Is medical therapy still the optimal treatment strategy for patients with acute type B aortic dissections?

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Objective: The optimal treatment of patients with acute type B dissections continues to be debated.

Methods: A 36-year clinical experience of medical and surgical treatments in 189 patients was retrospectively analyzed (multivariable Cox proportional hazards model) with respect to three outcome end points: all deaths, freedom from reoperation, and freedom from late aortic complications or death. Propensity score analysis identified 2 quintiles (quintiles I and II, consisting of 142 comparable patients) for further comparison of the effects of surgical versus medical treatment.

Results: Shock (hazard ratio 14.5, 95% confidence interval 4.7-44.5, $P < .001$) and visceral ischemia (hazard ratio 10.9, 95% confidence interval 3.9-30.3, $P < .001$) largely predominated as determinants of death, along with 6 other risk factors (arch involvement, rupture, stroke, previous sternotomy, and coronary or lung disease), which roughly doubled the hazard of death. Female sex was a significant but weaker predictor of death. Renal dysfunction, year of presentation, age, and mode of therapy (medical vs 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. Reoperation and late aortic complications were predicted by the presence of Marfan syndrome. For the propensity-matched patients in quintiles I and II, survival, freedom from reoperation, and freedom from aortic complications were almost identical in the medically treated and surgical subsets.

Conclusions: The prognosis for patients with acute type B aortic dissection is bleak and determined primarily by dissection-related and patient-specific risk factors, which do not appear to be readily modifiable.

Consensus exists regarding the need for emergency surgical intervention in patients with acute ascending aortic dissection (Stanford type A), but the optimal treatment strategy for those with acute Stanford type B aortic dissection remains somewhat controversial. Wheat and associates^{1,2} recommended medical treatment, but in 1970 Daily and colleagues³ from Stanford concluded that there was no major difference in early outcome between patients treated medically and those treated surgically. Most groups today favor a complication-specific approach, reserving surgical replacement of the descending aorta for patients with rupture, organ ischemia, refractory pain, uncontrollable hypertension, sizable dilatation of the false lumen, or other life-threatening conditions.⁴⁻⁸ On the other hand, our group⁹ has advocated consideration of early operation for selected patients with acute Stanford type B aortic dissection who are younger and relatively good operative candidates, irrespective of the presence or absence of complications.^{10,11} If operation is successful, these individuals theoretically would be at lower risk of sustaining late dissection-related aortic complications or requiring late aortic reoperation than would patients treated medically. Whether this proposition is valid has remained a matter of debate because of the relatively small numbers of patients treated for acute Stanford type B aortic dissection each year at any given hospital (even tertiary referral centers).¹¹ Further, the introduction of percutaneous interventional techniques to alleviate dissection-induced distal ischemia (or thoracoabdominal malperfusion) has shifted traditional surgical indications, with more patients now being treated medically despite the presence of complications that in the past would have prompted operative treatment. This change has further complicated the decision-making dilemma. Superiority of one treatment method over any other cannot be definitively established short of a multicenter, prospective, randomized trial of medical versus surgical treatment in patients with uncomplicated acute Stanford type B aortic dissections, which is probably unrealistic. Even indirect evidence supporting this more aggressive surgical approach remains elusive because of patient selection and patient referral biases, as well as the heterogeneity of the study populations.⁹⁻¹¹ Application of new statistical tools, such as propensity score analysis, can help to overcome some of these problems by reducing the entire set of background characteristics to a single, composite feature that appropriately summarizes the collection.^{12,13} This approach allows identification of patient subsets at similar risk in which outcome can be rigorously compared, thereby avoiding the fallacious conclusions that can be reached when different treatment methods are used to treat markedly dissimilar patient cohorts.

To explore this dilemma, we performed a retrospective

TABLE 1. Clinical characteristics at presentation for all 189 patients with acute type B aortic dissections, subdivided into those treated medically and those who underwent early operation

	Medical	Surgical	χ^2 P value
Total (No.)	122 (65%)	67 (35%)	
Age (y, mean $\pm$ SD)	62 $\pm$ 13	62 $\pm$ 12	
Sex (No.)			
Male	83 (68%)	47 (70%)	
Female	39 (32%)	20 (30%)	
Previous dissection (No.)	2 (2%)	5 (8%)	.043
Previous surgery (No.)	16 (13%)	9 (13%)	
Hypertension	98 (80%)	46 (69%)	
Coronary artery disease* (No.)	23 (19%)	13 (19%)	
CHF	11 (9%)	1 (2%)	.042
Smoking	68 (59%)	33 (55%)	
Pulmonary disease†	31 (25%)	9 (13%)	.054
Liver disease‡	2 (2%)	1 (2%)	
Diabetes	5 (4%)	2 (3%)	
Stroke	11 (9%)	3 (5%)	
Rupture	6 (5%)	19 (29%)	
Visceral ischemia§	34 (28%)	18 (27%)	
Renal dysfunction	40 (33%)	19 (28%)	
Peripheral pulse deficit¶	28 (23%)	18 (27%)	
Arch extension	6 (5%)	20 (30%)	<.001
Site of tear			
None	5 (4%)	0 (0%)	
Unknown	3 (3%)	4 (6%)	
Arch	2 (2%)	7 (11%)	.02
Descending aorta	109 (89%)	55 (82%)	
Abdominal aorta	3 (2%)	1 (2%)	

*As indicated by a previous diagnosis of coronary disease or myocardial ischemia or infarction.

†Diagnosis of chronic obstructive pulmonary disease or significant lung ailment.

‡Total bilirubin greater than 2.0 mg/dL at the time of diagnosis.

§Compromised arterial perfusion of any intra-abdominal organ diagnosed by angiography, computed tomography, or magnetic resonance imaging.

||Compromised renal perfusion by angiography, acute anuria, renal infarction or serum creatinine level of at least 3 mg/dL or blood urea nitrogen of at least 40 mg/dL.

