Immediate operation for acute type A aortic dissection complicated by visceral or peripheral malperfusion

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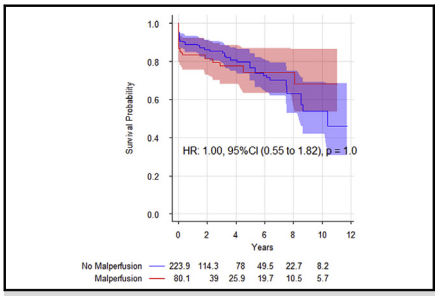
ABSTRACT

Objective: To evaluate the effect of visceral, renal, or peripheral malperfusion on the outcome of acute type A aortic dissection.

Methods: We performed a retrospective review of the acute type A aortic dissection experience at Stanford Hospital between January 2005 and December 2015. Inverse probability weighting was used to account for differences between patients who experienced malperfusion syndromes and those who did not. Weighted logistic regression was used to evaluate in-hospital mortality, and midterm survival was assessed with the restricted mean survival time and weighted Cox regression. Reintervention was assessed with death as a competing risk.

Results: There were 305 patients with type A dissection extending beyond the ascending aorta, and 82 (26.9%) presented with a malperfusion syndrome. In-hospital mortality in the malperfusion subgroup was no different compared with patients without malperfusion in weighted logistic regression, odds ratio, 1.50 (95% confidence interval, 0.65-3.47; $P = .3$). There was no difference in midterm survival using restricted mean survival time, −50.2 days (95% CI, −366.8 to 266.4; $P = .8$) in patients with malperfusion compared with patients without malperfusion at 8 years. Patients with malperfusion had an increased risk of interventions (12.5%) on aortic branches compared with patients without (5.7%) in weighted analysis at 10-years, hazard ratio, 3.06 (95% CI, 1.24-7.56; $P = .02$). The median time to reintervention on aortic branches was 2 days for patients with malperfusion compared with 230 days without malperfusion, $P = .01$.

Conclusions: Immediate operation for acute type A aortic dissection complicated by malperfusion is associated with good results. (J Thorac Cardiovasc Surg 2018;156:18-24)



There was no survival difference between patients with and without malperfusion.

Central Message

Immediate operation for acute type A aortic dissection complicated by malperfusion remains the gold standard therapy.

Perspective

Given the rise of the "endovascular-first" approach in acute type A aortic dissection complicated by malperfusion, the role of immediate surgical therapy is uncertain. We demonstrate that repair of the ascending aorta with reconstitution of true lumen flow remains the gold standard approach to patients with malperfusion and is not associated with increased risk of death in a contemporary cohort.

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Acute type A aortic dissection is a life-threatening emergency that is treated with emergent surgery.[1] When this process is complicated by malperfusion, perioperative mortality has been reported to range from 29% to 89%.[2-4] Despite the potential increase in risk, the practice at Stanford has been to perform immediate surgery to reconstitute antegrade true lumen flow, resolve dynamic flow obstruction in aortic branches, and depressurize the false lumen.[5] However, in an effort to mitigate the increased risk associated with malperfusion syndromes, surgeons have advocated for the restoration of true lumen flow to threatened end-organs first. Historically, this task was

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Abbreviations and Acronyms
CI = confidence interval
HR = hazard ratio
OR = odds ratio

accomplished with open fenestration, but more recently endovascular techniques have been developed to achieve this goal.[4,6-9] Patel and colleagues[7] have reported excellent outcomes for patients with malperfusion treated by a strategy of operative delay who eventually underwent surgery; the Michigan group also reported 33% mortality (23 of 70) in patients waiting for an operation. In light of this, the optimal management of malperfusion remains controversial.

Advocates of the "endovascular-first" approach to malperfusion have recommended subcategorizing patients with acute type A aortic dissection into a "type A—no malperfusion" group, who would proceed immediately to surgery, and a "type A—malperfusion" group, who would initially proceed with endovascular therapy and experience operative delay.[10] This is despite the lack of evidence that a strategy of endovascular reperfusion truly attenuates the risk directly attributable to malperfusion syndromes. We undertook the current study to evaluate the effect of malperfusion on outcomes of immediate operative repair of all patients with acute type A aortic dissection in a contemporary cohort.

