

What Is the Best Treatment for Patients With Acute Type B Aortic Dissections—Medical, Surgical, or Endovascular Stent-Grafting?

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Background. Controversy continues regarding treatment for patients with acute type B aortic dissection.

Methods. One hundred eighty-nine patients with acute type B aortic dissection managed over a 36-year period were analyzed retrospectively for three outcome end-points: survival; freedom from reoperation, and freedom from late aortic-related complications or late death. Risk factors for death were identified using a multivariable Cox proportional hazards model. Then to account for patient selection bias, heterogeneity of the population, and continuous evolution in techniques, propensity score analysis was used to identify risk-matched cohorts (quintiles I and II) in which the results of medical ($n = 111$) or surgical ($n = 31$) therapy were compared more comprehensively.

Results. The two main determinants of death were shock (hazard ratio [HR] = 14.5, 95% confidence level [CL] 4.7, 44.5; $p < 0.001$) and visceral ischemia (HR = 10.9, 95% CL 3.9, 30.3; $p < 0.001$). Arch involvement, rupture, stroke, previous sternotomy, and coronary or lung dis-

ease roughly doubled the hazard. Female sex was also a significant but weaker independent predictor of death. Actuarial survival estimates for all patients were 71%, 60%, 35%, and 17% at 1, 5, 10, and 15 years, respectively, and were similar for the medical and surgical patients. The Marfan syndrome predicted reoperation and late aortic complications or late death. In a separate analysis of the 142 patients in quintiles I and II, survival, freedom from reoperation, as well as freedom from late aortic complications or death were almost identical in the medical and surgical subsets.

Conclusions. The poor long-term prognosis of patients with acute type B aortic dissection is determined primarily by dissection-related and patient-specific risk factors, which are not readily modifiable. Whether the outlook in the future will be improved using stent-grafts remains to be determined.

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While most currently favor a “complication-specific” approach to acute type B aortic dissections (AcBAoD) with the great majority receiving medical therapy [1–5], our group has advocated a more aggressive stance for younger, good operative candidates. Logic dictates that a successful operation should result in a surviving patient who is neurologically intact and has a lower risk of late dissection-related complications or need for aortic reoperation. Proving this hypothesis is made particularly difficult by the heterogeneity of the patient population, inherent referral biases, and continuous evolution of therapeutic options including the advent of percutaneous interventional techniques. A prospective, randomized, multicenter study would be the only way to establish definitely the superiority of one management method over another but that is unrealistic. With the aid of new statistical tools such as propensity score analysis [6–8], we reviewed our entire experience in the management of AcBAoD, identified subsets of patients with similar risk factors, and rigorously com-

pared them with respect to three outcome end-points: survival, freedom from reoperation, and freedom from late aortic complications or late death.

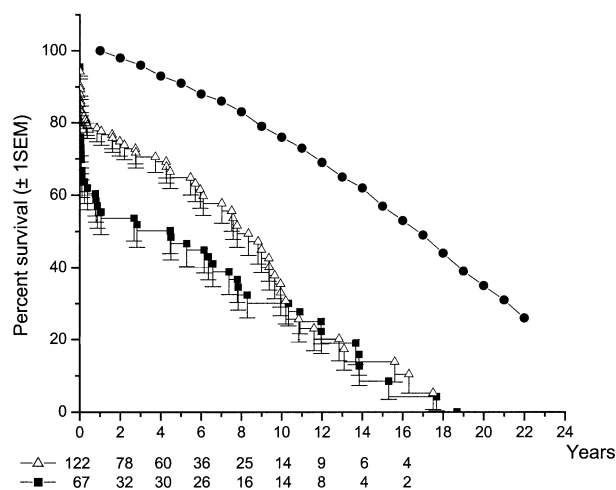
Patients and Methods

This report encompasses the Stanford experience in the treatment of 189 patients (130 male, 59 female) with AcBAoD over a 36-year period. Diagnoses were established within 14 days of the onset of symptoms according to the Stanford system [9]. Data were obtained by chart review, and follow-up was conducted by telephone or written communication or both. Follow-up was 98% complete, extended to a maximum of 19 years (mean 4.5 ± 4.7 years), and totaled 842 patient-years.

