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The International Registry of Acute Aortic Dissection (IRAD)

New Insights Into an Old Disease

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Context Acute aortic dissection is a life-threatening medical emergency associated with high rates of morbidity and mortality. Data are limited regarding the effect of recent imaging and therapeutic advances on patient care and outcomes in this setting.

Objective To assess the presentation, management, and outcomes of acute aortic dissection.

Design Case series with patients enrolled between January 1996 and December 1998. Data were collected at presentation and by physician review of hospital records.

Setting The International Registry of Acute Aortic Dissection, consisting of 12 international referral centers.

Participants A total of 464 patients (mean age, 63 years; 65.3% male), 62.3% of whom had type A dissection.

Main Outcome Measures Presenting history, physical findings, management, and mortality, as assessed by history and physician review of hospital records.

Results While sudden onset of severe sharp pain was the single most common presenting complaint, the clinical presentation was diverse. Classic physical findings such as aortic regurgitation and pulse deficit were noted in only 31.6% and 15.1% of patients, respectively, and initial chest radiograph and electrocardiogram were frequently not helpful (no abnormalities were noted in 12.4% and 31.3% of patients, respectively). Computed tomography was the initial imaging modality used in 61.1%. Overall in-hospital mortality was 27.4%. Mortality of patients with type A dissection managed surgically was 26%; among those not receiving surgery (typically because of advanced age and comorbidity), mortality was 58%. Mortality of patients with type B dissection treated medically was 10.7%. Surgery was performed in 20% of patients with type B dissection; mortality in this group was 31.4%.

Conclusions Acute aortic dissection presents with a wide range of manifestations, and classic findings are often absent. A high clinical index of suspicion is necessary. Despite recent advances, in-hospital mortality rates remain high. Our data support the need for continued improvement in prevention, diagnosis, and management of acute aortic dissection.

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On 25 October 1760 George II, then 76, rose at his normal hour of 6 AM, called as usual for his chocolate, and repaired to the closet-stool. The German valet de chambre heard a noise, memorably described as 'louder than the royal wind', and then a groan; he ran in and found the King lying on the floor, having cut his face in falling. Mr. Andrews, surgeon of the household, was called and bled his Majesty but in vain, as no sign of life was observed from the time of his fall. At necropsy the next day Dr. Nicholls, physician to his late Majesty, found the pericardium distended with a pint of coagulated blood, probably from an orifice in the right ventricle, and a transverse fissure on the inner side of the ascending aorta 3.75 cm long, through which blood had recently passed in its external coat to form a raised ecchymosis, this appearance being interpreted as an incipient aneurysm of the aorta.¹

Disease is very old, and nothing about it has changed. It is we who change as we learn to recognize what was formerly imperceptible.
—Jean Martin Charcot

ACU TE AORTIC DISSECTION IS A challenging clinical emergency first described by Morgagni more than 200 years ago.² In 1958, Hirst et al³ reviewed 505 patients with the condition, highlighting the high mortality rate and the infrequency of antemortem diagnosis. Prior to the introduction of cardiopulmonary bypass in the mid 1950s, surgical options were severely limited.⁴ Since DeBakey first reported surgical repair of a thoracic aortic aneurysm, management techniques have steadily advanced.⁵⁻¹⁴ Recently, percutaneous fenestration and/or stent placement have been used in select patients.¹⁵⁻¹⁹ Similarly, diagnostic imaging modalities, including computed tomography, transesophageal echocardiography, and magnetic resonance imaging, have been developed and are widely available.²⁰⁻²⁵

Aortic dissection is the most common acute aortic condition requiring urgent surgical therapy.²⁶⁻²⁹ Separation of the layers within the aortic wall characterizes dissection. Blood enters the intima-media space with further propagation of the dissection. Typically, 1 or more tears in the intimal layer allow communication between the 2 lumens. Intramural hematoma without an intimal tear is a distinct pathological le-

sion that is being observed with increasing frequency. Presenting features are similar, and progression to dissection may occur.³⁰⁻³² While the initiating event is unknown, most patients have a structural abnormality of the arterial wall and/or systemic hypertension.^{3,33-35}

Classification of aortic dissection is based on anatomical location and time from onset. Stanford type A dissections involve the ascending aorta and type B dissections occur distal to the left subclavian artery.³⁶ The 14-day period after onset has been designated the acute phase, because morbidity and mortality rates are highest and surviving patients typically stabilize during this time.