METHODS

After approval from the institutional review board at Stanford University, we performed a retrospective review of patients treated for acute type A aortic dissection at Stanford Hospital between January 1, 2005, and December 31, 2015 using departmental databases and a query of billing data in the Stanford Translational Research Integrated Database Environment. We excluded patients undergoing definitive endovascular repair, preoperative endovascular revascularization, and iatrogenic aortic dissection (either from manipulation during cardiac surgery or due to thoracic aortic endograft implantation). Patients with aortic dissection limited to the ascending aorta also were excluded.

Malperfusion was defined as patients with signs and symptoms of compromised blood flow to a limb, visceral vessel, or renal artery by using a combination of clinical history, physical examination, radiographic studies, and laboratory values. For limb malperfusion, clinical documentation of a pulse deficit (not just pressure differential) was necessary, and available radiographic evidence was used to corroborate the clinical findings. Visceral malperfusion was determined via a combination of clinical and radiographic factors, including radiographic evidence of flow obstruction with clinical evidence of ischemia to the abdominal viscera including melena or abdominal pain with distention. Evaluation of renal malperfusion may be challenging, given the multiplicity of factors that can precipitate acute kidney injury in the setting of aortic dissection; we used radiographic evidence of delayed enhancement or renal artery dissection in conjunction with a rise in creatinine. The isolated presence, radiographically, of a dissection flap into a branch vessel without demonstrable flow impedance was not considered malperfusion.

Patients with neurologic deficit (attributable to either the brain or spinal cord) were not categorized in the malperfusion group—and were thus distributed between the 2 arms of our study—for 2 reasons. First, many of the neurologic deficits appeared to be related to hypotension and low cardiac output and not necessarily obstruction of a carotid artery. Second, patients with neurologic deficits may in fact be best served with immediate operation,[10-12] and so this did not appear to be the pertinent question. Patients with coronary malperfusion also were not categorized in the malperfusion group for the same reason: these patients require immediate restoration of true lumen flow with either ostial reconstruction or coronary artery bypass grafting.

Normally distributed continuous variables are presented with standard deviation and were compared with Student t test; non-normally distributed continuous variables are presented with interquartile ranges and were compared with the Wilcoxon rank-sum test. Categorical variables are reported with absolute counts and percentages, and comparisons were made with the χ^2 test or Fisher exact test. Odds ratios (ORs) and hazard ratios (HRs) are presented with 95% confidence intervals (CIs). A 2-tailed P-value <.05 was considered to be statistically significant. Because of the exploratory nature of this study, no adjustment was made for multiple comparisons.[13] All analyses were performed in R 3.2.2 (R foundation, Vienna, Austria).

Outcomes

The primary endpoint was overall midterm survival, and this was verified by using a combination of the Social Security Death Index, integrated electronic medical records, and direct patient contact through our thoracic aortic monitoring program. Patients were censored at the time of last contact. Our protocol is similar to that reported by the Yale group and involves a dedicated group of advanced practice practitioners, surgeons, radiologists, and administrative assistants.[14] Use of the Social Security Death Index alone was not appropriate, given substantial missingness.[15] Our secondary endpoints were reoperation on the distal aorta (aortic arch, descending thoracic aorta, abdominal aorta) or aortic branch revascularization. As part of an exploratory analysis, we evaluated the incidence of perioperative morbidities including respiratory insufficiency, tracheostomy, acute kidney injury, hemodialysis, and heparin-induced thrombocytopenia and thrombosis.

Statistical Analysis

Assuming an absolute difference for in-hospital mortality of 15%,[2,3] this study had 88% power to detect a difference with an alpha of 0.05. Inverse probability weighting was used to account for baseline differences between patients with and without malperfusion. We began by constructing a nonparsimonious logistic regression to estimate the probability of experiencing malperfusion based on observed covariates (Table E1). Stabilized weights were then estimated by multiplying the marginal probability of malperfusion by the inverse of the probability of the actual designated group (malperfusion group weights: $\frac{[\text{proportion of patients experiencing malperfusion}]}{\text{probability of malperfusion}}$; control weights: $\frac{[1-\text{proportion of patients experiencing malperfusion}]}{1-\text{probability of malperfusion}}$).[16] This yielded the average exposure effect as opposed to the average exposure effect on the exposed. Balance was assessed by using standardized mean differences; a difference of <20% was considered to be appropriate, and a difference of <10% was considered ideal.[17,18]

