Long-Term Survival in Patients Presenting With Type B Acute Aortic Dissection
Insights From the International Registry of Acute Aortic Dissection

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Background—Follow-up survival studies in patients with acute type B aortic dissection have been restricted to a small number of patients in single centers. We used data from a contemporary registry of acute type B aortic dissection to better understand factors associated with adverse long-term survival.

Methods and Results—We examined 242 consecutive patients discharged alive with acute type B aortic dissection enrolled in the International Registry of Acute Aortic Dissection (IRAD) between 1996 and 2003. Kaplan-Meier survival curves were constructed, and Cox proportional hazards analysis was performed to identify independent predictors of follow-up mortality. 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). Independent predictors of follow-up mortality included female gender (hazard ratio [HR], 1.99; 95% confidence interval [CI], 1.07 to 3.71; P=0.03), a history of prior aortic aneurysm (HR, 2.17; 95% CI, 1.03 to 4.59; P=0.04), a history of atherosclerosis (HR, 2.48; 95% CI, 1.32 to 4.66; P<0.01), in-hospital renal failure (HR, 2.55; 95% CI, 1.15 to 5.63; P=0.02), pleural effusion on chest radiograph (HR, 2.56; 95% CI, 1.18 to 5.58; P=0.02), and in-hospital hypotension/shock (HR, 12.5; 95% CI, 3.24 to 48.21; P<0.01).

Conclusions—Contemporary follow-up mortality in patients who survive to hospital discharge with acute type B aortic dissection is high, approaching 1 in every 4 patients at 3 years. Current treatment and follow-up surveillance require further study to better understand and optimize care for patients with this complex disease. (Circulation. 2006;114:2226-2231.)

Key Words: aorta ■ risk factors ■ mortality ■ follow-up studies

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.1 In patients presenting with evolving complications such as signs of imminent rupture, expansion, retrograde dissection, or malperfusion syndromes, however, classic open surgery for acute type B aortic dissection carries a 14% to 67% risk of irreversible spinal injury or postoperative mortality.2-4 Over the last 10 years, endovascular techniques including fenestration and stent grafting have emerged as less invasive alternatives to surgery in patients with complicated type B dissections and have been reported to translate into better short-term outcomes.5-7

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Short- and long-term prognosis after discharge from the hospital for acute type B dissection remains unclear. Previous studies are inconsistent and have reported survival rates between 56% and 92% at 1 year and 48% to 82% at 5 years.8-15 However, most of these studies were single-center
experiences with enrollment periods spanning decades and excluded patients treated with endovascular therapies. This lack of contemporary data on survival, as well as improved surgical techniques and the advent of new endovascular therapies such as stenting and fenestration, has led to the need to reassess optimal therapy for acute type B aortic dissection and evaluate how patients currently fare after hospital discharge.

The International Registry of Acute Aortic Dissection (IRAD) currently represents 21 large referral centers from around the world with consecutively enrolled patients presenting with acute type B aortic dissection. It includes clinical information on in-hospital clinical outcomes and follow-up data. Investigators and in-hospital covariates are listed in the appendices, which are found in the online-only Data Supplement. The purpose of the present study was to evaluate long-term survival rates in a contemporary registry of acute type B aortic dissection after hospital discharge and to report the clinical correlates of death based on in-hospital presentation and complications.

### Methods

IRAD is a multinational registry of 21 referral centers in 11 countries designed to provide an unbiased representative population of patients with acute aortic dissection. Treatment during the index hospitalization or in follow-up was not standardized but was at the discretion of each patient’s treating physician. Full details of the IRAD structure and methods used have been published previously.1,16

### Study Population

We examined data on all patients with acute type B aortic dissection enrolled in IRAD between January 1, 1996, and December 31, 2003. Acute type B aortic dissection was defined as any nontraumatic dissection that involved the descending aorta and that appeared within 14 days of symptom onset.17,18 Patients were identified prospectively at presentation or retrospectively via discharge diagnoses, imaging, and surgical databases. Diagnosis was based on confirmatory imaging, intraoperative visualization, or autopsy.

Of the 1417 patients enrolled in IRAD with acute aortic dissection, 532 (37.5%) had type B dissections. To minimize bias with regard to differences in follow-up, the present study included 317 patients (59.6%) from the 8 of 15 referral centers with >80% follow-up, of whom 39 (12.3%) died in the hospital. The remaining 242 (87.1%) had follow-up death data and comprised the present study population. Median follow-up time was 2.3 years.