Because presenting clinical features are diverse and serious complications occur rapidly, antemortem diagnosis has proven difficult.^{3,37,38} One would predict that the advent of modern imaging combined with progress in both surgical and nonsurgical therapy should result in improved outcomes. Little is known about the effect of these developments. Therefore, The International Registry of Acute Aortic Dissection (IRAD) was established in 1996, enrolling patients at large referral centers, to assess the current presentation, management, and outcomes of acute aortic dissection.

METHODS

Patient Selection

Twelve large referral centers in 6 countries are participating in the registry. All patients with acute aortic dissection were enrolled beginning January 1, 1996. Patients were 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 postmortem examination. Patients with aortic disruption secondary to trauma were excluded.

Data Collection

A questionnaire of 290 variables, defined according to standard defini-

tions, including demographics, history, physical findings, management, imaging studies, and outcomes, was developed by IRAD investigators.³⁹ Data were collected at presentation or by physician review of hospital records and were forwarded to the IRAD Coordinating Center at The University of Michigan. Forms were reviewed for clinical face validity and analytical internal validity. External validation was performed through a random (5%) field selection and error audit. More than 33% of patient report forms were re-reviewed for validation by each site.

Data Analysis

Data analysis was performed using statistical analysis software. Univariate analyses were used to compare frequency, proportion, or distribution of demographic and comorbidity variables between samples. χ^2 Cross-tabulations, t tests, or nonparametric Wilcoxon rank sum tests were applied as appropriate. To determine a trend across groups, regardless of condition, the extended Mantel-Haenszel correlation statistic at 1 df was used. Categorical modeling was used to test statistical trends and associations using the likelihood ratio test for model determination. Models were selected using likelihood ratio tests, with a significance level of .05. Corrections due to multiple comparisons were used to determine appropriate levels of significance.

RESULTS

Demographics

As of December 31, 1998, 464 patients have been enrolled (TABLE 1). Two thirds of those patients were male. Mean age of all patients was 63.1 years (95% confidence interval, 61.8-64.4 years). Type A dissection was identified in 62.3% of patients. Patients with type B dissection were, on average, older ($P < .001$). A history of cardiac surgery was present in 83 patients (17.9%). Iatrogenic dissection was reported in 20 patients (4.3%). Sixty percent of patients initially presented to an outside hospital and were referred to IRAD centers

for continued management. A history of hypertension was elicited in 72.1% of all patients. Marfan syndrome was present in 4.9% of all patients (mean age, 36 years; range, 13-52 years).

Presenting Symptoms and Signs

Severe pain was the most common presenting symptom, and 84.8% of patients recalled abrupt onset (TABLE 2). The majority of patients complained of chest pain (72.7%). Anterior chest pain was typical in patients with type A dissection, whereas patients with type B dissection more often experienced pain in the back and abdomen, although there was substantial overlap ($P < .001$). Of note, pain was described as sharp more often than tearing or ripping. Hypertension at initial presentation was more common among patients with type B dissection (70.1% vs 35.7%, $P < .001$). One in 4 patients with type A dissection had an initial systolic blood pressure below 100 mm Hg. When

documented, a pulse deficit was noted more often in patients with type A dissection ($P = .006$). Most patients who presented with stroke also gave a history of pain. Among patients with type A dissection, 12.7% presented with syncope, and most did not have other neurological findings.

Initial Investigations

Chest radiography showed absence of mediastinal widening in 37.4% of patients with type A dissection and an abnormal aortic contour was noted in the minority of those patients (TABLE 3). Chest radiography showed both absence of mediastinal widening and absence of abnormal aortic contour in 21.3% of all patients. No chest radiography abnormality was noted in 12.4% of patients. The 12-lead electrocardiogram most frequently showed nonspecific abnormalities; results were normal for 31.3% of patients.

