensive individuals. It has been postulated that cocaine users have premature atherosclerosis from abnormal lipoprotein homeostasis which can lead to weakening of the aortic wall leaving it to be more amenable to injury due to the profound sympathetic stimulation of cocaine abuse.[10—12] (Table 2). Nonetheless, these rare but preventable exposures must not be forgotten as potential causes of an acute aortic dissection and must be asked about in the routine review of systems of patients presenting with chest and/or back pain syndromes.

## Natural History and Prognosis

### Type A (proximal) dissection

AAD of the ascending aorta is highly lethal in the absence of surgical treatment. However, even in the presence of early identification and timely surgery, operative mortality remains high. Different reports from single centers and/or single surgeons have reported mortality rates between 7% and 30%.[13—15] Some of these studies are from single center cohorts stretching over decades or studies focusing on the surgically treated cohort only and not all patients presenting to their institution. This excludes the high risk patients who are either turned down for surgery or die in the operating room. Others do not distinguish between Type A or B dissections or their acuity thereby mixing high and low risk groups. IRAD was designed to enroll consecutive patients from a broad geographic region to minimize inherent biases seen in small surgical registries.

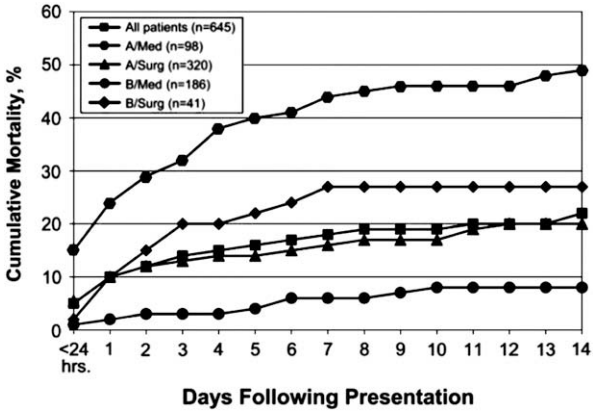



**Figure 1** 14-day mortality in 645 patients from IRAD stratified by medical and surgical treatment in both type A and B aortic dissection. Reproduced with permission from *JAMA*.[7]

The in-hospital mortality rate for acute type A patients in IRAD receiving surgery was 26.6% and 55.9% for those treated with medical therapy alone (overall 32.5%) (Fig. 1). Therefore, nearly 1 in 3 patients will die after presenting to centers with extensive expertise and interest in aortic dissection in the real world. Furthermore, this is likely an under-estimation of mortality given that over 60% of IRAD patients are transferred from outside facilities. Patients who die at the transferring facility or on route are not captured in IRAD. Patients who reach an IRAD facility alive have already undergone an element of selection. Predictors

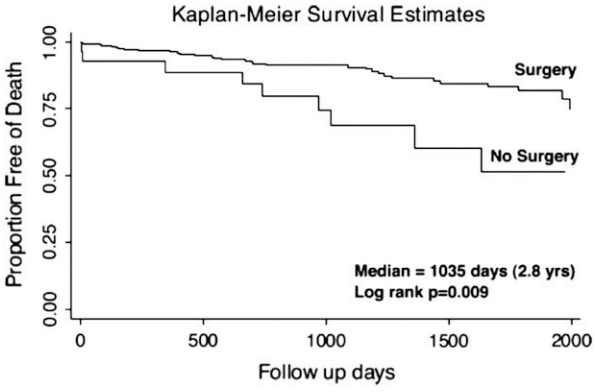



**Figure 2** Unadjusted Kaplan—Meier survival curve stratified by in-hospital management from date of hospital discharge in patients with Acute type A aortic dissection. Reproduced with permission from *Circulation*.[18]

of in-hospital death were age > 70 years old (OR, 1.70: 95% CI, 1.05–2.77; $P = 0.03$); abrupt onset of chest pain (OR, 2.60: 95% CI, 1.22–5.54; $P = 0.01$); hypotension/shock/tamponade (OR, 2.97: 95% CI, 1.25–3.29; $P = 0.004$); and abnormal ECG (OR, 1.77: 95% CI, 1.06–2.95; $P = 0.03$).[16] Similar to coronary artery disease, gender is predictive of adverse events in acute aortic syndromes. In-hospital complications of hypotension and tamponade occurred with greater frequency in women and surgical outcomes were worse in women compared to men ultimately resulting in higher in-hospital mortality ($P = 0.013$).[17]

The short- and long-term follow-up survival of acute type A patients has also been variable with reported survival rates between 52% and 94% at one year and 45 and 88% at 5 years.[18] Our registry provides a unique opportunity to evaluate long-term mortality rates over a short span of enrollment (1996–2003) minimizing the impact of changing strategies of care such as surgical techniques, anesthesia, cardiopulmonary support, ICU care and follow-up imaging for surveillance after discharge. IRAD examined 303 patients who survived to hospital discharge and had documented clinical follow-up data. 273 (90.1%) patients were managed surgically and 30 (9.9%) were managed medically. Survival for patients treated with surgery was 96.1% ± 2.4% and 90.5% + 3.9% at 1 and 3 years versus 88.6% + 12.2% and 68.7% + 19.8% without surgery (mean follow-up overall 2.8 years, log rank $P = 0.009$) Fig. 2. Therefore, in contrast to the high-mortality rates seen during the initial hospitalization and peri-operative period, contemporary 1- and 3-year survival in patients who are repaired and survive to hospital discharge is excellent.