### Table 1. Clinical, Imaging, and In-Hospital Complications According to Management

<table>
<thead>
<tr>
<th>Variable</th>
<th>Medical Treatment (n=189)</th>
<th>Surgery (n=26)</th>
<th>Endovascular Therapy (n=27)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean±SD, y</td>
<td>63.3±12.9</td>
<td>55.3±13.8</td>
<td>60.2±10.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Female gender, n (%)</td>
<td>62 (33)</td>
<td>4 (15)</td>
<td>9 (33)</td>
<td>0.19</td>
</tr>
<tr>
<td>Marfan syndrome, n (%)</td>
<td>4 (2)</td>
<td>3 (12)</td>
<td>1 (4)</td>
<td>0.04</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>135 (72)</td>
<td>13 (50)</td>
<td>22 (82)</td>
<td>0.03</td>
</tr>
<tr>
<td>Atherosclerosis, n (%)</td>
<td>58 (31)</td>
<td>4 (16)</td>
<td>6 (22)</td>
<td>0.21</td>
</tr>
<tr>
<td>Prior aortic dissection, n (%)</td>
<td>15 (8)</td>
<td>2 (8)</td>
<td>0 (0)</td>
<td>0.31</td>
</tr>
<tr>
<td>History of prior aortic aneurysm, n (%)</td>
<td>30 (16)</td>
<td>4 (17)</td>
<td>3 (11)</td>
<td>0.79</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>8 (4)</td>
<td>1 (4)</td>
<td>3 (11)</td>
<td>0.32</td>
</tr>
<tr>
<td>Prior cardiovascular surgery, n (%)</td>
<td>28 (16)</td>
<td>4 (17)</td>
<td>4 (15)</td>
<td>0.99</td>
</tr>
<tr>
<td>SBP on admission, mean±SD, mm Hg</td>
<td>168±37</td>
<td>150±51</td>
<td>177±40</td>
<td>0.04</td>
</tr>
<tr>
<td>DBP on admission, mean±SD, mm Hg</td>
<td>95±21</td>
<td>86±27</td>
<td>99±20</td>
<td>0.08</td>
</tr>
<tr>
<td>Hypertension on admission, n (%)</td>
<td>133 (72)</td>
<td>9 (38)</td>
<td>20 (77)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Any pulse deficit on admission, n (%)</td>
<td>24 (14)</td>
<td>7 (27)</td>
<td>6 (25)</td>
<td>0.12</td>
</tr>
<tr>
<td>Arch involvement, n (%)</td>
<td>7 (4)</td>
<td>4 (19)</td>
<td>1 (4)</td>
<td>0.02</td>
</tr>
<tr>
<td>Pleural effusion on chest radiograph, n (%)</td>
<td>22 (13)</td>
<td>3 (13)</td>
<td>2 (8)</td>
<td>0.88</td>
</tr>
<tr>
<td>Intramural hematoma, n (%)</td>
<td>28 (16)</td>
<td>2 (8)</td>
<td>1 (4)</td>
<td>0.17</td>
</tr>
<tr>
<td>Diameter of descending aorta, mean±SD, cm</td>
<td>4.5±1.3</td>
<td>5.2±1.8</td>
<td>4.6±1.3</td>
<td>0.15</td>
</tr>
<tr>
<td>Periaortic hematoma, n (%)</td>
<td>24 (14)</td>
<td>3 (12)</td>
<td>5 (20)</td>
<td>0.67</td>
</tr>
<tr>
<td>Mesenteric ischemia</td>
<td>3 (2)</td>
<td>4 (17)</td>
<td>4 (15)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>17 (10)</td>
<td>4 (17)</td>
<td>3 (19)</td>
<td>0.28</td>
</tr>
<tr>
<td>Extension of dissection</td>
<td>6 (4)</td>
<td>6 (26)</td>
<td>2 (8)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Limb ischemia</td>
<td>7 (4)</td>
<td>6 (26)</td>
<td>9 (35)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Neurological deficit</td>
<td>11 (7)</td>
<td>1 (4)</td>
<td>4 (15)</td>
<td>0.28</td>
</tr>
<tr>
<td>Myocardial ischemia</td>
<td>1 (0.6)</td>
<td>1 (4)</td>
<td>1 (4)</td>
<td>0.17</td>
</tr>
</tbody>
</table>