Diagnostic Imaging

Most patients had multiple imaging studies performed (Table 3). Computed tomography was more often the initial study tool, particularly in patients with type B dissection. Aortography and magnetic resonance imaging were rarely used initially. Aortic insufficiency was noted by imaging in half of patients with type A dissection. Intramural hematoma was noted in 46 patients and two thirds of these had type B dissection ($P < .001$).

Management and Outcomes

Of 289 patients with type A dissection, 72% were managed surgically (TABLE 4). Surgery was not performed in 28% of patients with type A dissection because of advanced age, comorbidity, patient refusal, intramural hematoma, and death prior to planned surgery. Surgical therapies in ascending aortic dissection included coro-

Table 1. Demographics and History of Patients (N = 464) With Acute Aortic Dissection*

Category	No.† (%)	Type A, No. (%) (n = 289)	Type B, No. (%) (n = 175)	P Value, Type A vs B
Demographics				
Age, mean (SD), y	63.1 (14.0)	61.2 (14.1)	66.3 (13.2)	<.001
Male sex	303 (65.3)	182 (63.0)	121 (69.1)	.18
Referred from primary site to IRAD center	280 (60.3)	177 (61.2)	103 (58.9)	.61
Ethnicity (n = 407)				
White	337 (82.8)	205 (84.4)	132 (80.5)	.51
Asian	55 (13.5)	31 (12.8)	24 (14.6)	
Black	7 (1.7)	2 (0.8)	5 (3.0)	
Other	8 (2.0)	5 (2.0)	3 (1.9)	
Patient history				
Marfan syndrome	22/449 (4.9)	19 (6.7)	3 (1.8)	.02
Hypertension	326/452 (72.1)	194 (69.3)	132 (76.7)	.08
Atherosclerosis	140/452 (31.0)	69 (24.4)	71 (42)	<.001
Known aortic aneurysm	73/453 (16.1)	35 (12.4)	238 (2.2)	.006
Prior aortic dissection	29/453 (6.4)	11 (3.9)	18 (10.6)	.005
Diabetes mellitus	23/451 (5.1)	12 (4.3)	11 (6.6)	.29
Prior cardiac surgery‡				
83 (17.9)	46 (15.9)	37 (21.1)	.16	
Aortic valve replacement	24/444 (5.4)	16 (5.8)	8 (4.8)	.66
Aortic aneurysm and/or dissection	43/444 (9.7)	20 (7.2)	23 (14)	.02
Coronary artery bypass graft surgery	19/442 (4.3)	14 (5)	5 (3.0)	.32
Mitral valve surgery	3/444 (0.7)	1 (0.3)	2 (0.1)	NA
Iatrogenic				
20 (4.3)	14 (4.8)	6 (3.4)	.47	
Catheterization/PTCA	10/454 (2.2)	5 (1.7)	5 (2.8)	NA
Cardiac surgery	10/454 (2.2)	9 (3.1)	1 (0.6)	NA

*IRAD indicates The International Registry of Acute Aortic Dissection; PTCA, percutaneous transluminal coronary angioplasty; NA, not applicable; type A dissections involve the ascending aorta; and type B dissections occur distal to the left subclavian artery.

†Denominator of reported responses is given if different than stated in the column heading.

‡Prior cardiac surgery includes aortic valve surgery, coronary artery bypass graft surgery, aortic aneurysm and/or dissection, mitral valve surgery, or other aortic surgery.

Table 2. Presenting Symptoms and Physical Examination of Patients With Acute Aortic Dissection (N = 464)*