## Type B (distal) dissection

In-hospital outcomes are generally acceptable in patients with uncomplicated acute type B dissection, 90% of whom survive to hospital discharge after receiving effective antihypertensive therapy.[19] In patient presenting with evolving complications such as signs of imminent rupture, expansion, retrograde dissection, or malperfusion syndromes, classic open surgery for acute type B aortic dissection carries a 14%–67% risk of irreversible spinal injury or post-operative mortality.[20–22]

In IRAD, overall in-hospital mortality was 13% with most deaths occurring within the first week. In patients with indications for surgery, mortality was 32.1% versus 9.6% when treated with medical therapy alone and 6.5% when treated by an endovascular approach (Table 3). After adjusting for age and gender, 3 key variables collectively named ''the deadly triad'' emerged as highly significant predictors of death: hypotension/shock (odds ratio [OR] 23.8, $P < 0.001$), absence of chest/back pain on presentation [OR 3.5, $P = 0.01$], and branch vessel involvement [OR 2.9, $P = 0.02$].[19] In patients who survived to hospital discharge, three-year survival for patients treated medically, surgically, or with endovascular therapy was 77.6 ± 6.6%, 82.8 ± 18.9%, and 76.2 ± 25.2%, respectively (median follow-up 2.3 years, log-rank $P = 0.61$) (Fig. 3). Independent predictors of follow-up mortality included female gender (HR, 2.17; 95% CI, 1.03–4.59; $P = 0.04$), a history of atherosclerosis (HR, 2.48; 95% CI, 1.32–4.66; $p < 0.01$), in-hospital renal failure (HR, 2.55; 95% CI, 1.15–5.63; $P = 0.02$), pleural effusion on chest radiograph (HR, 2.56; 95% CI, 1.18–5.58; $P = 0.02$), and in-hospital hypotension/shock (HR, 12.5; 95% CI, 3.24–48.21; $P < 0.01$).[23]

## Intramural hematoma (IMH)

The natural history of acute intramural hematoma continues to be debated. In patients presenting with acute aortic syndromes, acute IMH accounts for 5–20% of cases.[24,25] Regression is seen in approximately 10% of patients but progression to classic aortic dissection occurs in 28–47% of patients and carries a risk of rupture in 20–45%.[26] However, Asian registries have suggested that IMH is a more benign condition in which aggressive medical therapy and

**Table 3** In-hospital management and outcomes of all patients with type B aortic dissection

| Variable | Overall | Survived | Died | *P*-value |
|---|---|---|---|---|
| Definitive management | | | | |
| Surgery (%) | 56 (15) | 38 (67.9) | 18 (32.1) | <0.0001* |
| Medical Rx (%) | 282 (73) | 255 (90.4) | 27 (9.6) | |
| Percutaneous intervention (stent, fenestration) (%) | 46 (12) | 43 (93.5) | 3 (6.5) | |
| Initial medical treatment (excluding hypotensive patients) | | | | |
| Beta-blockers (%) | 277 (78.7) | 253 (79.6) | 24 (70.6) | 0.22 |
| All in-hospital complications (including post-operative) | | | | |
| Coma/altered consciousness (%) | 19 (5.1) | 8 (2.5) | 11 (23.9) | <0.0001 |
| Branch vessel involvement (%) | 76 (21.6) | 56 (18.1) | 20 (46.5) | <0.0001 |
| Hypotension/shock (%) | 40 (11.7) | 15 (5.0) | 25 (61.6) | <0.0001 |
| Malperfusion (%)[a] | 72 (20.6) | 52 (17.0) | 20 (45.5) | <0.0001 |
| Acute renal failure (%) | 46 (13.5) | 36 (11.8) | 10 (26.3) | 0.01 |
| Mesenteric ischemia/infarction (%) | 18 (5.3) | 12 (4.0) | 6 (15.8) | 0.002 |
| Limb ischemia (%) | 24 (7.1) | 17 (5.7) | 7 (17.5) | 0.006 |

*Chi-square *P*-value for differences in survival by management.
[a]Malperfusion is defined for a patient having one of the three conditions listed below.
Reproduced with permission from *Circulation*.[19]

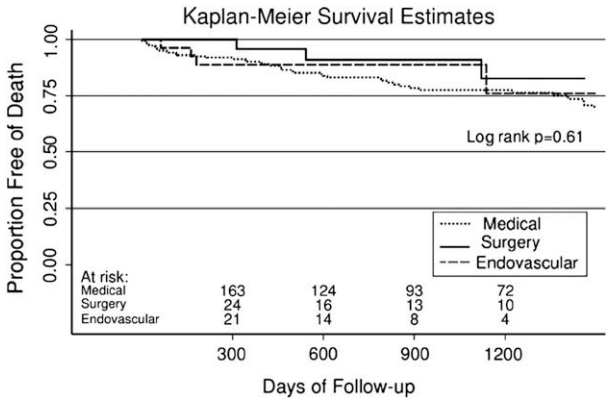



**Figure 3** Unadjusted Kaplan—Meier survival curve stratified by in-hospital management of patients with acute type B dissection who survive to hospital discharge. Reproduced with permission from *Circulation*.[23]