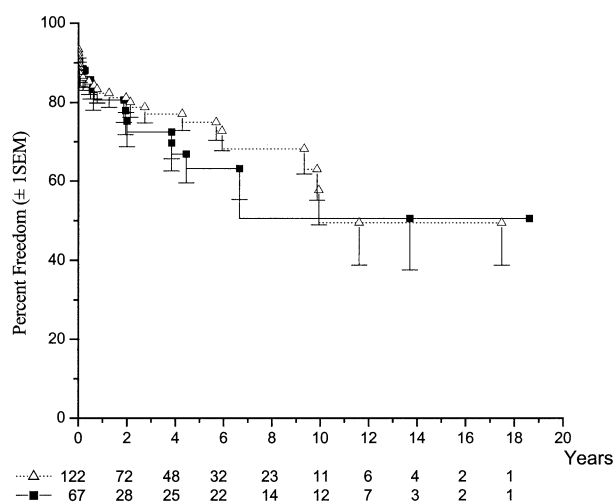
The principal objective was to determine the potential benefit of surgical versus medical therapy in patients with AcBAoD using propensity score analysis to neutralize the inherent “apples versus oranges” comparisons associated with retrospective analyses. To generate propensity scores reflecting the probability of receiving one treatment modality or the other, 21 independent variables were identified and entered into a univariable logistic regression model, with type of treatment being the dependent variable and ignoring outcome. Variables that emerged as significant ($p < 0.05$) were entered into a stepwise logistic multivariable regression model that identified pulmonary disease as

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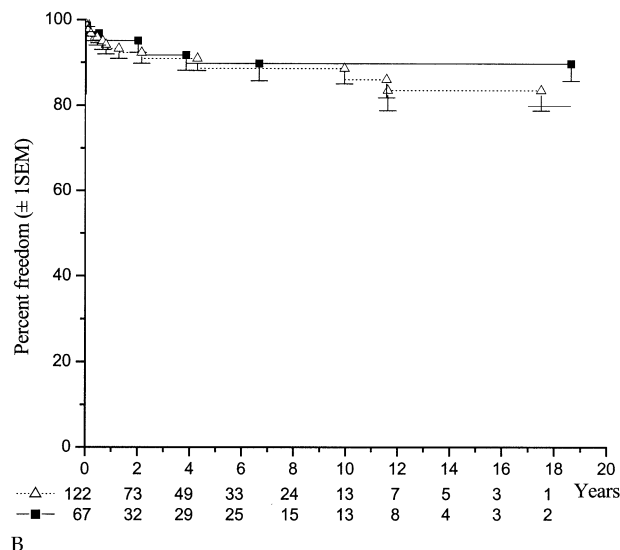
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A



C



B

Fig 1. (A) Actuarial survival estimates for all patients subdivided according to treatment mode. This graph also portrays the survival curve of an age- and sex-matched US population, indicating that only approximately 35% of American patients this age and sex can be expected to be alive 20 years later. (B) Freedom from reoperation for all patients expressed in actual (or observed cumulative frequency) terms. (C) Actuarial freedom from late aortic-related complications or death for all 189 patients. (Triangles = medical therapy; squares = surgery; circles = US population.)

favoring medical treatment, and rupture, arch dissection, and previous dissection favoring operative intervention. A propensity score was then calculated from the logistic equation for each patient which divided the entire patient sample into five propensity-matched quintiles. One hundred forty-two patients in quintiles I and II (111 medically treated and 31 surgically treated) constituted a relatively homogeneous cohort that was analyzed further to determine if the outcome was different between the two therapeutic approaches.

Actuarial estimates of survival and freedom from late aortic-related complications or death were performed using the nonparametric Kaplan-Meier method for the entire study group as well as for quintiles I and II. In the case of nonfatal events such as reoperation, actual (or observed cumulative frequency) probabilities for reoperation were calculated [10].

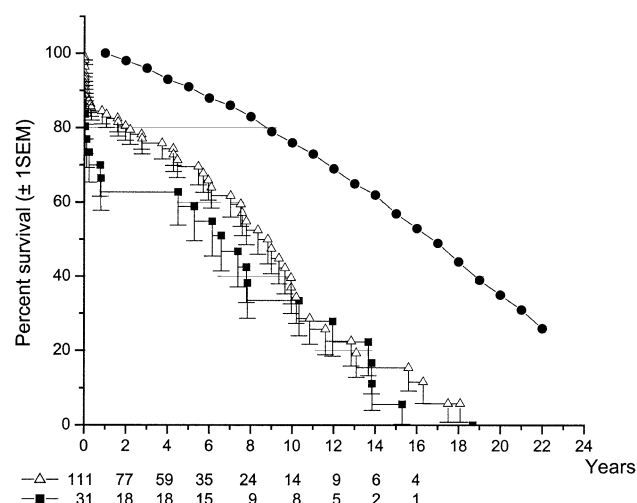
Results

One hundred twenty-two patients (64%) were managed medically, whereas 67 (36%) received early surgical treat-