Category	Present, No. Reported (%)	Type A, No. (%)	Type B, No. (%)	P Value, Type A vs B
Presenting symptoms				
Any pain reported	443/464 (95.5)	271 (93.8)	172 (98.3)	.02
Abrupt onset	379/447 (84.8)	234 (85.4)	145 (83.8)	.65
Chest pain	331/455 (72.7)	221 (78.9)	110 (62.9)	<.001
Anterior chest pain	262/430 (60.9)	191 (71.0)	71 (44.1)	<.001
Posterior chest pain	149/415 (35.9)	85 (32.8)	64 (41)	.09
Back pain	240/451 (53.2)	129 (46.6)	111 (63.8)	<.001
Abdominal pain	133/449 (29.6)	60 (21.6)	73 (42.7)	<.001
Severity of pain: severe or worst ever	346/382 (90.6)	211 (90.1)	135 (90)	NA
Quality of pain: sharp	174/270 (64.4)	103 (62)	71 (68.3)	NA
Quality of pain: tearing or ripping	135/267 (50.6)	78 (49.4)	57 (52.3)	NA
Radiating	127/449 (28.3)	75 (27.2)	52 (30.1)	.51
Migrating	74/446 (16.6)	41 (14.9)	33 (19.3)	.22
Syncope	42/447 (9.4)	35 (12.7)	7 (4.1)	.002
Physical examination findings				
Hemodynamics (n = 451)†				
Hypertensive (SBP ≥ 150 mm Hg)	221 (49.0)	99 (35.7)	122 (70.1)] <.001
Normotensive (SBP 100-149 mm Hg)	156 (34.6)	110 (39.7)	46 (26.4)	
Hypotensive (SBP < 100 mm Hg)	36 (8.0)	32 (11.6)	4 (2.3)	
Shock or tamponade (SBP ≤ 80 mm Hg)	38 (8.4)	36 (13.0)	2 (1.5)	
Auscultated murmur of aortic insufficiency	137/434 (31.6)	117 (44)	20 (12)	<.001
Pulse deficit	69/457 (15.1)	53 (18.7)	16 (9.2)	.006
Cerebrovascular accident	21/447 (4.7)	17 (6.1)	4 (2.3)	.07
Congestive heart failure	29/440 (6.6)	24 (8.8)	5 (3.0)	.02

*SBP indicates systolic blood pressure; NA, not applicable. For definitions of type A and B dissections, see footnote to Table 1.

†Systolic blood pressure is reported for 277 patients with type A and 174 patients with type B acute aortic dissection, respectively.

Table 3. Chest Radiography, Electrocardiography, and Initial Diagnostic Imaging Results for Patients With Acute Aortic Dissection*

Category	Present, No. Reported (%)	Type A, No. (%)	Type B, No. (%)	P Value, Type A vs B
Radiography findings (n = 427)				
No abnormalities noted	53 (12.4)	26 (11.3)	27 (15.8)	.08
Absence of widened mediastinum or abnormal aortic contour	91 (21.3)	44 (17.2)	47 (27.5)	.01
Widened mediastinum	263 (61.6)	169 (62.6)	94 (56)	.17
Abnormal aortic contour	212 (49.6)	124 (46.6)	88 (53)	.20
Abnormal cardiac contour	110 (25.8)	69 (26.9)	41 (24.0)	.49
Displacement/calcification of aorta	60 (14.1)	29 (11.3)	31 (18.1)	.05
Pleural effusion	82 (19.2)	46 (17.3)	36 (21.8)	.24
Electrocardiogram findings (n = 444)				
No abnormalities noted	139 (31.3)	85 (30.8)	54 (32.1)	.76
Nonspecific ST-segment or T-wave changes	184 (41.4)	116 (42.6)	68 (42.8)	.98
Left ventricular hypertrophy	116 (26.1)	67 (25)	49 (32.2)	.11
Ischemia	67 (15.1)	47 (17.3)	20 (13.2)	.27
Myocardial infarction, old Q waves	34 (7.7)	19 (7.1)	15 (9.9)	.30
Myocardial infarction, new Q waves or ST segments	14 (3.2)	13 (4.8)	1 (0.7)	.02
Initial modality (n = 453)				
Computed tomography	277 (61.1)	145 (50.2)	132 (75.4)	<.001
Echocardiogram (TEE and/or TTE)	148 (32.7)	122 (42.2)	26 (14.9)	<.001
Aortography	20 (4.4)	12 (4.2)	8 (4.6)	.92
Magnetic resonance imaging	8 (1.8)	2 (0.7)	6 (3.4)	.36
Images performed per patient, mean (SD)	1.83 (0.82)	1.64 (0.69)	2.15 (0.91)	<.001

*TEE indicates transesophageal echocardiography; TTE, transthoracic echocardiography. For definitions of type A and B dissections, see footnote to Table 1.

nary artery bypass in 33 patients, aortic valve repair/replacement in 34 patients, and aortic arch repair in 39 patients (21 partial; 18 complete). Of 175 patients with type B dissection, 20% underwent surgical therapy. Percutaneous fenestration and/or stenting was performed in 20 patients (4.3%). Median hospital stay among surviving patients was 16 days and did not differ between dissection types ($P = .19$).