¶Loss of blood flow to extremities as documented by physical examination, angiography, or computed tomography.

investigation focusing on three primary end points: overall survival, reoperation, and freedom from late aortic complications or death. By means of propensity score analysis, we identified comparable subsets of patients, which allowed more meaningful analysis. With the recent advent of endovascular stent grafting, it is important to establish what can be expected with our conventional medical or surgical treatment strategies to define which patients may benefit from this new endovascular therapy in the future.

Methods

Patient Population

One hundred eighty-nine patients (130 male and 59 female patients) with acute type B aortic dissection constitute the basis for this report. Patients with intramural hematoma (with or without an

Figure 1. Patient distribution by year according to whether they were treated medically (*white bars*) or surgically (*black bars*).

associated penetrating aortic ulcer) were excluded, as were those undergoing endovascular stent-graft treatment. One hundred twenty-two patients were treated medically (1972-1999) and 67 patients were treated surgically (1963-1999); patients treated nonsurgically between 1963 and 1972 were not identified (Figure 1). The vast majority of patients, irrespective of mode of therapy, were cared for on the cardiovascular surgery service. The diagnosis of dissection was confirmed with aortography, computed tomography, magnetic resonance imaging, transthoracic or transesophageal echocardiography, surgical findings, or autopsy reports. Dissections were classified according to the Stanford system, as proposed in 1970.³ Dissections without ascending aortic involvement were type B, even if some degree of retrograde arch involvement was present. If the ascending aorta proximal to the level of the innominate artery was involved, it was a Stanford type A, and the patient was excluded from this analysis. All patients had dissection diagnosed within 14 days of the onset of symptoms. Clinical data were obtained retrospectively through chart review, and current follow-up was obtained by telephone or written communication. Follow-up was 98% complete, extended to a maximum of 19 years (mean 4.5 ± 4.7 years), and totaled 842 patient-years.

Table 1 summarizes the clinical characteristics of the two groups. Mean ($\pm$ SD) patient age was 62 ± 13 years (range, 25-88 years) and was nearly identical for the medical and the surgical groups. Twenty-five patients (13%) had a history of previous cardiac or aortic surgery: 13 (7%) had undergone a previous sternotomy, and 7 (4%) had undergone an operation for previous aortic dissection (5 with acute type A, 1 with acute type B [this patient had a subsequent acute redissection of the descending aorta], and 1 with chronic type A). The patients in the medical group had higher incidences of renal and pulmonary disease, congestive heart failure (CHF), and stroke. These factors, alone or in combination, served as relative contraindications to surgical therapy whenever possible. Rupture, which occurred 3 times more frequently in the surgical group, constituted the main operative indication in 28% of cases. Peripheral arterial or visceral ischemia was present in 23% to 28% of patients in both groups.

In this series, the primary intimal tear was usually located in the descending aorta just distal to the left subclavian artery (87%),

whereas 9 patients (5%) had an arch tear, 3 (2%) had the primary intimal tear in the abdominal aorta, and 7 (4%) had no primary intimal tear identified (Figure 2). Acute dissections originating in the arch were rare, but they are a highly lethal problem.¹⁴ Extent of dissection has been implicated previously as a predictor of high risk for death. In this study, the descending aorta alone was involved in 45 cases (24%); the descending and abdominal aorta were involved in 117 cases (62%); the arch and descending aorta were involved in 11 cases (6%); the arch, descending, and abdominal aorta were involved in 14 cases (7%); the arch only was involved in 1 case (1%); and the abdominal aorta was involved in 1 case (1%). There was no significant difference between the medical and surgical groups with respect to the extent of dissection.

Patient Treatment

Medical therapy. All patients were treated in the intensive care unit with aggressive blood pressure control with intravenous vasodilators and negative inotropic therapy, consisting primarily of β -blockade (esmolol and labetalol are the current preferred intravenous agents, subsequently transitioning to oral labetalol or metoprolol). Pain in most cases resolved with adequate blood pressure control. Failure of medical therapy, defined as intractable pain despite optimal antihypertensive regimen, uncontrollable hypertension, rupture or leak, or progressive expansion of the false lumen, prompted consideration of operation. Additionally, 6 patients since 1992 with uncomplicated dissections were judged to be good operative candidates and underwent urgent open graft replacement of the descending aorta. Patients before 1992 with thoracoabdominal malperfusion syndromes (visceral or renal ischemia or peripheral arterial compromise) usually were operated on. Later, interventional radiologic catheter techniques became available for dissection flap fenestration and true lumen stenting.¹⁵

Surgical treatment. Through a left posterolateral thoracotomy and with either partial (femorofemoral) cardiopulmonary bypass or (in the last decade) total cardiopulmonary bypass and profound hypothermic circulatory arrest, a short segment of the descending thoracic aorta containing the most severe injury and whenever

Figure 2. Sites of primary intimal tear in groups treated medically and surgically.

possible the primary intimal tear was replaced with a double velour-woven Hemashield Dacron graft (Medi-Tech; Boston Scientific Corporation, Boston, Mass). Because these were acute dissections, the dissected walls of the aorta proximally and distally were reapproximated with layers of polytetrafluoroethylene felt, or Bioglu (CryoLife Inc, Kennesaw, Ga) since 1999, such that distal flow into the reconstructed aortic true lumen was restored. In most cases only 5 to 10 cm of the proximal descending thoracic aorta was replaced. Rarely, ligation of the destroyed (or thrombosed) aorta was performed, followed by axillofemoral bypass grafting or an ascending aortic to abdominal aortic extra-anatomic bypass graft (thromboexclusion). Few abdominal aortic surgical fenestrations were carried out as a primary procedure before 1992.

Negative inotropic drug treatment was advised indefinitely, even for normotensive patients, to minimize the incidence of late redissection, aortic rupture, and false lumen aneurysmal enlargement.^{9,11,16} Early postoperative monitoring for all patients included serial abdominal, neurologic, and pulse examinations to detect visceral, limb, or spinal ischemia. If suspected, the diagnosis was confirmed radiologically, and surgical (before 1992) or interventional catheter fenestration and stenting was performed.¹⁵ After discharge, it was recommended that all patients undergo serial aortic surveillance with annual computed tomographic or magnetic resonance imaging scans, but strict compliance with this recommendation could not be ensured because most patients were referred from long geographic distances and were covered by a wide variety of health care provider systems.