Adjusted survival curves were constructed,[19] and midterm survival was compared with weighted Cox proportional hazards regression with a robust variance estimator using the *survival* package.[20] The possibility of a surgeon effect was accounted for by using a separate mixed-effects Cox proportional hazards model with surgeon as a random intercept using the *coxme* package. Given the observed differences in perioperative mortality in the literature and the possibility of nonproportional hazards, we evaluated in-hospital mortality using weighted logistic regression with a robust variance estimator and additionally performed survival analysis using restricted mean survival time and weighted Cox regression.[21] Finally, we evaluated the risk of reoperation using a weighted form of the Fine–Gray subdistribution hazard.[22]

This technique accounts for death as a competing risk given that the two events may not be independent.

Previous studies have evaluated the influence of multiple malperfused sites on survival.[2,10] To evaluate the possibility that the number of malperfused sites affected perioperative mortality, we used backwards selection in 200 bootstrap replicates to develop a parsimonious logistic regression model with the available plausible preoperative demographic, clinical, and presenting variables (Table E2).[23] The number of malperfused sites was evaluated as a categorical rather than a continuous variable. Only variables that appeared frequently and with consistent signs were included in the final model; this analysis was performed with the *bootStepAIC* package.

RESULTS

There were 391 patients with acute type A aortic dissection who presented to Stanford Hospital in the time period studied. Of these, 31 (7.9%) patients were treated nonoperatively, 14 (3.6%) were treated with definitive endovascular therapy, and 2 (0.5%) patients underwent preoperative endovascular revascularization before proceeding with an open operation at a later time. The patients treated with definitive endovascular therapy underwent either stent grafting of the ascending aorta or thoracic endovascular aortic repair to cover a primary intimal tear in the descending thoracic aorta with retrograde propagation into the ascending aorta without reentry. Only 2 of these patients had experienced preoperative malperfusion. An additional 2 patients with malperfusion syndromes were initially treated with preoperative endovascular revascularization for malperfusion: 1 patient underwent celiac artery stenting and endovascular flap fenestration followed by replacement of the ascending aorta 2 days later. The second patient had a previous aortic root replacement with dissection of the residual ascending aorta; he underwent flap fenestration in the acute phase of his aortic dissection. This was followed by definitive ascending aortic and total arch replacement with frozen elephant trunk 329 days later.

After these exclusions, 344 patients underwent open repair of an acute type A aortic dissection at our institution during the time period under study, and 39 patients had aortic dissection limited to the ascending aorta, leaving 305 patients eligible for the current analysis. Of these patients, there were 82 (26.9%) who presented with a visceral, renal, or peripheral malperfusion syndrome. There were limited differences between the 2 populations at baseline, with more patients with diabetes in the cohort without malperfusion and more patients with neurologic deficits at presentation in the group with malperfusion. All variables were appropriately balanced after the

TABLE 1. Differences in covariates at baseline and after applying IPW: after applying stabilized weights, there was no observed difference