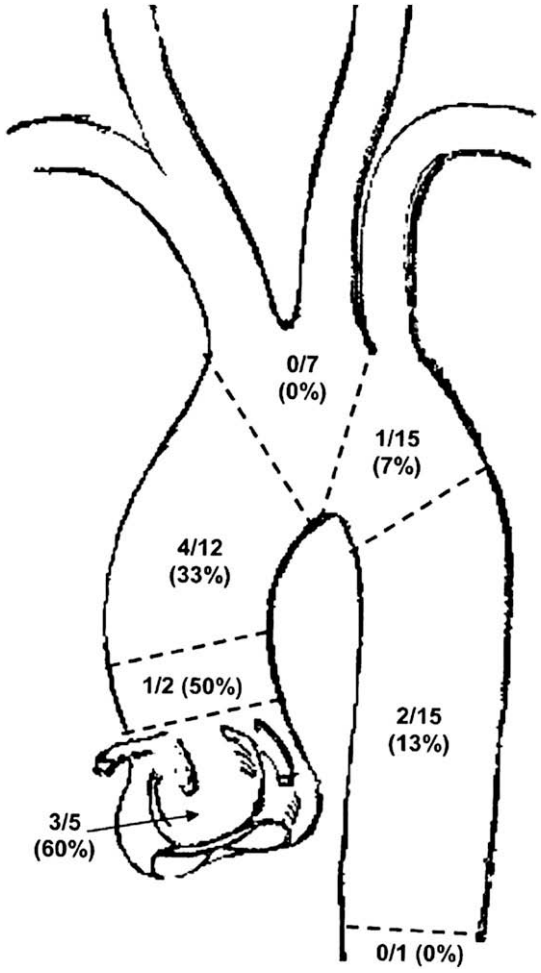



**Figure 4** In-hospital mortality for IMH according to site of origin. IMH was defined after first imaging test failed to demonstrate IMH or dissection but second test confirmed IMH or first study showed IMH but no evidence of dissection. Reproduced with permission from *Circulation*.[30]

serial imaging may allow for watchful waiting and the avoidance of surgery in selected patients.[27—29] These protocols often include serial imaging studies at frequent intervals which may not be practical in the current practice environment in the West. In the IRAD registry of 1010 patients with AAD, 58 (5.7%) patients had IMH.[30] 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%; $p < 0.0001$). The investigators demonstrated an association between increasing hospital mortality and the proximity of IMH to the aortic valve, irrespective of medical or surgical treatment (9 of 12 deaths occurred in the ascending aorta) (Fig. 4).

## Clinical Manifestations

The art of the diagnosis of AAD has evolved since the advent of rapid advanced imaging techniques and therapeutic modalities. The clinical manifestations are diverse and overlap with a broad differential diagnosis requiring a high index of suspicion to pursue and aggressively treat this disorder. Coupled with it's relative infrequency compared to other pain syndromes presenting to the emergency room, the diagnosis of AAD has been missed on initial exam in up to 38% of patients, and the diagnosis first established at post-mortem examination in up to 28% of patients.[7,31]

Patients often complain of the sudden onset of excruciating chest and/or back pain, radiating to the neck or shoulders. This is distinct from pain of coronary ischemia which can be more gradual and often less abrupt. In IRAD, the most common presenting symptom are the abrupt onset of pain, frequently described as severe or the ''worst ever'' in 84.8% of patients. The majority described the quality of the pain as sharp (64.4%) more often then tearing or ripping and localized the pain to the chest (72.7%).[7] Patients with acute type B dissection more often experienced pain in the back or abdomen, although there was substantial overlap.

Syncope is a well-recognized symptom of AAD, often indicating the development of dangerous complications such as cardiac tamponade, obstruction of cerebral vessels or activation of cerebral baroreceptors. Syncope was

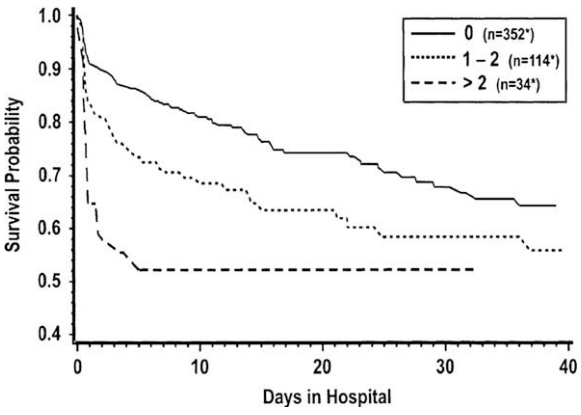



**Figure 5** Kaplan—Meier survival curves from patients with and without pulse deficits; log-rank for curves of patients with 1, 2, or 3 or more pulse deficits differ from patients with no pulse deficits (*P*_0.03 and 0.004). Reproduced with permission from *Am J Cardiol*.[35]