Statistical Methods

Preliminary analysis of the baseline data included χ^2 testing to detect significant differences between the two treatment groups. The main objective of the study was to assess whether there was any benefit of surgical rather than medical therapy for patients with acute Stanford type B aortic dissections by using statistical methods that would help neutralize the patient selection bias inherent in

this retrospective investigation. Variability of continuous data was expressed as mean $\pm$ SD, that of important fractions or ratios was expressed as [mean $\pm$ half the extent of the 70% confidence interval (CI)], and that of actuarial or actual estimates was expressed as $\pm$ SEM, roughly equivalent to the 70% CI.

A total of 21 preoperative characteristics or dissection-related complications (independent variables) were analyzed for their possible influence on death at any time, incidence of reoperation, and late aortic-related complications or death (dependent variables; Table 2). Early mortality was defined as death within 30 days of treatment or during the same hospitalization regardless of time. The categorical variable extent of dissection involvement was converted to a binary variable (arch extension) if the arch was involved. Predictors of outcome for the entire group were identified with Cox proportional hazards analysis and expressed as hazard ratios (HRs) and their 95% CIs.

To generate propensity scores reflecting the probability of receiving medical or surgical treatment, all independent variables were entered into a univariable logistic regression model, with type of treatment as the dependent variable and ignoring outcome. Significant variables ($P < .05$) were entered into a stepwise logistic multivariable regression model to discriminate those with the greatest power in predicting treatment type. Of the variables used to create the propensity model, only pulmonary disease (favoring medical treatment) and rupture, arch dissection, and previous dissection (favoring operative intervention) were significant in the logistic multivariable regression model. A propensity score was then calculated from the logistic equation for each patient. The patients were then divided into 5 propensity-matched quintiles (Figure 3). Quintiles III, IV, and V included patients more likely to receive surgical therapy because of the presence of rupture, shock, arch involvement, or previous dissection; these 47 patients (11 medical, 36 surgical), represented 25% of the patient sample. The remaining two quintiles (I and II) contained 142 patients (75% of the total patient sample) who did not have any

TABLE 2. Patient characteristics and disease-related variables selected for statistical analysis

Age
Sex
Hypertension
Coronary artery disease*
Pulmonary disease†
Liver disease‡
Renal dysfunction§
Diabetes mellitus
Smoking
Rupture
Shock
Visceral ischemia
Stroke
Peripheral pulse deficit¶
Site of tear**
Arch extension††
Previous surgery‡‡
Previous dissection§§
Previous sternotomy
CHF
Marfan syndrome
Cardiac disease

*As indicated by a previous diagnosis of coronary disease or myocardial ischemia or infarction.

†Diagnosis of chronic obstructive pulmonary disease or significant lung ailment.

‡Total bilirubin greater than 2.0 mg/dL at the time of diagnosis.

§Compromised renal perfusion by angiography, acute anuria, renal infarction or serum creatinine level of at least 3 mg/dL or blood urea nitrogen of at least 40 mg/dL.

||Compromised arterial perfusion of any intra-abdominal organ diagnosed by angiography, computed tomography, or magnetic resonance imaging.

¶Loss of blood flow to extremities as documented by physical examination, angiography, or computed tomography.

**0, No tear identified; 1, ascending aorta; 2, arch; 3, descending aorta; 7, abdominal aorta.

††1, Arch involvement; 0, no arch involvement.

‡‡History of previous cardiac or vascular surgery.

§§0, No dissection; 1, acute type A dissection; 2, acute type B dissection; 3, chronic type A dissection; 4, chronic type B dissection.

|||CHF or ischemia according to angiogram, history, or electrocardiogram.

compelling surgical indications and were well matched. This relatively homogeneous cohort of 111 medically treated and 31 surgically treated patients was analyzed further to determine whether there were any differences in outcome between the two treatment approaches.

Actuarial estimates of survival, freedom from reoperation, and freedom from late dissection-related aortic complications or death were performed with the Kaplan-Meier method. In the case of freedom from reoperation, which is a nonfatal event, actual (or observed cumulative frequency) probabilities of reoperation were also calculated. Statistical comparisons between the actuarial curves were performed with the log-rank test.

Results

Of the 189 patients, 122 (64%) were treated medically and 67 (36%) underwent an open operative procedure. Figure 1

TABLE 3. Statistically significant independent variables that predicted a higher likelihood of death (early or late) by Cox propensity hazards analysis

	β (HR)	95% CI	P value
Shock	14.5	4.7-44.5	<.001
Visceral ischemia*	10.9	3.9-30.3	<.001
Arch extension†	2.5	1.5-4.3	.001
Rupture	2.5	1.4-4.3	.001
Stroke	2.4	1.2-4.7	.01
Previous sternotomy	2.4	1.2-4.9	.019
Coronary artery disease‡	2.2	1.4-3.6	.001
Pulmonary disease§	2.1	1.3-3.4	.003
Sex	1.6	1.0-2.4	.035

*Compromised arterial perfusion of any intra-abdominal organ diagnosed by angiography, computed tomography, or magnetic resonance imaging.

†1, Arch involvement; 0, no arch involvement.

‡As indicated by a previous diagnosis of coronary disease or myocardial ischemia or infarction.

§Diagnosis of chronic obstructive pulmonary disease or significant lung ailment.

illustrates patient distribution by type of treatment across time. A relatively stable number of surgical patients were seen each decade, and until the 1990s this number was roughly equal to the number treated medically. After 1990, however, a large increase in the medical group occurred, with 43% ($n = 37/86$) of these patients undergoing adjunctive interventional dissection flap fenestration and stenting for thoracoabdominal malperfusion (23 true lumen stents and 14 fenestrations) in this era. The advent of these percutaneous techniques accounts for this shift in operative indications by allowing many complicated cases to avoid operation. In addition, two surgical patients (6%) required catheter interventions for ischemic complications after the operation.