Overall in-hospital mortality was 27.4%. Highest mortality occurred in patients with type A dissection not receiving surgery (58.0%), in contrast to surgically treated patients with type A dissection (26%). Patients with type B dissection treated medically had the lowest mortality (10.7%). However, mortality for patients with type B dissection who underwent surgery was 31.4%. Mortality was highest within the first 7 days of presentation (FIGURE). When reported, the most common causes of death among patients with type A dissection were aortic rupture or cardiac tamponade (41.6%) and visceral ischemia (13.9%). Aortic rupture (38.5%) and visceral ischemia (15.4%) were the most common causes of death in patients with type B dissection.

Female patients tended to be older (67.9 vs 60.6 years, $P < .001$) and had a higher mortality rate than males (33.5% vs 24.1%, $P < .001$). Patients with intramural hematoma had mortality rates similar to those with intimal tears. Among 46 patients (10% of total sample) with intramural hematoma, 17 were type A and 29 type B. Among type A patients, 9 received surgical therapy, of whom 4 died, and 8 received medical therapy, of whom 4 died. Of type B patients, 24 were managed medically resulting in 4 hospital deaths, and 5 required surgery, resulting in 1 death.

COMMENT

Acute aortic dissection may be uncommon, but complications occur often and early, and the outcome is frequently fatal.^{3,40-42} Since dissection is a dynamic process that may occur anywhere within the aorta, the clinical spectrum

Table 4. Management and Outcomes of Acute Aortic Dissection

	Type A (n = 289) Management, No. (%)		Type B (n = 175) Management, No. (%)	
	Surgical	Medical	Surgical	Medical
No.	208 (72)	81 (28)	35 (20)	140 (80)
In-hospital mortality	54 (26)	47 (58)	11 (31.4)	15 (10.7)
Total*	101 (34.9)		26 (14.9)	

*Total mortality for both groups was 127 (27.4%). For definitions of type A and B dissections, see footnote to Table 1.

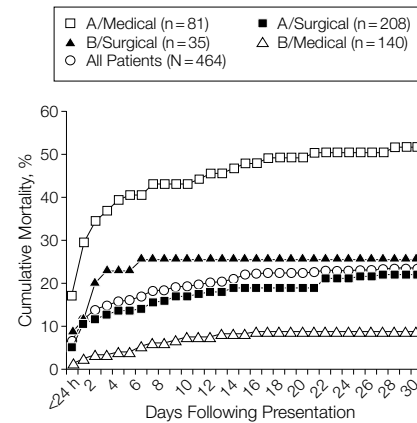
of presentation is broad. Symptoms may mimic more common disorders such as myocardial ischemia or stroke, and physical findings may be absent or suggestive of a diverse range of other conditions.^{3,38,43-45} Therefore, dissection is often difficult to diagnose, and a high clinical index of suspicion is mandatory. As recently as a decade ago, a large referral center reported on a series of patients in whom the diagnosis was frequently missed on initial evaluation (38%) and first established in 28% of patients at postmortem examination.³⁷ Although clinicians today are better equipped to deal with the complex threat posed by aortic dissection, mortality rates remain high.

The typical patient in the IRAD registry is a male in his seventh decade with a history of hypertension who presents with abrupt onset of chest pain. A history of hypertension, which is considered the most common predisposing factor for aortic dissection, was present in more than 70% of patients.^{3,46}

In contrast to classic teaching, tearing or ripping were not the characteristic descriptors of pain. While most clinicians would appropriately associate these terms with aortic dissection, our patients were more likely to describe their pain as sharp in nature. Migratory pain has been described as characteristic but was noted in only 16% of patients in IRAD.⁴⁷

Syncope occurred in more than 12% of patients with type A dissection, and 10 (2.2%) of these patients did not have pain or other neurological findings. Thus, aortic dissection should be considered in the differential diagnosis of syncope, even in the absence of pain. While the physical examination may