reported in 13% of patients in the IRAD registry.[32] These patients were more likely to die in the hospital (34% versus 23% without syncope) and were more likely to have had a proximal dissection (OR = 5.5; $P < 0.001$), cardiac tamponade (OR = 3.1; $P < 0.001$), or a stroke (OR = 3.5; $P < 0.001$). Therefore physicians must be vigilant regarding patients who present with syncope in the setting of chest pain and consider AAD and its major sequelae. Pulse deficits occurred in 30% of the patients in IRAD and are similar to the 30–50% of patients reported previously in other studies.[33,34] Like other reports, there is an incremental additive risk of in-hospital death with the number of pulse deficits noted on physical exam. This often serves as a surrogate finding indicating the extent of vascular compromise (Fig. 5).[35]

Perhaps the most challenging diagnostic cases of AAD are in those who present with abdominal pain or a painless aortic dissection. In IRAD, we reported on 46 patients (4.6%) who presented primarily with abdominal pain. Specifically in patients with acute type B dissection, in-hospital mortality was significantly higher (28% versus 10.2%; $p = 0.02$) and was associated with a higher incidence of malperfusion syndromes. We also reported on 63 (6.4%) patients who presented with a painless aortic dissection.[36] These patients more commonly presented with a history of diabetes (10.2%), previous aortic aneurysm (29.5%), and prior cardiovascular surgery (48.1%) and often presented with syncope (33.9%), congestive heart failure (19.7%) and stroke (11.3%). Because of these atypical features above and confounding comorbidites, in-hospital mortality was higher in the patients who presented with a painless dissection versus a painful dissection (33.3% versus 23.2%, $p = 0.05$).

After presentation to the hospital, one of the most ominous findings on physical exam is the presence of hypotension (systolic blood pressure <90 mmHg). Hypotension occurred in >25% of patients and was associated with neurologic deficits, altered mental status, myocardial and mesenteric ischemia, limb ischemia and death in 55% of patients. Congestive heart failure on presentation was detected in 6.4% of IRAD patients based on the impressions of the managing physicians but was not associated with an increased mortality in type A or B dissection.[37] However these patients were less likely to present with frank chest or back pain and were more likely on examination to have the murmur of aortic regurgitation.

Aortic dissection has a wide range of clinical presentations that may mimic other disorders such as stroke, myocardial infarction, vascular embolization, and abdominal pathology. Therefore, diagnosis of this disease requires a high index of suspicion and low threshold for diagnostic testing in patients with the appropriate risk factors.

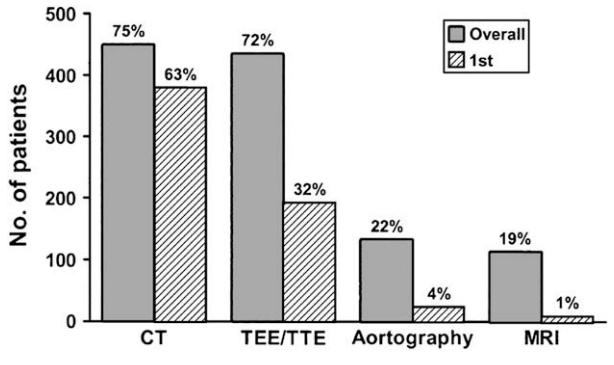



**Figure 6** Overall number and percentage of study patients according to imaging study and the number and percentage according to imaging study of first choice. TTE = transthoracic echocardiography. Reproduced with permission from *Am J Cardiol*.[38]

## Diagnostic Strategies

Given the frequency of missed dissections, atypical presentations, and time dependent morbidity and mortality, effective imaging is paramount to the detection and treatment of this disorder. The ideal imaging modality will definitively, safely and quickly confirm the diagnosis of AAD. It should also provide treatment specific anatomic information such as tear location, extent of dissection, classification, and evaluation for emergent complications such as pericardial, mediastinal, and pleural hemorrhage.

Over the last 2 decades, there has been a shift away from an invasive (aortography) to a noninvasive diagnostic strategy such as computed tomography (CT), magnetic resonance imaging (MRI), and transesophageal echocardiography (TEE) for evaluating thoracic dissections. In IRAD, almost 70% of patients had multiple imaging studies. The 1st diagnostic modality of choice was CT in 63%, then TEE in 32%, aortography in 4% and MRI in 1% (Fig. 6). The mean number of image modalities per patient at non-U.S. sites was significantly higher ($1.94 + 0.83$) than at U.S. sites ($1.71 + 0.76$) ($p = 0.0005$).[38] With similar sensitivity, CT and TEE have become the standard of care for the diagnosis of AAD. CT is usually readily available and performed near or in most emergency departments and TEE can be performed at the bedside. Both are safe and usually give complementary information for definitive treatment plans.