SBP indicates systolic blood pressure; DBP, diastolic blood pressure; atherosclerosis, any coronary, peripheral or cerebrovascular disease; and hypotension/shock, SBP <100 mm Hg.
Data Collection
Clinical variables were recorded on a standardized form that included information on patient demographics, history, clinical presentation, physical findings, imaging study results, details of medical and surgical treatment, and patient outcomes, including mortality. Completed data entry forms were forwarded to the IRAD data coordinating center at the University of Michigan and reviewed for internal consistency and face validity and then scanned electronically into an Access database (Microsoft Corp, Redmond, Wash).

Yearly follow-up data were obtained up to 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.

Statistical Analysis
We compared patients by in-hospital management. Summary statistics between the 3 groups are presented as frequencies for categorical variables and mean±SD for continuous variables. In all cases, missing data were not defaulted to negative, and denominators reflect only cases reported. Relationships with follow-up death were investigated with univariate Cox regression analysis. Stepwise Cox proportional hazards analysis was performed to identify independent predictors of follow-up mortality. Initial modeling used variables marginally suggestive of an unadjusted association with follow-up mortality (P<0.20; Appendix 2). Variables were reviewed for clinical significance before testing. Ascending stepwise selection of variables after controlling for age, gender, and in-hospital management were performed sequentially, with a default value for inclusion set at P<0.05. The estimated survival function for the fitted model was used to construct predicted survival curves for each predictor, with sample mean values used for the remaining covariates. SAS version 8.2 (SAS Institute, Cary, NC) and Stata version 8.0 (Stata-Corp LP, College Station, Tex) were used for analyses.
The authors had full access to the data and take full responsibility for its integrity. All authors have read and agree to the manuscript as written.

Results
Study Population, Baseline Characteristics, and Differences Between Groups
The mean age was 62.1±12.9 years, with the majority of patients being male (69%); 77 (32%) were aged 70 years or older, and 170 (71%) had a history of hypertension. Other comorbidities such as atherosclerosis (29%), a prior aortic aneurysm (16%), and a prior aortic dissection (7%) were not uncommon. Compared with patients receiving medical therapy alone, patients undergoing surgery or endovascular treatment were significantly more likely to have in-hospital complications such as mesenteric ischemia, extension of dissection, and limb ischemia (Table 1). Arch involvement and hypotension or shock on admission occurred significantly more often in the patients treated with surgery.

In-Hospital Management and Outcomes
All patients were initially subjected to intense medical therapy that focused on blood pressure lowering; of these, 189 patients (78%) continued to receive medical therapy for treatment of their acute type B aortic dissection, whereas 26 (11%) underwent surgery, and 27 (11%) received endovascular treatment. The reason for endovascular or surgical treatment was documented in 88% of cases. Recurrent pain, extension of dissection, or refractory hypertension was cited as the reason in 26% of cases, whereas limb ischemia and visceral ischemia were cited in 28% and 30% of cases, respectively. Refractory pain was cited least often (13% of cases). Of the 317 patients from centers with >80% follow-up, in hospital mortality was 12 (29%) of 41 patients treated with surgery, 4 (11%) of 36 patients treated with endovascular treatment, and 23 (10%) of 240 patients treated with medical therapy alone (P<0.001). Total in-hospital mortality was 39 (12%) of 317 patients.

Figure 1 shows the survival curves estimated by the Kaplan-Meier method stratified by in-hospital management. The unadjusted survival rate at 1 and 3 years for patients discharged from the hospital alive was 90.3±4.3% and 77.6±6.6% for medical therapy alone, 95.8±8.0% and 82.8±18.9% for surgery, and 88.9±11.9% and 76.2±25.2% for endovascular treatment (median 2.3 years, log-rank P=0.63).

Predictors of Follow-Up Mortality
Table 2 presents the univariate Cox regression analyses relating likelihood of death according to demographic, historical, and in-hospital patient variables.