The predictors of death at any time for the entire patient cohort were identified with a backward, stepwise multivariable Cox proportional hazards analysis. In terms of the magnitude of the adverse clinical impact on survival, shock (HR 14.9, 95% CI 4.7-44.5, $P < .001$) and visceral ischemia (HR 10.9, 95% CI 3.9-30.3, $P < .001$) dominated by a large margin (Table 3). Six other variables roughly doubled the probability of death: arch involvement (HR 2.5, 95% CI 1.5-4.3, $P = .001$), rupture (HR 2.5, 95% CI 1.4-4.3, $P = .001$), stroke (HR 2.4, 95% CI 1.2-4.7, $P = .01$), previous sternotomy (HR 2.4, 95% CI 1.2-4.9, $P = .019$), coronary artery disease (HR 2.2, 95% CI 1.4-3.6, $P = .001$), and pulmonary disease (HR 2.1, 95% CI 1.3-3.4, $P = .003$). Female sex, although a significant independent determinant of death, had only a modest effect on survival (HR 1.6, 95% CI 1.0-2.4, $P = .035$). Year of admission, age, treatment mode (medical vs surgical), and renal dysfunction did not emerge as significant predictors of death. Even though year

Figure 3. Quintiles I and II of 5 propensity-matched quintiles were used for further analysis of determinants of three primary outcome variables among patients treated medically (*white bars*) or surgically (*black bars*). These two quintiles included 142 patients, or 75% of entire sample. Note how numbers of patients treated either way were unbalanced in these quintiles to accomplish balancing of risk. Patients in quintiles I and II were comparable but were not necessarily low-risk patients, with many having thoracoabdominal malperfusion and other serious complications (see Table 3). Quintiles III through V (25% of patients) were not well matched, and most required operation.

Figure 4. Early (30-day) mortalities as function of time (decades) and broken down into medical (*white bars*) and surgical (*black bars*) subgroups. Variability in mortality is indicated as $\pm$ half extent of 70% CI.

of presentation was not a significant independent predictor of death, the early mortality risk did fall gradually in the surgical group, from $57\% \pm 19\%$ during the 1960s to $27\% \pm 10\%$ in the 1990s (Figure 4). Conversely, no such trend toward lower early mortalities across time was observed in the medical group.

With respect to the dependent variables of reoperation and freedom from late aortic complications or death, the only independent predictor that emerged from the Cox multivariable analysis was Marfan syndrome. For reoperation, the HR for Marfan syndrome was 6.3 (95% CI 2.4-16.8, $P < .001$); for the combined end point of late aortic complications or death, the HR was 5.9 (95% CI 2.5-114.3, $P < .001$).

For the propensity score calculations, univariate logistic

regression analysis identified CHF and pulmonary disease as predictors of medical therapy, whereas rupture, arch extension, previous (acute type A) dissection, and arch primary intimal tear predicted a higher likelihood of surgical intervention. The stepwise logistic multivariable regression model indicated that pulmonary disease, rupture, arch extension, and previous dissection significantly predicted whether the patient was more likely to be treated medically or surgically. These variables were entered into a logistic equation for each individual patient to compute the propensity scores. The entire population was then divided into propensity-matched quintiles to balance these characteristics. Quintiles III, IV, and V contained 47 patients who were most likely to be operated on because of the presence of rupture, shock, or arch extension (only 36 were actually

TABLE 4. Patient characteristics categorized by propensity-matched quintiles

	Quintiles I and II					Quintiles III-V				
	Medical		Surgical		χ^2 P value	Medical		Surgical		χ^2 P value
	No.	%	No.	%		No.	%	No.	%	
Total	111		31			11		36		
Hypertension	88	79	22	71	NS	10	91	24	67	NS
Coronary artery disease*	19	17	6	19	NS	4	36	7	19	NS
Pulmonary disease†	29	26	4	13	NS	2	18	5	14	NS
Liver disease‡	2	1.8	0	0	NS	0	0	1	3	NS
Renal dysfunction§	38	34	5	16	NS	2	18	14	39	NS
Diabetes mellitus	4	4	0	0	NS	1	9	2	6	NS
Smoking	63	57	17	55	NS	5	46	16	47	NS
Rupture	0	0	0	0	NS	6	55	19	53	NS
Shock	0	0	1	3	NS	0	0	6	17	NS
Visceral ischemia	31	27	6	19	NS	3	27	12	33	NS
Stroke	8	7	1	3	NS	3	27	2	6	.041
Peripheral pulse deficit¶	25	23	6	19	NS	3	27	12	33	NS
Arch extension**	0	0	0	0	NS	3	27	11	31	NS
Previous surgery††	11	10	5	16	NS	5	46	4	11	.011
Previous dissection‡‡	1	1	1	3	NS	1	9	4	11	NS
CHF	11	10	0	0	NS	0	0	1	3	NS
Marfan syndrome	6	5	3	10	NS	0	0	2	6	NS
Cardiac disease§§	4	4	0	0	NS	0	0	0	0	NS
Site of tear										
None	4	4	0	0	NS	1	9	0	0	NS
Unknown	2	2	2	7	NS	1	9	2	6	NS
Arch	0	0	1	3	NS	2	18	6	17	NS
Descending aorta	102	92	28	90	NS	7	64	27	75	NS
Abdominal aorta	3	3	0	0	NS	0	0	1	3	NS

Quintiles 1 and 2 were equally likely to be treated either surgically or medically and were relatively well matched in terms of risk. These two quintiles were combined (total of 142 patients) for further analysis. NS, Not significant.

*As indicated by a previous diagnosis of coronary disease or myocardial ischemia or infarction.

†Diagnosis of chronic obstructive pulmonary disease or significant lung ailment.

‡Total bilirubin greater than 2.0 mg/dL at the time of diagnosis.