## Treatment

### Ascending (type A) aortic dissection

Surgery provides definitive treatment for patients with type A AAD. Surgical treatment aims to treat or prevent the common and lethal complications such as aortic rupture, stroke, visceral ischemia, cardiac tamponade and circulatory failure. Successful surgery and discharge from the hospital have been associated with excellent 1- and 3-year follow-up survival rates of greater than 90% in IRAD. However, operative mortality for ascending aortic dissections at experienced centers varies widely between 15% and 35% and has not changed appreciably in the last two decades.

In IRAD, 526 patients were operated on for their acute type A dissection. Their in-hospital mortality was highly dependent on their risk profiles prior to surgery. Patients categorized as unstable (cardiac tamponade, shock, congestive heart failure, CVA, coma, myocardial infarction, acute renal failure, or mesenteric ischemia) had a much higher in-hospital mortality of 31.4% versus 16.7% in those

**Table 4** Prediction model with variables during operation

| Variable | Overall type A (%) | % Among survivors | % Among death | Coefficient | Score assigned | *p* Value | Death OR (95% CI) |
|---|---|---|---|---|---|---|---|
| Age ≥70 years | 27.3 | 24.1 | 37.4 | 0.58 | 0.6 | 0.04 | 1.79 (1.02–3.15) |
| History aortic valve replacement | 4.5 | 3.8 | 6.6 | 1.78 | 1.8 | <0.01 | 5.93 (2.07–16.97) |
| Presenting hypotension, shock, or tamponade | 28.8 | 22.4 | 49.0 | 0.92 | 0.9 | <0.01 | 2.52 (1.40–4.54) |
| Migrating chest pain | 13.8 | 12.1 | 19.3 | 0.70 | 0.7 | 0.04 | 2.02 (1.02–4.02) |
| Any pulse deficit | 28.6 | 25.7 | 37.8 | 0.64 | 0.6 | 0.02 | 1.90 (1.10–3.29) |
| In operation | | | | | | | |
| Hypotension or shock | 30.7 | 21.1 | 61.7 | 1.34 | 1.3 | <0.01 | 3.81 (2.16–6.71) |
| RV dysfunction | 7.0 | 3.6 | 18.2 | 1.59 | 1.6 | <0.01 | 4.90 (2.00–12.00) |
| Partial arch | 27.3 | 28.9 | 21.6 | −0.65 | −0.7 | 0.04 | 0.52 (0.28–0.98) |
| CABC | 14.6 | 12.4 | 22.1 | 0.93 | 0.9 | 0.01 | 2.54 (1.23–5.24) |

Reproduced with permission from *J Thorac Cardiovasc Surg*.[39]

patient without unstable features ($P < 0.001$).[39] Unfortunately, unstable patients made up the majority of patients operated upon in IRAD (53.5% versus46.5%). The independent pre-operative predictors of operative mortality was a history of aortic valve replacement (OR 3.12; CI, 1.16–8.40, $P = 0.02$), migrating chest pain (OR 2.77; CI, 1.49–5.15, $P = 0.001$), presenting hypotension (OR 1.95; CI, 1.08–3.52, $P = 0.02$), presenting shock or cardiac tamponade (OR 2.69; CI, 1.41–5.11, $P = 0.002$), and pre-operative limb ischemia (OR 2.10; CI, 1.00–4.38, $P = 0.04$). The mean time interval from onset of symptoms to surgical intervention for all IRAD patients showed an average of 93 h for survivors and 37.9 h for those who died ($P < 0.001$). Not surprisingly, the time period was shorter in unstable patients than in stable patients and suggests that the major predictors of death such as tamponade and shock also force the hand of the surgeon to operate sooner on the most moribund patients. Furthermore, the mortality in patients with acute type A dissection has not changed appreciably in the last 2 decades which might reflect both technical surgical challenges and attempted surgical intervention on patients in extreme conditions.

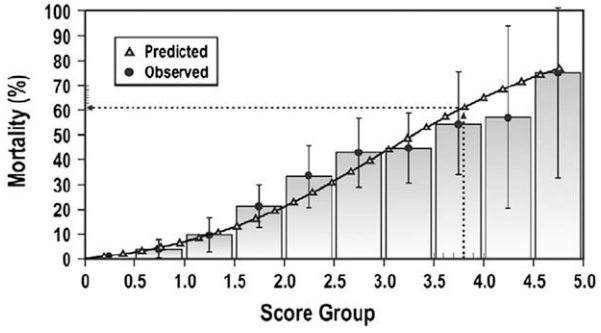



**Figure 7** Model 1: observed versus model probabilities of death by score. Example: 77-year-old woman with migrating chest pain, pre-operative cardiac tamponade, a pulse deficit, and ST elevation. Her model score is 0.7 (age > 70) + 0.9 (migrating chest pain) + 1.0 (pre-operative cardiac tamponade) + 0.6 (pulse deficit) + 0.6 (ST elevation). Total score = 3.8. Drawing a line straight up from her risk score, the estimate of her surgical mortality risk is 61%. Reproduced with permission from *Ann Thorac Surg*.[40]

In 2007, IRAD developed a bedside pre-operative and post-operative risk prediction tool of mortality to better educate co-providers, patients and their family regarding the expected risk with surgical intervention. Intra-operative parameters of hypotension, right ventricular dysfunction and other parameters were added to the pre-operative model to obtain a post-operative score (Table 4).[40] Fig. 7 shows it's application to a patient scenario. An individual's risk score may help the provider, patient and patient advocates in making difficult decisions about whether to forego surgery in critically ill patients and provide realistic expectations of survival.