	Baseline variables			After IPW		
	No malperfusion n = 223	Malperfusion n = 82	SMD	No malperfusion n = 223.9	Malperfusion n = 80.1	SMD
Patient demographics						
Operative year, median [IQR]	2011 [2008, 2014]	2010 [2008, 2013]	0.076	2011 [2008, 2014]	2010 [2008, 2013]	0.027
Age, y, mean (SD)	58.87 (13.53)	58.18 (11.35)	0.055	58.67 (13.38)	58.48 (11.52)	0.015
Female sex, n (%)	64 (28.7)	18 (22.0)	0.156	(26.4)	(22.9)	0.082
White, n (%)	116 (52.0)	43 (52.4)	0.008	(50.8)	(55.5)	0.093
Black, n (%)	11 (4.9)	9 (11.0)	0.225	(7.0)	(6.9)	0.004
Comorbidities						
Previous stroke, n (%)	5 (2.2)	2 (2.4)	0.013	(2.7)	(2.2)	0.029
Heart failure, n (%)	11 (4.9)	6 (7.3)	0.100	(5.3)	(4.6)	0.034
Hypertension, n (%)	190 (85.2)	74 (90.2)	0.154	(86.6)	(87.2)	0.019
Coronary artery disease, n (%)	20 (9.0)	9 (11.0)	0.067	(9.4)	(8.7)	0.022
Atrial fibrillation, n (%)	18 (8.1)	3 (3.7)	0.189	(6.8)	(4.6)	0.093
COPD, n (%)	28 (12.6)	9 (11.0)	0.049	(12.2)	(10.7)	0.048
Home O_2, n (%)	1 (0.4)	1 (1.2)	0.085	(0.7)	(0.7)	0.002
Diabetes, n (%)	15 (6.7)	2 (2.4)	0.206	(5.6)	(6.7)	0.047
Hyperlipidemia, n (%)	59 (26.5)	18 (22.0)	0.105	(24.7)	(22.6)	0.05
Chronic renal insufficiency, n (%)	33 (14.8)	18 (22.0)	0.185	(17.0)	(16.8)	0.005
Dialysis, n (%)	5 (2.2)	1 (1.2)	0.078	(1.9)	(1.4)	0.043
Bicuspid aortic valve, n (%)	11 (4.9)	6 (7.3)	0.100	(5.1)	(7.4)	0.097
Marfan syndrome, n (%)	9 (4.0)	2 (2.4)	0.090	(3.4)	(3.5)	0.006
Other connective tissue disease, n (%)	8 (3.6)	1 (1.2)	0.155	(3.1)	(2.3)	0.052
Clinical characteristics						
Redo sternotomy, n (%)	11 (4.9)	6 (7.3)	0.100	(4.9)	(6.0)	0.051
Shock, n (%)	26 (11.7)	14 (17.1)	0.155	(12.7)	(11.8)	0.025
Persistent neurologic deficit, n (%)	17 (7.6)	12 (14.6)	0.224	(9.9)	(10.8)	0.032

IPW, Inverse probability weighting; *SMD*, standardized mean difference; *IQR*, interquartile range; *SD*, standard deviation; *COPD*, chronic obstructive pulmonary disease.

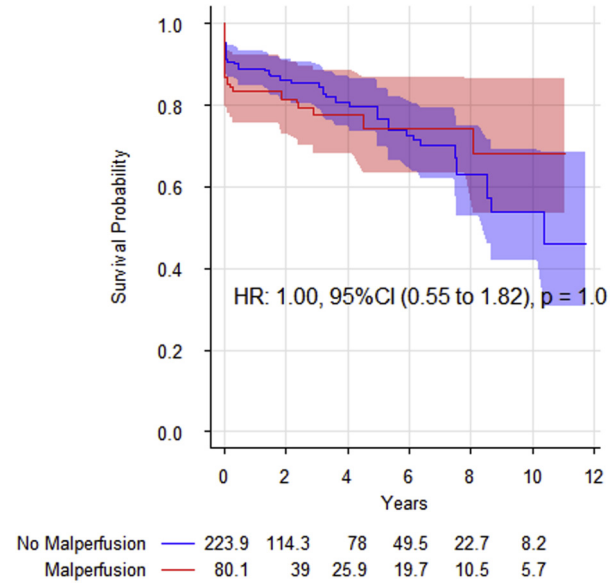

FIGURE 1. Adjusted survival curves comparing patients with malperfusion (*red*) with patients without malperfusion (*blue*). There was no difference in midterm survival. *Shading* represents 95% confidence intervals (*CIs*). *HR*, Hazard ratio.

application of inverse probability weighting with stabilized weights (Table 1). There were no differences with respect to cardiopulmonary bypass time or extent of operation between patients with and without malperfusion. The vast majority of patients (89.8%) received blood or blood products during the index hospitalization, and there was no difference between groups after weighting. Of 305 patients, 284 (93.1%) were transferred from another institution, and the time from presenting symptoms to skin incision was <24 hours in 79.3% of patients (242/305). Median follow-up was 2.0 years (interquartile range: 0.2-5.3 years).