§Compromised renal perfusion by angiography, acute anuria, renal infarction or serum creatinine level of at least 3 mg/dL or blood urea nitrogen of at least 40 mg/dL.

||Compromised arterial perfusion of any intra-abdominal organ diagnosed by angiography, computed tomography, or magnetic resonance imaging.

¶Loss of blood flow to extremities as documented by physical examination, angiography, or computed tomography.

**Retrograde dissection involving the aortic arch but stopping short of the proximal limit of the innominate artery.

††History of previous cardiac or vascular surgery.

‡‡0, No dissection; 1, acute type A dissection; 2, acute type B dissection; 3, chronic type A dissection; 4, chronic type B dissection.

§§CHF or ischemia according to angiogram, history, or electrocardiogram.

offered operation). Therefore these patients were not analyzed further. The 142 patients in quintiles I and II were well matched but did not necessarily constitute a low-risk subpopulation. Because of the small numbers of surgical patients in quintiles I and II (4 in quintile I and 27 in quintile II, these two quintiles were combined for a total of 142 patients (111 medical and 31 surgical) and examined further. The effectiveness of the propensity score matching was validated in that there were no significant differences between these medical and surgical patients (Table 4). More detailed analyses focusing on treatment method were then performed on the 142 patients within quintiles I and II with respect to survival, freedom from reoperation, and freedom from late dissection-related complications or death.

Actuarial survival estimates for all patients at 1, 5, 10, and 15 years were 71%, 60%, 35%, and 17%, respectively. Survivals at these same times were 85% $\pm$ 4%, 71% $\pm$ 5%, 38% $\pm$ 6%, and 20% $\pm$ 6% for the medically treated patients, versus 67% $\pm$ 6%, 63% $\pm$ 6%, 39% $\pm$ 6%, and 12% $\pm$ 5% for the surgical cohort ($P = .11$), as shown in Figure 5, A, which also contains the survival curve for an age- and gender-matched US population. There was no significant difference between the treatment groups in actuarial reoperation rates at these intervals (94% $\pm$ 2%, 86% $\pm$ 4%, 83% $\pm$ 7%, and 62% $\pm$ 14% for the medical group and 96% $\pm$ 3%, 87% $\pm$ 6%, 83% $\pm$ 7%, and 83% $\pm$ 7% for the surgical group; Figure 5, B). Calculating the freedom from reoperation in actual terms shifted the curves upward (as

expected, given the strong competing risk of death) and further emphasized the lack of any difference between them. The estimates of actual freedom from reoperation at 1, 5, and 10 years were $93\% \pm 2\%$, $91\% \pm 3\%$, and $89\% \pm 4\%$, respectively, for medically treated patients, versus $97\% \pm 2\%$, $92\% \pm 4\%$, and $90\% \pm 4\%$ for the surgical group (Figure 5, C). Finally, the actuarial estimates of freedom from late aortic-related complications or death at 1, 5, 10, and 15 years were $83\% \pm 4\%$, $77\% \pm 4\%$, $59\% \pm 8\%$, and $51\% \pm 11\%$, respectively, in the medical group, versus $83\% \pm 5\%$, $67\% \pm 7\%$, $64\% \pm 8\%$, and $52\% \pm 12\%$ in the surgical group ($P = .79$; Figure 5, D). The causes of death are listed in Table 5. Combining deaths from progression of dissection or rupture, those that were sudden and unexplained (which could possibly have been due to aortic rupture), and those for which a cause was unknown, 34% of the medical and 31% of the surgical groups could theoretically have died of an aortic complication. Comorbidities such as CHF, renal failure, cancer, and stroke accounted for 50% of the deaths in the medical subset, compared with 40% of the surgical patients.

Turning to the results among the 142 comparable patients in quintiles I and II, the actuarial and actual curves are depicted in Figure 6. Survivals at 1, 5, 10, and 15 years were $85\% \pm 4\%$, $71\% \pm 5\%$, $38\% \pm 7\%$, and $20\% \pm 7\%$, respectively, in the medical subset, versus $67\% \pm 9\%$, $63\% \pm 9\%$, $39\% \pm 10\%$, and $12\% \pm 7\%$ in the surgical subset ($P = .47$), as shown in Figure 6, A. Again, the expected survival curve for an age- and gender-matched US population is illustrated for perspective. Actuarial freedoms from reoperation in quintiles I and II at 1, 5, 10, and 15 years were $93\% \pm 3\%$, $88\% \pm 4\%$, $83\% \pm 7\%$, and $62\% \pm 14\%$, respectively, for medically treated patients and $96\% \pm 4\%$, $86\% \pm 8\%$, $86\% \pm 8\%$, and $86\% \pm 8\%$ for surgically treated patients ($P = .62$; Figure 6, B). Actual freedoms from reoperation again were similar (Figure 6, C). Actual freedoms from reoperation in quintiles I and II at 1, 5, 10, and 15 years were $94\% \pm 2\%$, $90\% \pm 3\%$, $87\% \pm 4\%$, and $82\% \pm 5\%$, respectively, for medically treated patients and $97\% \pm 3\%$, $90\% \pm 6\%$, $90\% \pm 6\%$, and $90\% \pm 6\%$ for surgically treated patients ($P = .62$). Finally, examination of survivals free of late aortic-related complications (including reoperation) showed no significant differences between the subsets, with $88\% \pm 3\%$, $82\% \pm 4\%$, $62\% \pm 9\%$, and $53\% \pm 11\%$ of medically treated patients surviving free of aortic complications at 1, 5, 10, and 15 years, respectively, versus $92\% \pm 5\%$, $68\% \pm 10\%$, $68\% \pm 10\%$, and $49\% \pm 18\%$ of surgically treated patients ($P = .78$; Figure 6, D). For all three end points, inspection of Figures 5 and 6 reveals that the curves were even closer together for the comparable quintile I and II patients than for all patients. This verifies that the propensity score selection process was valid.