## Descending (type B) aortic dissection

In the current era, surgeries for type B AAD are reserved for complications because surgical repair has no proven superiority over medical or interventional treatment in stable patients. Patients with uncomplicated aortic dissections confined to the descending thoracic aorta (Stanford type B or DeBakey type III) are at present treated with medical therapy but have recently been considered candidates for endovascular therapy.[41]

In our first report on type B aortic dissection, we included 384 patients from the IRAD registry, of which 73% were managed medically, 15% with surgery and 12% with endovascular interventions. In-hospital mortality was 9.6%, 32.1%, and 6.5% respectively.[19] Currently, optimal therapeutic management of patients with complicated acute type B dissection remains controversial. A significant one-third of patients with acute type B dissection present with complications such as peripheral malperfusion syndromes and or hemodynamic instability. These patients have a high risk of subsequent death. Endovascular treatment has emerged over the last decade and now exceeds standard open surgery as the dominant modality to treat most complications of acute type B aortic dissection. In a recent propensity analysis from IRAD, open surgical repair was associated with an independent increased risk of in-hospital mortality (OR: 3.41, 95% CI, 1.00–11.67,

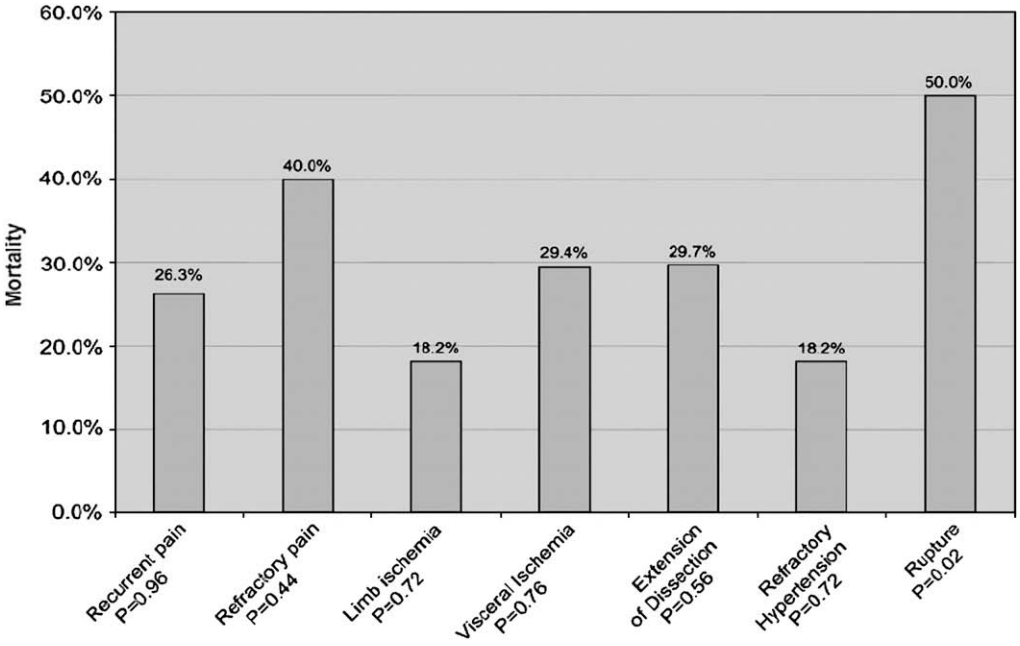


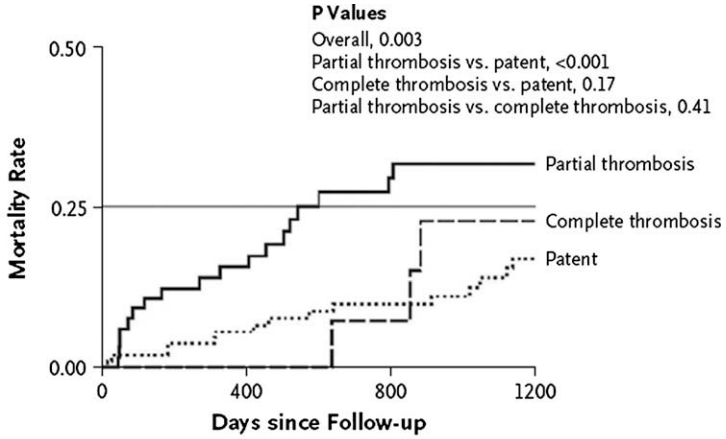

**Figure 8** Bar graph showing the incidence of mortality in type B AAD patients with different indications for surgical treatment. Reproduced with permission from *Circulation*.[44]

$P = 0.05$).[42] In-hospital complications occurred in 20% of patients subjected to endovascular techniques, and in 40% after open surgical repair. In-hospital mortality was significantly higher after open surgery (33.9%) than after endovascular treatment (10.6%, $p = 0.002$).[43] However, surgical mortality is highly dependent on the indication for surgery (Fig. 8).[44] In IRAD, endovascular treatment seems to offer better short-term outcomes in terms of mortality and associated complications than open repair.