Survival

Adjusted survival curves demonstrated no difference in midterm survival with malperfusion, HR 1.00 (95% CI, 0.55-1.82; $P = 1.0$) (Figure 1), and this was no different after accounting for surgeon with a mixed-effects Cox regression, HR 1.00 (95% CI, 0.57-1.74; $P = 1.0$) (Table 2). The relative hazard of death was not constant between groups throughout the follow-up period, ie, proportional hazards assumption was violated, and this was handled by separately evaluating in-hospital mortality and restricted mean survival time.

In-hospital mortality in the malperfusion subgroup was no different (11/82, 13.4%) compared with patients without malperfusion (19/223, 8.5%) when we used unadjusted univariable logistic regression, OR, 1.66 (95% CI, 0.75-3.67; $P = .2$), and weighted univariable logistic regression with a robust variance estimator confirmed this finding, OR 1.50 (95% CI, 0.65-3.47; $P = .3$) (Table 2). Using restricted mean survival time, we found there was no difference in midterm survival with a mean difference in survival of −50.2 days (95% CI, −366.8 to 266.4; $P = .8$) in patients with malperfusion compared with patients without malperfusion at 8-year follow-up.

In our exploratory analysis, patients with malperfusion had a greater incidence of perioperative morbidity, including acute kidney injury (50.7% vs 35.0%, $P = .02$), hemodialysis (20.1% vs 7.0%, $P = .003$), fasciotomy (7.2% vs 0.5%, $P = .002$), and heparin-induced thrombocytopenia and thrombosis (8.7% vs 1.8%, $P = .008$) after we accounted for differences in baseline variables with inverse probability weighting. There were no other differences in postoperative morbidities (Table 3).

Reoperation

Reoperation was separated into interventions on aortic branches (renal, celiac, superior mesenteric, or iliac artery) and reoperations on the distal aorta (arch, descending, abdominal aorta, or thoracoabdominal operations). Some patients underwent multiple procedures over the course of time; time to first reintervention was used in this analysis. There were 19 patients who underwent reinterventions on aortic branches in unweighted analysis resulting in 5 visceral stents, 8 iliac operations, and 12 renal stents. In the weighted analysis, patients with malperfusion had a significantly increased risk of interventions on aortic branches (12.5% at 10 years) compared with patients without malperfusion (5.7% at 10 years), HR, 3.06 (95% CI, 1.24-7.56; $P = .02$) (Figure 2). The median time to aortic branch intervention among patients with malperfusion was 2 days as compared with 230 days among patients without malperfusion, $P = .01$.

With respect to aortic reoperations, there were 27 patients who underwent 32 distal aortic reoperations: 6 total arch replacements, 2 hemiarch replacements, 5 thoracoabdominal repairs, 7 thoracic endovascular aortic repairs, 5 open descending thoracic aortic aneurysm repairs, 5 endovascular aortic repairs of the abdominal aorta, and 2 open abdominal aortic aneurysm repairs. In weighted analysis, there was no difference observed between patients with and without malperfusion, HR, 0.55 (95% CI, 0.20-1.50; $P = .31$) (Figure 3).

Malperfused Sites

Most patients (60/82, 73.2%) had only 1 site of malperfusion (limb, renal, or visceral), whereas 19 (23.2%) had 2 affected sites and only 3 (3.7%) had 3 affected sites. Unadjusted in-hospital mortality for patients with limb malperfusion was 14.5% (10 of 69), renal malperfusion was 16.1% (5 of 31), and mesenteric malperfusion was 28.6% (2 of 7). In multivariable logistic

TABLE 2. Effect of malperfusion on postoperative survival and in-hospital mortality

Survival	Hazard ratio (95% CI)	*P*
Cox regression, weighted	1.00 (0.55-1.82)	1.0
Cox regression, weighted with mixed effects	1.00 (0.57-1.74)	1.0
Perioperative mortality	**Odds ratio (95% CI)**	***P***
Logistic regression, unadjusted	1.66 (0.75-3.67)	.2
Logistic regression, weighted with robust variance estimator	1.50 (0.65-3.47)	.3

Weighted comparisons are univariate as weighting created appropriately balanced groups. *CI*, Confidence interval.

regression with bootstrap backwards selection, presenting with 3 malperfused sites increased the odds of in-hospital mortality compared with no malperfusion, OR 108.4 (95% CI, 6.0-1945.1, $P = .001$) (Tables E2 and E3). Additional variables that reached statistical significance were presence of a persistent neurologic deficit, shock at presentation, presentation with myocardial infarction, obstructive sleep apnea, and older age; malperfusion of 1 or 2 sites was not associated with an increased risk of perioperative mortality.