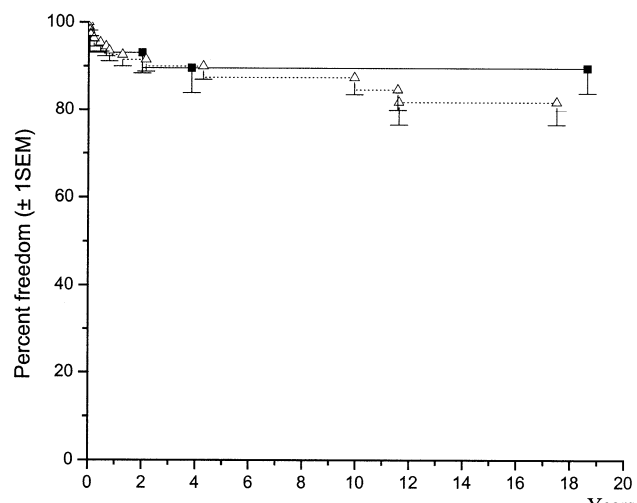
ment. Of interest was the observation that the number of surgical patients treated during each decade remained relatively stable (18 to 22 patients per decade), while the number of medically managed patients increased to 86 in the 1990 to 1999 period from 26 treated during the previous decade. This shift was linked to the introduction of transcatheter techniques of revascularization, with 37 of 86 subjects undergoing percutaneous interventional flap fenestration with or without stenting procedures between 1990 and 1999.

All Patients

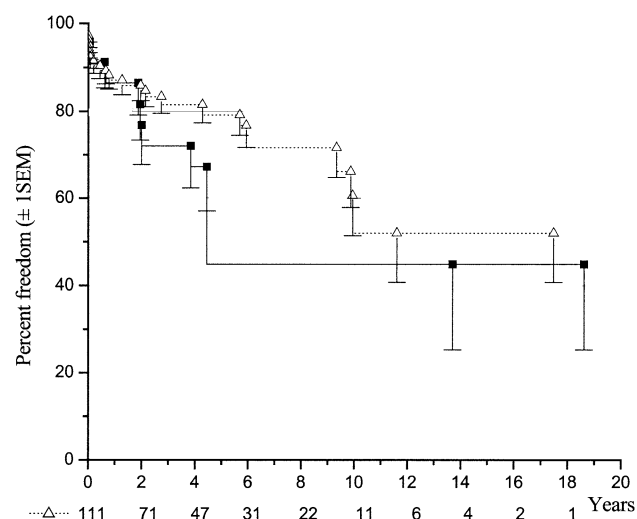
Analysis of the entire experience demonstrated a trend toward a lower mortality risk over the years—from 57% between 1963 and 1969, to 27% between 1990 and 1999—for surgical patients but, interestingly, not for those treated medically. Multivariable Cox proportional hazards analysis revealed that shock (hazard ratio [HR] = 14.5 (95% confidence level [95%CL] 4.7, 44.5; $p < 0.001$) and visceral ischemia (HR = 10.9, 95%CL 3.9, 30.3, $p < 0.001$) largely dominated as determinants of death along with six other factors (arch involvement, rupture, stroke, previous sternot-



A



B



C

Fig 2. (A) Actuarial survival estimates for the 142 comparable patients in quintiles I and II along with the expected survival curve of an age- and sex-matched US population. (B) Actual freedom from reoperation for the patients in quintiles I and II. (C) Actuarial freedom from late aortic-related complications or death in quintiles I and II. (Triangles = medical therapy; squares = surgery; circles = US population.)

omy, and coronary or lung disease), which roughly doubled the hazard of death. Female sex was a significant but weaker independent predictor of death. Renal dysfunction, year of presentation, age, and mode of therapy (medical versus surgical) had no important bearing on overall survival. The actuarial survival estimates for all patients were 71%, 60%, 35%, and 17% at 1, 5, 10, and 15 years, respectively, and were similar for the medical and surgical patients (Fig 1, A). Overall, early operation did not provide normal life expectancy as both curves were substantially inferior compared with the age- and sex-matched US general population. The incidence of reoperation (in actual—not actuarial—terms; Fig 1, B) and actuarial freedom from late aortic related complications or late death (Fig 1, C) were also similar; for both end-points, the only independent predictor was the Marfan syndrome.