## Follow-up

These reports illustrate that the in-hospital mortality rate for acute type A AAD is high but relatively stable after discharge from the hospital with surgical repair whereas hospital mortality for acute type B dissection is relatively low but increases substantially after discharge from the hospital. Three main management issues are predominant in these patients during the follow-up phase and include: medical therapy; serial imaging to detect signs of dissection progression, redissection, or aneurysm formation; and reoperation when indicated. Multiple factors such as advanced age, aortic size, and false-lumen physiology may identify a higher risk cohort for complications.

Aortic diameter has long been used as the mainstay of prevention of aortic dissection in patients with aortic aneurysm and for decisions to operate on remaining dissecting aneurysm in those recovering from acute type A or B




| No. at Risk | | | | |
|---|---|---|---|---|
| Patent | 111 | 96 | 75 | 56 |
| Partial thrombosis | 67 | 48 | 32 | 24 |
| Complete thrombosis | 19 | 17 | 12 | 4 |

**Figure 9** Kaplan—Meier mortality cure stratified according to the status of the false lumen. *P* values were calculated by the log-rank test. Overall denotes comparison of all three curves. Reproduced with permission from *N Engl J Med*.[55]

AAD. IRAD has challenged the concept that most patients who suffer aortic dissection have enlarged aneurysms which emphasizes the need for additional risk markers for early surgical repair. We examined 591 patients with acute type A dissection and found the maximum aortic diameter averaged 5.3 cm and 59% had aortic diameters <5.5 cm and 40% had aortic diameters <5.0 cm.[45] Therefore, almost 60% of patients who suffered an aortic dissection did not fall within the current guidelines for elective aneurysm repair.

In addition to aortic diameter, a reported predictor of poor outcomes in acute type B AAD has been the patency of the false lumen which has been linked to false-lumen expansion and rupture over time.[46–48] Other studies have implicated thrombus as a cause of arterial wall weakening from local inflammation and neovascularization as a mode of worse outcomes in abdominal aortic aneurysms (AAA).[49–51]

The interplay of thrombus and flow on pressure dynamics within the aneurysm sack has also been evaluated in phantom models of stent graft endoleaks which suggests increased pressure in the lumen with the presence of both flow and thrombus.[52–54] In response to clinical anecdotes of patients with acute type B dissections in the recovery phase, who exhibited tremendous expansion of the false lumen in the presence of partial thrombosis, IRAD subsequently evaluated the impact of partial thrombosis of the false lumen on long-term outcomes in patients with chronic type B aortic dissection. Partial thrombosis of the false lumen was present in 33.8% of acute type B aortic dissection on imaging and was a significant independent predictor of death at 3 years (RR, 2.69; 95% CI, 1.45–4.98; $P = 0.002$) showing a 3-year mortality of 31.6% (Fig. 9).[55] The conceptual model explaining the increased mortality in this