Independent Predictors of Follow-Up Mortality
Cox proportional hazards analysis adjusted for age (≥70 years old), gender, and in-hospital management identified female gender (hazard ratio [HR], 1.99; 95% CI, 1.07 to 3.71; P=0.03), a history of prior aortic aneurysm (HR, 2.17; 95% CI, 1.03 to 4.59; P=0.04), a history of atherosclerosis (HR, 2.48; 95% CI, 1.32 to 4.66; P<0.01), in-hospital renal failure (HR, 2.55; 95% CI, 1.15 to 5.63; P=0.02), pleural effusion on chest radiograph (HR, 2.56; 95% CI, 1.18 to 5.58; P=0.02), and in-hospital hypotension/shock (HR, 12.5; 95% CI, 3.24 to 48.21; P<0.01) as significant independent predictors of follow-up mortality (Table 3).

Discussion
Mortality Rates in Patients With Acute Type B Aortic Dissection
This report shows that follow-up mortality rates are relatively high in patients discharged alive from the hospital after acute type B aortic dissection, approaching 1 in 4 patients dying.
Predictors of Follow-Up Mortality in Patients With Acute Type B Aortic Dissections

The present analysis identified several clinical variables as important predictors of follow-up death in patients with acute type B aortic dissection (Table 3). Similar to previous studies reporting on in-hospital and follow-up predictors of mortality, markers of malperfusion or rupture such as renal failure, hypotension, and shock were significant independent predictors of follow-up death in the present study.\textsuperscript{12,15,19}

Evidence of a pleural effusion on chest radiograph was also found to be an independent predictor of follow-up mortality.\textsuperscript{23} We speculate that the presence of a pleural effusion on chest radiograph may be an indication that a periaortic hematoma has complicated the acute dissection, which may herald the possibility of rupture. This corroborates previous findings in IRAD of periaortic hematoma as an independent predictor of in-hospital mortality for acute aortic dissection.\textsuperscript{23}

Not surprisingly, female gender, with age adjustment, was also an independent predictor of follow-up death in the present analysis, which is in line with the existing literature on other cardiovascular disorders and that on acute aortic dissection.\textsuperscript{24,25} IRAD has previously reported on the gender-related differences in acute aortic dissection and showed that women had a significant delay in presentation to the hospital and a higher in-hospital and surgical perioperative mortality than men.\textsuperscript{25} Finally, comorbidities such as atherosclerosis and a diseased aneurysmatic aorta have been shown in previous studies to predict in-hospital and follow-up outcomes. These factors also appear to predict perioperative mortality and all-cause mortality and morbidity.\textsuperscript{11,15} Patency of the false lumen has been implicated as a significant predictor of both aneurysm expansion and outcomes in aortic dissection. Progressive enlargement of the false lumen by 3.3 mm/y has been observed even in stable, uncomplicated type B cases.\textsuperscript{26}

Owing to a paucity of imaging data on the false lumen from IRAD, we have not analyzed the impact of false lumen size on survival. In addition, we have not investigated the potential impact on survival of treatment modality, in-hospital management, and long-term outcomes in patients with in-hospital mortality. These are important aspects that require further study.

**TABLE 3. Independent Predictors of Death After Multivariate Cox Regression Adjustment**

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female gender</td>
<td>1.99</td>
<td>0.03</td>
</tr>
<tr>
<td>History of prior aortic aneurysm</td>
<td>2.17</td>
<td>0.04</td>
</tr>
<tr>
<td>History of atherosclerosis</td>
<td>2.48</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>In-hospital renal failure</td>
<td>2.55</td>
<td>0.02</td>
</tr>
<tr>
<td>Pleural effusion on chest radiograph</td>
<td>2.56</td>
<td>0.02</td>
</tr>
<tr>
<td>In-hospital hypotension/shock</td>
<td>12.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Age ≥70 y</td>
<td>1.41</td>
<td>0.29</td>
</tr>
<tr>
<td>Medical treatment</td>
<td>1.00</td>
<td>...</td>
</tr>
<tr>
<td>Surgical treatment</td>
<td>0.90</td>
<td>0.86</td>
</tr>
<tr>
<td>Endovascular treatment</td>
<td>1.77</td>
<td>0.26</td>
</tr>
</tbody>
</table>

Within 3 years, follow-up mortality after type B dissection exceeds the follow-up mortality seen after acute type A aortic dissection and exceeds the cumulative incidence of mortality in other diseases such as coronary artery disease, moderate chronic obstructive pulmonary disease, and stage II colon cancer.\textsuperscript{20,22} Furthermore, even though the present study fails to provide full information on cause-specific morality, previous studies have suggested that 31% to 66% of follow-up deaths are due to aorta-related complications such as rupture, extension of dissection, and perioperative mortality from subsequent aortic or vascular repairs.\textsuperscript{8–10,15} In contrast, the survival curve in the present study began on the day of hospital discharge. This allowed us to focus on the impact of in-hospital variables on subsequent outcomes without including those who died in the hospital.