Figure. Thirty-Day Mortality by Dissection Type and Management



See footnote to Table 1 for descriptions of type A and type B dissections.

provide valuable clues to the diagnosis of aortic dissection, typical signs were often absent. For example, pulse deficit, which was reported previously in up to 50% of patients with type A dissection, was recorded in less than 20% of patients in IRAD. The murmur of aortic regurgitation, reported previously in approximately two thirds of patients, was documented in 44% of patients with type A dissection.^{37,47}

Earlier studies describe the value of the abnormal chest radiography findings in the evaluation of suspected aortic dissection.^{46,48} While chest radiography may be helpful, a substantial number of patients did not have evidence of widened mediastinum or abnormal aortic contour.

The incidence of aortic dissection has been estimated at from 5 to 30 per 1 million people per year, and the incidence of acute myocardial infarction in the United States has been estimated at

4400 per 1 million per year.^{28,29,49} Differentiating aortic dissection from myocardial ischemia is a common clinical dilemma, and because the therapeutic strategy is very dissimilar, rapid, accurate diagnosis is essential.^{50,51} Occasionally, dissection and myocardial infarction may occur concomitantly. Normal electrocardiogram findings have been touted as a marker to move clinicians away from a diagnosis of myocardial ischemia or infarction and toward dissection.^{34,47} Normal electrocardiogram findings were present in less than a third of our patients, suggesting that this test was not especially helpful in the differential diagnosis.

The choice of initial imaging modality may reflect availability rather than preference. Although transesophageal echocardiography is accurate and can be performed quickly at the bedside with minimal risk, computed tomography was the most common initial assessment performed. Despite recent reports of high sensitivity and specificity of magnetic resonance imaging, it was rarely used as a first diagnostic imaging method.^{24,25} Availability, time delay, restricted ability to monitor patients during imaging, and incompatibility with implanted metal devices are likely explanations for its limited use. Aortography, previously the criterion standard, was used infrequently, and rarely as the initial study.

Despite improved diagnostic and therapeutic techniques, overall in-hospital mortality for acute aortic dissection was 27.4%. As expected, highest mortality occurred early after symptom onset, emphasizing the urgency of diagnosis and institution of appropriate therapy. A minority of patients with type A dissection did not receive surgery, primarily because of advanced age and comorbidity. Accordingly, these patients had the poorest outcome, with more than half dying in the hospital. Patients with type B dissection who underwent surgery also had a high mortality rate, mainly because of aortic rupture and complications of visceral ischemia. The majority of patients with type B dissection had

an uneventful hospital course and were managed medically. Patients with intramural hematoma had similar outcome to those with classic dissection.

While the IRAD experience is the largest study of aortic dissection in recent years, there are limitations. Since high-volume referral sites were selected, the data may not be applicable to the general community. Most patients were white. Many patients with aortic dissection die before presentation to the hospital or prior to diagnosis. We studied only patients who were alive at the time of diagnosis. Since some data were gathered by chart review, the limitations of these methods apply. However, data were rigorously reviewed, and we did not impute for any missing variables. The diagnosis remains unconfirmed by surgical or pathologic correlation in medically managed survivors. However, because patients were evaluated at referral centers and had presentations and imaging studies consistent with acute dissection, we do not believe that this is a significant limitation. While the outcome data are striking, inferences should be made with caution. Patient survival to hospitalization varies, and the choice of therapy was influenced by many factors, including age and condition of the patient.

CONCLUSIONS

Acute aortic dissection is uncommon, but complications develop rapidly and the outcome is often fatal. The typical presentation is characterized by acute onset of severe pain. However, clinical manifestations are diverse, and what were previously considered to be classic symptoms and signs are often absent. Therefore, a high clinical index of suspicion is necessary.

Despite significant advances in diagnostic and therapeutic techniques, morbidity and mortality rates remain high. Although it is clear that during the past 2 centuries much progress has been made, these data support the need for continued improvements in our ability to understand, diagnose, and manage this devastating condition.

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Disease is very old, and nothing about it has changed.
It is we who change, as we learn to recognize what
was formerly imperceptible.
—Jean Martin Charcot (1825-1893)