DISCUSSION

Perioperative and midterm mortality for immediate open surgical repair of patients with acute type A aortic dissection complicated by malperfusion were no different from patients without malperfusion after we adjusted for available clinical variables. However, there were more peripheral, renal, and visceral revascularization procedures among patients with malperfusion, and these operations typically occurred soon after the repair. Patients with distal malperfusion syndromes also had a greater incidence of perioperative morbidity, including hemodialysis and fasciotomy. On the one hand, this finding suggests that surgeons caring for these complicated patients have to maintain vigilance during the postoperative period and aggressively evaluate potential peripheral vascular threat. On the other hand, our results appear to challenge the current trend toward using an ''endovascular-first'' approach in the management of patients with malperfusion complicating acute type A aortic dissection.

The practice at Stanford Hospital has always been to operate immediately in an effort to reconstitute true lumen flow.[5] The rationale for this strategy has been supported in a study by Chung and colleagues[24] using bench-top models with pulsatile flow demonstrating that true lumen collapse was attributable to either a large inflow tear with false lumen non-reentry or low cardiac output with low true lumen outflow resistance. A follow-up report by Chung and colleagues[25] further suggested that addressing the primary intimal tear was more effective than creating fenestrations in the intimal flap in their model. Providing additional circumstantial evidence for the effectiveness of an approach focused on addressing the primary intimal tear and restoration of true lumen flow, Czerny and colleagues[10] recently reported in the German Registry for Acute Aortic Dissection Type A that ascending aortic primary intimal tears, which are addressed in the standard operation for type A dissection, reduced the odds of postoperative visceral malperfusion syndromes. Conversely, descending aortic primary intimal tears, ie, tears not addressed during a standard type A aortic dissection operation, were associated with an increased odds of visceral malperfusion.

These findings suggest theoretical limitations to the approach of operating immediately. Firstly, immediate operation will not resolve static flow obstructions. Secondly, large distal fenestrations or a distal primary intimal tear may cause ongoing false lumen pressurization even after replacement of the ascending aorta resulting in persistent postoperative malperfusion syndromes. Whether retrograde type A dissections represent a special case that might be better treated endovascularly to address the primary intimal tear is uncertain, and this is an area of active interest for our group.

Despite the inability to address distal fenestrations and primary intimal tears of the descending aorta with

TABLE 3. Postoperative morbidities

	No malperfusion	Malperfusion	*P*
Intubation >48 h, n (%)	81.1 (36.2)	35.0 (43.7)	.3
Acute kidney injury, n (%)	78.4 (35.0)	40.6 (50.7)	.02
Hemodialysis, n (%)	15.7 (7.0)	16.1 (20.1)	.003
Fasciotomy, n (%)	1.2 (0.5)	5.8 (7.2)	.002
Heparin-induced thrombocytopenia and thrombosis, n (%)	4.1 (1.8)	6.9 (8.7)	.008
Mediastinal re-exploration, n (%)	23.1 (10.3)	13.4 (16.7)	.2
ICU length of stay, d [IQR]	5 [3, 10]	5 [3, 8]	.9
Hospital length of stay, d [IQR]	10 [7, 17]	10 [7, 17]	.8

ICU, Intensive care unit; *IQR*, interquartile range.