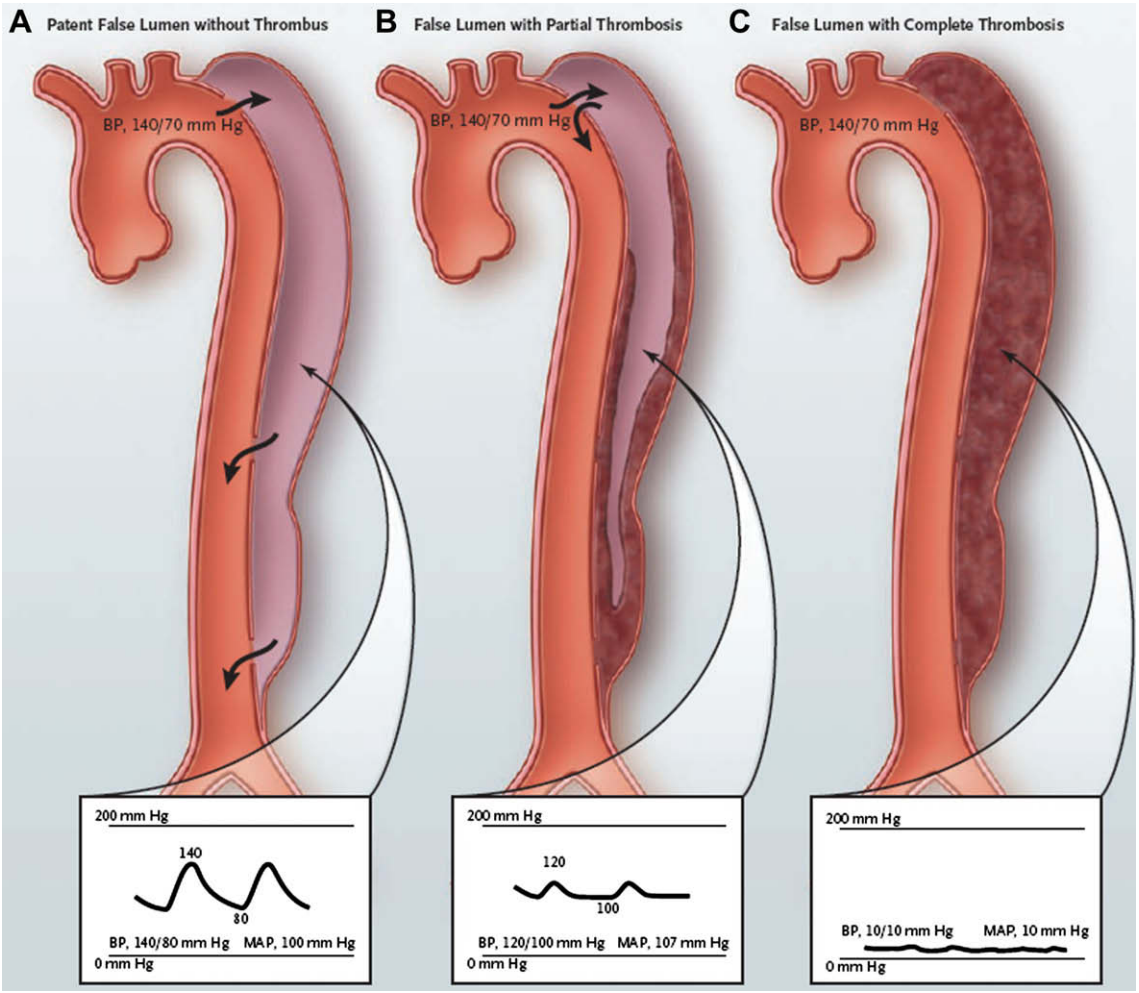



**Figure 10** Conceptual model of risk according to the status of the false lumen: The figure shows a proposed model of the physiological consequences of false-lumen patency or thrombosis, based on hemodynamic studies in ex vivo models and in patients with aortic dissection. Panel A shows type B aortic dissection with patent proximal and patent distal reentry tears in the absence of thrombus. The blood-pressure tracing shows systolic, diastolic, and mean arterial pressures in the false lumen similar to the pressures in the true lumen. Panel B shows type B aortic dissection with a patent entry tear and partial thrombosis that occupies the inner circumference of the false lumen and obstructs the reentry tears, forming a blind sac. The blood-pressure tracing shows diastolic and mean arterial pressures in the false lumen that exceed the pressures seen in Panel A, with identical pressures in the true lumen. Panel C shows type B aortic dissection with a false lumen filled with thrombus and no longer communicating with the true lumen. The pressure within the false lumen is likely to be low and nonpulsatile. BP denotes blood pressure, and MAP mean arterial pressure. Reproduced with permission from *N Engl J Med*.[55]

patient subset challenges the therapeutic landscape in the recovery phase of these patients and resurrects support for treatments that encourage remodeling of the false channel (Fig. 10).

## IRAD: Future Directions

As IRAD has already revolutionized the contemporary understanding of acute aortic conditions and introduced the concept of acute aortic syndromes, the attitude in the medical community towards dissection and its precursors (such as intramural hematoma) has already changed.[26,56,57] There is growing interest in an early and definitive (confirmatory) diagnosis of acute aortic syndrome for prognostic purposes. Moreover, with the new data on the incidence and outcomes of AAD, the medical community has understood the alarming signal sent out by IRAD which has heightened the awareness of the disease and the importance of pathways in the hospital environment and in referring networks in the attempt to manage acute aortic syndromes at a high level of excellence. This task may require expert platforms such as regional aortic centers to meet an increasing demand for the delivery of diagnostic and therapeutic care. The problems have been recognized and the efforts to improve care are currently being monitored in IRAD. In addition to the mission of IRAD to both enlighten the understanding of acute and chronic aortic conditions and to offer appropriate expedited treatment, IRAD will branch out to regional activities enabling the comparison of genetic clustering and regional idiosyncrasies and will focus on genetic sub-studies as well as regional differences in treatment strategies.

Finally, the access to acute cases of suspected and confirmed aortic dissection will provide the opportunity to look at early biomarkers potentially instrumental in the prediction of aortic catastrophes, similar to the impact of troponins for acute coronary syndrome.

## Conclusions

The IRAD activities emerged from the urgent need for contemporary data on acute aortic dissection, as strongly felt by its founders in 1996. Since then the textbook on aortic dissection has been expanded and offers updated highly valuable and realistic data on diagnostic and therapeutic strategies as well as outcomes of acute aortic syndrome at the wake of the 3rd millennium.

There is no comparable database available in the world that provides contemporary, multi-national outcomes data for surgical, endovascular and medical therapy in various forms of acute aortic syndromes. Thus, with contemporary information on acute aortic conditions, IRAD is unique and provides a valuable platform for modern strategic planning and teaching, and serves at the same time (on the scientific scope) as a hypothesis generating source of new information on an old disease.

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