TABLE 5. Causes of the late deaths among the 189 patients subdivided according to treatment method

	Medical		Surgical	
	No.	%	No.	%
Dissection rupture or extension	8	18	3	10
Sudden unexplained death	2	5	4	14
Arrhythmia	1	2	2	7
Myocardial infarction	2	5	3	10
CHF	5	11	2	7
Prosthetic valve structural valve dysfunction	1	2	0	0
Renal failure	3	7	1	3
Respiratory failure or pneumonia	5	11	2	7
Stroke	3	7	0	0
Anticoagulant hemorrhage	0	0	1	3
Multisystem organ failure	1	2	1	3
Sepsis	3	7	0	0
Malignancy	3	7	2	7
Suicide or accident	1	2	1	3
Gastrointestinal disease	0	0	1	3
Unknown	5	11	2	7
Other	1	2	2	7
Total	44		27	

The early postoperative mortality for surgical patients in quintiles I and II was 20% during all 36 years of the study, which was lower than the mortality for all patients, reflecting the impact of patient selection factors as elucidated by the propensity score analysis. Since 1992, none of the 6 surgical patients in quintiles I and II died within 30 days, yielding a surgical mortality of 0 for this small sample. This was due to some extent to the fact that after 1992 desperately ill patients with thoracoabdominal malperfusion syndromes were treated with percutaneous interventional catheter techniques coupled with conventional medical therapy.

Discussion

The controversy surrounding the optimal therapy for aortic dissections dates back to the 1960s, when DeBakey and colleagues¹⁷ published a series of 179 patients treated surgically. Given that this report was 36 years ago, the 21% early mortality and 5-year survival of 50% were impressive. After comparing their data with a large number of patients treated nonoperatively by Hirst and coworkers,¹⁸ with a survival of 7% at 1 year, DeBakey and colleagues¹⁷ concluded that all patients with aortic dissection should undergo surgical intervention. Nonetheless, breakdown of these data reveals a highly skewed patient population: 121 (68%) of the patients had a chronic dissection, and most had DeBakey type III dissections. In contrast, a few years later Wheat and associates² advocated a selective approach to the treatment of patients with acute aortic dissection on the basis of the observation that surgery carried a 25% early mortality, compared with 16% for pharmacologic therapy. They believed that rupture resulted from continued dissec-

Figure 5. A, Actuarial survival for all patients subdivided according to treatment mode (triangles, medical, squares, surgical). For perspective, this graph also portrays survival curve for age- and gender-matched US population (circles); this indicates that only approximately 35% of patients this age can be expected to be alive 20 years later. B, Estimates of actuarial freedom from reoperation for all patients subdivided according to treatment mode (triangles, medical, squares, surgical).

tion caused by high blood pressure and the impulse of myocardial contractility and recommended a pharmacologic regimen that decreased not only systemic pressure but also the myocardial impulse (aortic dp/dt); this gave rise to modern anti-impulse therapy. Rupture, impending rupture, overwhelming aortic insufficiency, and dissection-related ischemic complications constituted their only operative in-

dications. In 1970 Daily and associates³ first reported on how important it was (with respect to both prognosis and choice of treatment method) to differentiate between dissections that involve the ascending aorta and those that do not; this article introduced the Stanford type A and B dissection classification system, which is independent of the site of the primary intimal tear. For 30 years the consensus

Figure 5. Cont'd. C, Freedoms from reoperation for all patients expressed in actual (or observed cumulative frequency) terms subdivided according to treatment mode (triangles, medical, squares, surgical). D, Actuarial freedom from late aortic-related complications or death for all 189 patients subdivided according to treatment mode (triangles, medical, squares, surgical).

opinion has been that patients with acute type B dissections should be treated medically unless life-threatening complications are present. Fann and coworkers¹⁹ reported the Stanford results for 3 decades. Early mortalities varied considerably across time ($13\% \pm 12\%$ to $57\% \pm 20\%$),¹⁹ with better results more recently. Another earlier Stanford report showed that the operative risk for patients with an acute type B aortic dissection was markedly influenced by the presence of several risk factors, including renal or vis-

ceral ischemia, aortic rupture, and older age.⁹ Operative mortality climbed from 23% to 80% if renal or visceral ischemia was present and from 21% to 71% if aortic rupture had occurred.¹⁶ These observations were corroborated by our current analysis; moreover, a trend toward progressively lower early mortality risk across time was apparent for surgical patients but not for those treated medically (Figure 4). Since catheter interventional procedures for malperfusion were introduced in 1992, this has been even more

Figure 6. A, Actuarial survival for the 142 comparable patients in quintiles I and II subdivided according to treatment mode (triangles, medical, squares, surgical), along with expected survival curve for age- and sex-matched US population (circles). B, Actuarial freedom from reoperation in quintiles I and II subdivided according to treatment mode (triangles, medical, squares, surgical).

apparent, with no early deaths among 6 quintile I and II patients treated with open graft replacement of the descending thoracic aorta.

The long-term survivals reported by Fann and colleagues¹⁹ for patients with acute B dissections were 56%, 48%, 29%, and 11% at 1, 5, 10, and 15 years, respectively. Fann and colleagues¹⁹ had previously hypothesized that this sobering prognosis might be due to suboptimal serial imaging surveillance after the operation, which theoretically

would detect potential downstream aortic problems before rupture or death; however, in our analysis the causes of late death (Table 5) were similar in the two treatment groups, with most patients dying of underlying comorbidities, as the survival curves for a matched US population in Figures 5, A, and 6, A, reflect.