Quintiles I and II

Using propensity score analysis the entire cohort was divided into five quintiles. Patients in quintiles III, IV,

and V were more likely to require surgical intervention owing to rupture, shock, or arch extension. Quintiles I and II encompassed 142 patients well matched for all preoperative variables. Propensity score matching was validated using χ^2 analysis, finding no significant difference in risk of death between groups.

Actuarial survival curves were nearly identical in comparable quintile I and II patients (Fig 2, A). Analysis of actual freedom from reoperation (Fig 2, B) and actuarial freedom from late aortic-related complications or late death (Fig 2, C) again failed to show any significant difference between modes of treatment. The early post-operative mortality rate for surgical patients in quintiles I and II was 20% during all 36 years of the study, which was lower than the surgical mortality rate for all 67 surgical patients, reflecting the adverse impact of the selection factors elucidated by the propensity score analysis. Since 1992 none of 6 surgically treated patients in quintiles I and II died within 30 days.

Comment

For the last 30 years the consensus has been that patients with acute type B dissection should be treated medically except in the presence of life-threatening complications. The sobering prognosis of patients with AcBAoD treated surgically was reported by Fann and associates [10] from Stanford: long-term survival rates were 56%, 48%, 29%, and 11% at 1, 5, 10, and 15 years respectively. Early mortality varied over time ($57\% \pm 20\%$ during the early years and $13\% \pm 12\%$ more recently). At that time we hoped that this prognosis might be improved if more diligent postoperative serial imaging was carried out to detect potential downstream aortic problems before fatal complications occurred. In our current analysis, the causes of death were similar in both treatment groups, with patients succumbing mostly to underlying comorbidities (Fig 1, A, and Fig 2, A). Looking at the rate of reoperation and late dissection-related complications or late death also showed no statistically significant differences between groups. The survival free from reoperation curve stabilized at 86% after 3 years in the surgical group whereas that for medically treated patients continued to decline to 62% after 10 years (Fig 1, B, and Fig 2, B). It should be cautioned, however, that the number of patients remaining at risk beyond 5 to 10 years is small.

Analysis of the entire experience demonstrated a trend toward lower early surgical mortality risk over the decades from 57% (1963 to 1969) to 27% (between 1990 and 1999) with the most encouraging results obtained after 1992 with no surgical deaths among 6 uncomplicated patients operated on for AcBAoD. That could be due in part to the introduction of transcatheter revascularization methods, which decreased the number of moribund patients with irreversible visceral or renal ischemia undergoing operation.

In summary, after neutralizing selection and referral bias variations in techniques, and the heterogeneity of the patient population as best we could using propensity score analysis, the prognosis was identical for patients treated medically or surgically (Fig 2). Consequently one observer could infer that all patients should be treated medically whereas another individual could make a completely opposite interpretation. Our tactic in the light of these findings will continue to be what we have advocated in the past. Early operation should be offered selectively to more patients, particularly younger individuals: those judged to be good operative candidates, those with sizable localized false aneurysms, and those with the Marfan syndrome. Justification for this approach resides in a low operative morbidity and mortality risk as evidenced by our results in uncomplicated patients operated on since 1992 and the Mt. Sinai experience yielding zero mortality among 29 patients who underwent operation for AcBAoD between 1985 and 1997 [5].

Although percutaneous interventional flap fenestration/stenting has become a valuable adjunct to both medical and surgical treatment the real role of endo-

vascular aortic stent-grafts remains to be elucidated. Recently we showed that stent-grafting was associated with an early mortality rate of 16% in patients with AcBAoD who had life-threatening complications [11]. The same patients treated conventionally with an emergency thoracotomy would be facing an early risk in the range of 40% or perhaps even exceeding 70% if treated medically [10-12]. We speculate that emergency stent-grafting will be a life-saving therapeutic advance for patients with complicated AcBAoD but its effectiveness must be confirmed in prospective, multicenter randomized trials where this endovascular approach can be rigorously compared with conventional open operation in complicated cases or with medical therapy for uncomplicated patients. More detailed discussion of these and other unsolved issues can be found in our full report [14] from which this brief work was excerpted.

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