The design of the present analysis also allowed us to investigate the potential impact of surgery, any endovascular technique (fenestration and/or stenting), or medical therapy alone on follow-up outcomes. Previous reports have shown significant differences with respect to in-hospital mortality stratified by type of treatment for patients with acute type B aortic dissection. IRAD reported an in-hospital mortality rate of 32% for those treated with surgery, 7% for those managed with endovascular techniques, and 10% for those managed with medical therapy alone (P<0.0001).\textsuperscript{19} Despite these differences for in-hospital mortality, in-hospital management by surgery, endovascular procedures, or medical therapy alone does not appear to impact long-term survival in patients who survive to hospital discharge (Figure 1; Table 3).
and hypotension/shock appear to have a stronger impact on follow-up survival than predisposing risk factors such as gender and a history of atherosclerosis or a previous aortic aneurysm. Therefore, although initial in-hospital management appeared to stabilize these serious hemodynamic and end-organ insults, such complications still negatively impacted patient survival after hospital discharge.

Differences From Prior Studies
IRAD represents the largest reported cohort of patients with acute aortic dissection and represents consecutive patients treated at tertiary referral centers with an expertise and interest in acute aortic dissection. The patients described in the present report represent 15 referral centers with patients enrolled between 1996 and 2003. Previous reports on acute type B aortic dissection were typically single-center registries spanning decades of enrollment and either predated or excluded patients managed with endovascular techniques.8–15,22 In contrast, the present study cohort represents a contemporary reflection of patients from a broad geographic region and may more accurately represent the results of using advanced imaging and the more widespread use of endovascular techniques. Furthermore, by presenting our survival analysis and multivariate models based on patients who survive to hospital discharge, we focus exclusively on predictors of follow-up survival than predisposing risk factors such as gender and a history of atherosclerosis or a previous aortic aneurysm. Therefore, although initial in-hospital management appeared to stabilize these serious hemodynamic and end-organ insults, such complications still negatively impacted patient survival after hospital discharge.

Implications for Management
The optimal treatment of patients with acute type B aortic dissection will continue to be debated. Predictors of in-hospital morbidity and mortality such as signs of malperfusion or imminent rupture should continue to dictate in-hospital treatment decisions. Unsettled indications for active interventions, differing expertise, patient selection, and insufficient power make direct comparisons between surgery and endovascular techniques difficult. The present analysis provides predictors of follow-up mortality after successful in-hospital treatment that may have implications for subsequent imaging protocols and management considerations, however.

Study Limitations
The findings of the present study may not be generalizable to patients treated in community hospitals, because we only included patients treated at IRAD centers. Of these patients, 70% were transferred to an IRAD center from another hospital. Therefore, the majority of the present cohort reflects patients who survived the initial emergency triage and transfer period and may not be representative of patients treated directly. Furthermore, to minimize selection bias, we only included patients from the 8 of 15 centers with >80% follow-up. However, these patients resembled those from the centers with <80% follow-up with regard to mortality rates (33% versus 26%, P = 0.17). Additionally, there was not a significant difference in the percentage of patients lost to follow-up when grouped according to medical, surgery, and endovascular therapy (13% versus 10% versus 16%, P = 0.83). This suggests a nondifferential loss to follow-up between groups and therefore limits the bias attributable to any particular group. The unbalanced sample of patients in the endovascular (n = 27) and surgical (n = 26) groups compared with the medical group (n = 189), however, challenges the power of the present study to detect differences in survival between treatment modalities. Finally, data available to us on follow-up mortality did not include information on cause of death. We were therefore unable to evaluate cause-specific mortality or other end points such as freedom from reoperation, rupture, or redissection.

Conclusions
Contemporary follow-up mortality in patients with acute type B aortic dissection who survive to hospital discharge is high, approaching 1 in every 4 patients at 3 years despite access to and availability of modern therapeutic strategies. Current management and follow-up strategies are yielding unsatisfactory results, and there is a need to evaluate other therapeutic and surveillance strategies.

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Disclosures
None.

References


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