Recently, Schor and associates⁵ from Griep's group at Mt Sinai Medical Center reported on a group of 68 patients with acute type B dissections between 1985 and 1995

Figure 6. Cont'd. C, Actual freedom from reoperation for the patients in quintiles I and II subdivided according to treatment mode (triangles, medical, squares, surgical). D, Actuarial freedom from late aortic-related complications or death in quintiles I and II subdivided according to treatment mode (triangles, medical, squares, surgical).

treated with a selective approach. Indications for operation during the acute phase included rupture or substantial aortic dilatation. Malperfusion, initially an operative indication, had since 1993 been treated with balloon fenestration at their institution.⁵ Patients without any of these characteristics were treated medically. Overall actuarial survival estimates at 1 and 5 years were $92\% \pm 4\%$ and $82\% \pm 8\%$, respectively, and were similar in the two treatment groups ($93\% \pm 6\%$ and $68\% \pm 14\%$ for the surgical group and $96\% \pm 3\%$ and $93\% \pm 4\%$ for the medical group). Oper-

ative morbidity, however, was considerable, because 59% of patients had one or more serious complications. Schor and associates⁵ attributed their success to the selected nature of their patient population, coupled with improved spinal cord protection and better perioperative care. Lansman and coworkers⁸ updated this Mt Sinai experience in 1999. Among 29 patients with acute type B aortic dissection operated on during a 12-year interval (1985-1997) with this selective approach, there were no early postoperative deaths and only 1 case of paraplegia (4%).⁸ These commendable

results parallel our experience after 1992, confirming the influence of assiduous patient selection. Longer follow-up is needed, however, to establish conclusively whether this approach affects the long-term natural history of this disease.

In a large series from Bern, Switzerland, Gaze and colleagues²⁰ reported a 21% surgical mortality, versus 18% for medical therapy. Because 30% of patients subsequently required operation, they concluded that surgical indications should be expanded to include younger patients. They recommended early intervention for patients with Marfan syndrome, arch involvement,^{11,14} and expectation of poor medical compliance.^{21,22}

The series reported here represents one of the largest groups of patients treated for acute type B dissection at a single institution, but a previous study combining patients from Stanford and Duke²³ addressed the same question. The problem faced at that time was the same. How does one define comparable cohorts? Glower and colleagues²³ studied patients with acute or chronic type B dissections with multivariable analysis. Group I was defined as the entire 136 subjects in the study. Patients without compelling indications for emergency surgery constituted group II. From this group, individuals who had no severe cardiac or renal disease comprised group III, a low-risk group that theoretically could have been treated either way. For all patients, the significant determinants of overall mortality were aortic rupture, other dissection complications, increasing age, and cardiac disease. Type of treatment did not emerge as a significant predictor in any of the three groups. In the low-risk group III, the only predictor of mortality was advanced age. Survival estimates for the entire group at 1, 5, and 10 years were 80%, 59%, and 30%, respectively, for medically treated patients, versus 75%, 52%, and 25% for surgical patients ($P = \text{NS}$). When the low-risk cohort (group III) was analyzed, survivals at the same intervals were 94%, 87%, and 32% for the medical subgroup, versus, 90%, 80%, and 50% for those undergoing operation (P not significant).

Subsequent analysis of this same database by Miller¹¹ focusing on the acute dissections framed the argument for offering operation to more young patients without complications with acute type B dissections. Focusing only on the 89 patients with acute Stanford type B aortic dissections, there were 30 patients remaining after exclusion of those with life-threatening complications ($n = 24$) and those who were not good surgical risks on the basis of other medical problems ($n = 35$). This low-risk cohort of patients was considered suitable for either medical or surgical therapy. Of these, 19 were treated medically and 11 were treated surgically. The early mortality for the medical patients was 16%, versus 9% for the surgical patients. This subset of patients without complications who otherwise are reason-

able operative candidates probably is representative of the 29 patients operated on at Mt Sinai⁸ with no deaths. We continue to advocate that such carefully selected patients be considered for early operation.

This study reviews our entire experience for a period of 36 years with the treatment of patients with acute Stanford type B aortic dissection. The obstacles, as previously encountered by our group and others, are the heterogeneous nature of the study populations, inherent selection and referral biases, continuous evolution of established treatment methods, and the advent of new percutaneous interventional therapies. Analysis of the entire experience demonstrated a trend toward lower surgical mortality risk through the years, from 57% between 1963 and 1969 to 27% between 1990 and 1999 (Figure 4). Our most recent experience is more encouraging (no early surgical deaths in 6 patients without complications operated on after 1992); this may be due in part to the introduction of percutaneous interventional revascularization, which has increased the number of extremely sick patients undergoing medical treatment.

To address selection bias and the heterogeneous patient population, we used propensity score analysis to discriminate a group of patients that allowed more meaningful comparison of medical and surgical therapies. This group (quintiles I and II) included 142 patients (31 surgical and 111 medical), which were well matched. Analysis of these comparable patients in quintiles I and II showed that late survivals in the medical and the surgical groups were remarkably similar. For the 31 patients in quintiles I and II who were operated on, the operative mortality was 20%.

The long-term results reported here are consonant with those reported previously by Glower and colleagues²³ in the Duke-Stanford database study. Unfortunately, this sobering prognosis seems to reflect the fact that most patients who sustain an acute type B aortic dissection have other life-limiting illnesses (Figures 5, A, and 6, A). We therefore specifically looked at the rates of reoperation and dissection-related complications in quintiles I and II. Survivals free of dissection-related complications (Figure 6, D) at 5 and 10 years were 82% and 62% in the medical group and 68% and 68% among the surgical patients ($P = .8$). The difference in survival free of reoperation (Figure 6, B and C) also failed to reach statistical significance, although the curves for the surgical group stabilized after 3 years at 86%, whereas that for the medically treated patients continued to decline to 62% after 10 years. It is important to remember, however, that only small numbers of patients remained at risk beyond 5 to 10 years.