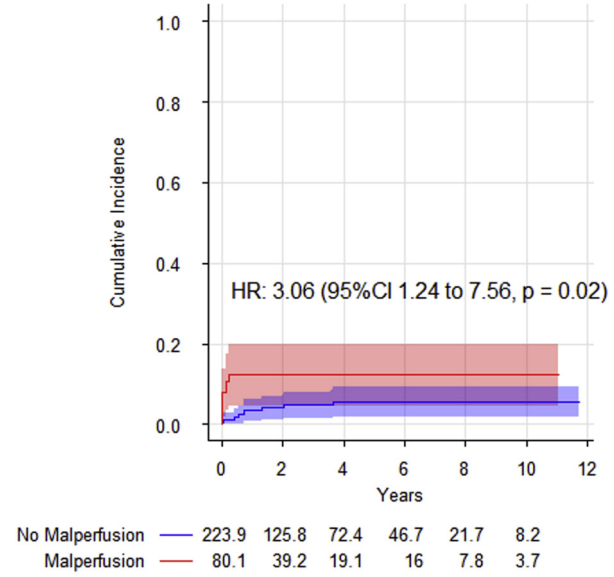

FIGURE 2. Weighted Fine–Gray subdistribution hazard demonstrating the increased risk for aortic branch intervention (iliac arteries, renal arteries, celiac artery, or superior mesenteric artery) after repair of acute type A aortic dissection in patients with malperfusion (*red*) as compared with patients without malperfusion (*blue*). *Shading* represents 95% confidence intervals (*CIs*). *HR*, Hazard ratio.

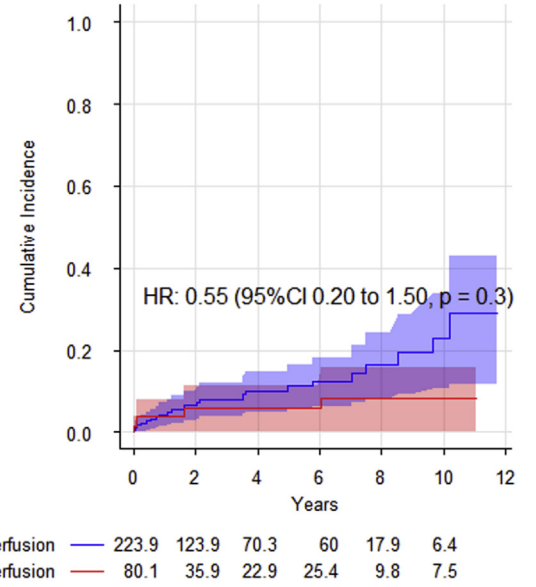

FIGURE 3. Weighted Fine–Gray subdistribution hazard demonstrating no difference in the risk for distal aortic reintervention (aortic arch, descending thoracic aorta, abdominal aorta, or thoracoabdominal aorta) after repair of acute type A aortic dissection in patients with malperfusion (*red*) as compared with patients without malperfusion (*blue*). *Shading* represents 95% confidence intervals (*CIs*). *HR*, Hazard ratio.

immediate open surgical repair, the vast majority of patients with malperfusion in our series did not require postprocedural revascularization. This suggests that a strategy of operative delay to perform an endovascular reperfusion maneuver would not have helped most of the patients afflicted by malperfusion in our series. Conversely, the 33% mortality (23 of 70) reported while waiting for an operation after endovascular reperfusion is of some concern.[7] One half of these patients died of aortic rupture, which may have been prevented with an expedient surgical intervention; the other half of the patients died of complications of malperfusion despite technical success in the catheterization laboratory. Although this strategy may have prevented the ''doomed'' patients from undergoing an operation from which they would never benefit, it appears difficult to allege that many of these patients would not have benefited from early reconstitution of true lumen flow, given the outcomes observed in our cohort.

One of the challenges facing evaluations of the data available in the literature has been the lack of an appropriate comparator arm. Patel and colleagues[7] used 9 historical controls from 1992 to 1994 to compare with a more contemporary group of aortic dissection patients; conversely, neither the German Registry for Acute Aortic Dissection Type A report nor our cohort contained an ''endovascular-first'' arm. Despite the limitations of published reports, the apparent lack of evidence supporting an ''endovascular-first'' approach is not reflected in the literature. Whether the field should continue to move toward an unproven therapy that fails to address the potential risk of aortic rupture, aortic insufficiency, or propagation of the dissection remains uncertain. The practice of initial endovascular reperfusion requires further investigation and stronger evidence before the introduction of a subclassification system.

Limitations

Our analysis was limited by virtue of being a single high-volume aortic referral center. Despite the large number of referrals for acute type A aortic dissection, our study may not have been large enough to determine whether small differences in risk existed between patients with and without malperfusion syndromes. However, other large centers have reported absolute risk differences of up to 15% to 20%,[2,3] and our study was adequately powered to detect a difference this large.