In summary, these data indicate that medical therapy appears to confer some survival advantage during the short term (Figure 5, A), but this is not statistically significant; other patient-related and dissection-related factors truly determine outcome (Table 3). Furthermore, the comparable

patients in quintiles I and II had an identical prognosis whether treated medically or surgically (Figure 6, A). If expected survivals among these comparable patients were the same regardless of whether a patient was treated surgically or medically, these results can be interpreted two completely different ways. One could logically infer that all patients should be treated medically; conversely, but equally logically, another observer could infer that all patients should be treated surgically. Because our surgical experience with 6 patients without complications since 1992 and that at Mt Sinai with 29 patients⁸ between 1985 and 1997 have demonstrated that extremely low operative mortalities and morbidity rates are realistic, we interpret the results of this analysis as justification for offering early operation on a selective basis to more patients, even in the absence of complications, including those with Marfan syndrome, younger patients, and those judged to be good operative candidates. Indeed, Marfan syndrome was the only significant independent predictor of reoperation or late aortic complications or death. Overall, early operation certainly did not provide normal life expectancy (Figures 5, A, and 6, A), but on the basis of contemporary results here and elsewhere,⁸ we believe that consideration of early operation may potentially reduce the need for reoperation and perhaps the incidence of fatal events. Only more follow-up of patients currently surviving early operation will answer this question in the future.

Percutaneous fenestration and stenting techniques to correct ischemic complications related to thoracoabdominal malperfusion have become a valuable adjunct to both medical and surgical therapy, but what is the role of endovascular stent-grafts in the future for these patients? Recently we showed that stent-grafts are associated with an early mortality of 16% among patients with acute Stanford type B aortic dissections who have life-threatening complications²⁴; if treated conventionally with an emergency thoracotomy, these patients would be facing an early risk in the range of 40%, or upward of 60% to 70% if treated medically.^{11,16,19,23} The effectiveness of stent-grafts for patients with complicated acute Stanford type B aortic dissections, however, must be confirmed in prospective randomized trials in which this endovascular approach can be rigorously compared with conventional open operation. A bigger unanswered clinical question pertains to the patients with acute Stanford type B aortic dissection who do not have complications, for whom stent-grafts have also been used successfully.²⁵ To address this quandary, we strongly endorse proceeding with multicenter randomized trials in which medical therapy is compared head to head with stent-grafting. Only such controlled trials can conclusively provide the information that we need to guide our therapeutic strategies in the future.

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Discussion

Dr Dave Fullerton (*Chicago, Ill*). This is a complex subject, and all of us around the country have looked to Stanford during the last several decades for guidance in how to treat these difficult problems. What Umaña and colleagues have provided us with today is enlightening.

When I saw the title of the abstract, I assumed that it would reinforce what most of us continue to teach: type B dissections should be treated medically. The thought process behind that was some data suggesting that outcomes were substantially better if such patients were treated medically rather than surgically. I am sure that this series reflected a bias of the worst patients getting operated on. Nonetheless, Umaña and colleagues showed there was really no difference in need for reoperation, no difference in aortic or other complications, and, most impressively, really no difference in survival when patients were treated medically or surgically.

Because the patients undergoing surgery almost certainly represented the worst cases, yet surgical outcomes were not different from medical outcomes, this really begs the question of whether we should operate on these patients, rather than treat them medically. Dr Umaña, would you extrapolate on that a little bit? Second, I know that your group has experience with the development of the endovascular stent technology. You probably have some experience in treating these patients off protocol. Could you share some of that with us?

Dr Umaña. In terms of whether we should operate more on these patients, I think that what we need to do is individually tailor patient treatment. If you have a patient at low risk who has a reasonable life expectancy and is a good operative candidate, our belief is that you probably should operate if you can achieve an operative mortality less than 5%. In those cases, the outcome should be better. In looking at our own series during the last decade those results are essentially reflected.

Regarding the stent grafts, we have published our experience with use of stent grafts in complicated acute type B aortic dissection. Patients who would otherwise have a mortality of approximately 50% had an operative mortality of about 16%. These stent-grafts can be used. This was a small patient group of only 19 patients, 16 of whom were treated at Stanford, and that study, as I said, needs to be validated in a prospective fashion.

The question is, should we be using stent grafts for patients without complications? I think the answer to that lies only in a prospective randomized study, again comparing stent-graft and medical treatment.

Dr Vaughn Starnes (*Los Angeles, Calif*). I want to add a sense of Western Thoracic Surgical Association tradition to your nice

presentation, Dr Umaña. This is the 27th Western Thoracic Surgical Association meeting, and you are a candidate for the Samson resident prize. Dr Fullerton, who discussed the article at the invitation of our program committee, was a recipient of this prize 11 years ago in 1990. We wish you well, and we look forward to your being an invited discussant in years to come on the basis of your accomplishments.

Dr Edward Verrier (*Seattle, Wash*). I think that this is an important article, and I have a two-part question. Why do the patients die every time? Mortality does not seem to be directly related to thrombotic disease. Aren't the preoperative risk factors the predictors of long-term outcome, rather than the aortic disease itself?

Dr Umaña. That is exactly right. If you look at the causes of late death, we found that aortic-related deaths accounted only for about 30% of those, whereas most patients died of their comorbidities, such as pulmonary disease, renal dysfunction, and underlying cardiac disease.

Dr Verrier. Now if we believe that, I will just make one more extrapolation. Why should we change our current teaching on therapy for acute type B dissection?

Dr Umaña. That is why I started by saying that if we are going to change our practice, we should individually tailor it. We have to customize it to the patient. If you have a patient who is young and who has no cardiac disease or pulmonary disease (and I know that they are rare, but the study from Mount Sinai includes 29 patients with those characteristics), then you should probably operate on them.

Dr Verrier. Would that group be the patients with Marfan syndrome, then?

Dr Umaña. Not necessarily. It would probably include the patients with Marfan syndrome, but it would not necessarily be all patients with Marfan syndrome.

Dr Starnes. The third corollary to that question is, why does a surgical group end up being at the same spot even though survival does not go down in parallel. You have a higher mortality with surgery at the time of surgery, and you would think that survivals would go down in parallel if they were not related to the aortic disease. That is why it remains so ambiguous in terms of how to interpret these data.

Dr Umaña. This is something we have been discussing among ourselves. We believe that if you can get rid of that operative mortality, then your survival curve will come up 15 points and all of a sudden your surgical group will stay up higher. What I interpret your question to mean is that survival in the surgical group of patients drops off acutely but then seems to be flatter, if you will, than the medical curve. If you can get rid of the operative mortality, then presumably your midterm or long-term results and outcome are going to be better.