Approximately 70% of patients in the International Registry of Acute Aortic Dissections, which primarily consists of high-volume aortic referral centers, were transferred from outlying hospitals; more than 90% of the patients treated at Stanford were transferred from other hospitals. Whether this introduced bias in the form of either survivor bias or selection bias is unclear, but the proportion of patients experiencing malperfusion syndromes in our series was on par with other large centers, the German registry, and a population-based study in Iceland.[2,3,10,26] Finally, it is possible that there may have been differential loss to follow-up, which would have biased our outcome evaluation.

CONCLUSIONS

Immediate operative intervention for acute type A aortic dissection complicated by visceral, renal, or peripheral malperfusion was associated with good in-hospital outcomes at a high-volume thoracic aortic referral center. Midterm survival after discharge did not appear to be influenced by malperfusion, although patients with malperfusion more frequently underwent early aortic branch intervention. Reconstitution of true lumen flow with immediate operation is associated with good outcomes, and this approach rendered visceral and peripheral intervention unnecessary in the majority of cases. Before the institution of a sub-classification system and recommendation for operative delay, the ''endovascular-first'' approach still has to prove itself superior to the gold-standard therapy of immediate operative repair.

Conflict of Interest Statement

Dr Fischbein has received speaking honoraria from Abbott. Additionally, he receives funding from the National Institutes of Health (NIH R01AR066629-01A1). All other authors have nothing to disclose with regard to commercial support.

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Key Words: aorta, aortic dissection, malperfusion, reoperation, outcomes

TABLE E1. Propensity score model

	Estimate	Std. error	*P*
(Intercept)	60.422	89.003	.5
Age	−0.005	0.012	.7
African American	0.542	0.533	.3
Sex	−0.172	0.327	.6
Connective tissue disease	−0.822	0.685	.2
Chronic renal insufficiency	0.664	0.408	.1
Dialysis	−0.897	1.226	.5
Coronary disease	0.463	0.496	.4
Home oxygen	1.158	1.449	.4
Hyperlipidemia	−0.427	0.373	.3
Hypertension	0.435	0.440	.3
Diabetes	−0.939	0.790	.2
Atrial fibrillation	−0.935	0.686	.2
Preoperative shock	0.458	0.402	.3
Preoperative neurologic injury	0.664	0.435	.1
Operative year	−0.031	0.044	.5

TABLE E2. Variables explored in 200 bootstrap replicates

Variables explored	Final model
Number of malperfused sites	Number of malperfused sites
Shock at presentation	Shock at presentation
Tamponade at presentation	Persistent neurologic deficit at presentation
Persistent neurologic deficit at presentation	Myocardial infarction at presentation
Syncope as initial symptom	Sex
Myocardial infarction at presentation	Previous stroke
Paraplegia at presentation	Coronary disease
Sex	Diabetes
Caucasian	Sleep apnea
Ethnicity	History of aortic disease
Previous stroke	Age
History of smoking	
Heart failure	
Coronary disease	
Atrial fibrillation	
Diabetes	
Renal failure	
Dialysis	
Chronic obstructive pulmonary disease	
Home oxygen	
Sleep apnea	
Illicit drug use	
History of aortic disease	
Marfan syndrome	
Marfanoid	
Age	
Operative year	
Previous sternotomy (reoperative)	

TABLE E3. Multivariable logistic regression exploring the effect of the number of malperfused sites on in-hospital mortality

	Estimate	Std. error	*P*
(Intercept)	−5.427	0.845	<.001
Malperfused sites: 1	0.477	0.573	.4
Malperfused sites: 2	0.791	1.027	.4
Malperfused sites: 3	4.686	1.473	.001
Shock at presentation	1.303	0.558	.02
Persistent neurologic deficit at presentation	2.658	0.626	<.001
Myocardial infarction at presentation	3.385	1.033	.001
Female sex	0.865	0.530	.1
Previous stroke	−17.033	1288.069	1.0
Coronary artery disease	−1.608	1.109	.1
Diabetes	1.540	0.794	.05
Sleep apnea	1.539	0.767	.04
History of aortic disease	1.142	0.585	.05
Age, y	0.010	0.005	.02