Operative delay for peripheral malperfusion syndrome in acute type A aortic dissection: A long-term analysis

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Background: We previously reported an improvement in early mortality for patients presenting with acute type A dissection with malperfusion using a strategy of initial percutaneous intervention to restore end-organ perfusion and delayed operative repair after resolution of the malperfusion syndrome. This study evaluates the late outcomes with this approach.

Methods: A total of 196 patients were admitted with acute type A dissection (1997–2007). Seventy patients with ischemic end-organ dysfunction underwent percutaneous fenestration or branch vessel stenting. Operative therapy was planned after resolution of the reperfusion injury. Outcomes were compared for patients with (MP) and without (UC) dissection with ischemic end-organ dysfunction.

Results: The mean age of the patients was 57.1 years, and 173 patients underwent operative repair (n = 126 UC group; n = 47 MP group). The remaining 23 patients in the MP group died before repair from complications of malperfusion (11) or aortic rupture (12) while awaiting resolution of the malperfusion syndrome. Operative mortality was seen in 9.2% of all patients (9.5% in UC group vs 8.5% in MP group; $P = 1.0$). On analysis of the entire cohort (n = 196), the mean survival was higher for the uncomplicated group (95.9 months for UC group vs 53.7 months for MP group; $P < .001$). A subgroup analysis of patients who underwent operation (n = 173) revealed similar mean survival (95.9 months for UC group vs 80.5 months for MP group; $P = .45$).

Conclusion: A strategy of immediate reperfusion, stabilization, and planned operative repair for acute type A dissection with malperfusion still carries a significant risk for early and late mortality. However, those patients who survive the initial malperfusion and undergo repair have a similar operative and late survival when compared with those patients presenting with uncomplicated dissection.

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Aortic dissection remains the most frequent and lethal complication of thoracic aortic disease. Although several groups, including the multicenter International Registry of Acute Dissection, have demonstrated improving outcomes with operative therapy, malperfusion syndrome associated with acute type A dissection remains a significant adverse risk factor for survival.¹⁻³ Reported in-hospital mortality rates for patients presenting with malperfusion with end-organ dysfunction have varied from 4% to 90%.⁴⁻¹⁰

In 1997, we described our early results for a strategy of operative delay for those patients presenting with acute type A dissection, malperfusion, and ischemic end-organ dysfunction.⁴ In that study, a historical cohort of patients presenting with similar ischemic end-organ dysfunction from malperfusion taken directly for open repair were compared with a cohort managed with initial percutaneous fenestration, selective branch vessel stenting, and delayed operative repair after resolution of the reperfusion injury. In contrast with an in-hospital mortality of 89% in the historical group, those patients who underwent operative delay had an overall 25% mortality, including a 15% mortality from rupture. These early results led to a consistent strategy at our institution of restoring end-organ perfusion before operation for all those patients

Abbreviation and Acronym

CT = computed tomography

presenting with acute type A dissection with significant end-organ ischemia from malperfusion. The current study reports the long-term results of this approach and describes the outcomes for the single largest cohort of patients with acute type A dissection, malperfusion, and ischemic end-organ dysfunction reported in the literature.

Materials and Methods

This study was approved by the University of Michigan Hospitals Institutional Review Board (no. 2003-0128). Informed consent requirements were waived for this study.

We performed a retrospective analysis of data from all patients who were admitted to the University of Michigan Hospitals with a diagnosis of acute type A aortic dissection from 1997 to April of 2007. Acute dissection for this study was defined as its occurrence within 14 days of presentation to the hospital. A combination of clinic and hospital records, imaging studies, and query of the National Death Index was used to obtain long-term information. A total of 196 consecutive patients who were evaluated for operative repair constituted the study cohort. Diagnosis of acute type A dissection was made by the combination of clinical factors, including history and physical examination, and either the use of dynamic computed tomography (CT) or transesophageal echocardiography.

Acute type A dissection without severe ischemic end-organ dysfunction (UC) was suspected in 126 patients, and they proceeded directly to operative repair. This group included patients without evidence of angiographic or clinical malperfusion, and patients who had angiographic malperfusion but did not display evidence of ischemic end-organ dysfunction (eg, absent femoral pulses but adequate sensation and motor function of legs, elevated creatinine with adequate perfusion on CT scan, or compromised true lumen on CT scan without clinical evidence of ischemia). In these patients, the standard operative procedure consisted of a median sternotomy with the rapid institution of cardiopulmonary bypass. An alpha-stat pH strategy was used on bypass. The extent of proximal resection generally included native aortic valve preservation and resuspension, unless contraindicated by the presence of root aneurysm (≥ 4.5 cm) or leaflet pathology. In patients who had a dissection present in the arch, resection of the proximal hemiarch under deep hypothermic circulatory arrest was initially performed as a standard procedure. Extended arch resection was reserved for those patients in whom the entry tear was identified within the arch, or if an arch aneurysm of 4.5 to 5.0 cm or more was identified. With increasing experience with arch resection during the course of the study period, extended arch repair was also preferentially performed in younger patients (< 65 years) or patients with connective tissue disease in the presence of dissected aorta alone. The ascending aorta was resected in all patients. Deep hypothermic circulatory arrest was used as a surgical adjunct in all patients in whom the dissection extended into the distal ascending aorta or beyond. Neuroprotective adjuncts during circulatory arrest consisted of retrograde cerebral perfusion only or a combination of antegrade and retrograde cere-

bral perfusion depending on the operating surgeon preference. However, in all cases of extended arch resection, antegrade cerebral perfusion was used to prevent prolonged cerebral ischemic times. In addition, the head was packed in ice in all patients during the period of cerebral ischemia to prevent rewarming during longer periods of circulatory arrest. In these situations, cerebral ischemic times were calculated as the period of time that the patient did not receive antegrade cerebral flow (ie, either straight hypothermic circulatory arrest or hypothermic circulatory arrest with retrograde cerebral perfusion time). Additional pharmacologic adjuncts included use of intravenous thiopental (1 g), methylprednisolone sodium succinate (Solu-Medrol; Pfizer Inc, New York, NY) (1 g), and mannitol (25 g) administered during the cooling phase when the bladder temperature reached 19°C.

On admission to the hospital, 70 patients (35.7%) had suspected neurologic (stroke or spinal cord ischemia), visceral (abdominal pain or tenderness, acidosis, hyperamylasemia, elevated transaminases, or diarrhea), renal (elevated creatinine and CT evidence of malperfusion), or limb (absent pulses with limb compromise) malperfusion with end-organ dysfunction (MP). This group underwent immediate angiography with percutaneous fenestration and aortic true lumen stenting with or without branch vessel stenting where appropriate. Operative therapy was then planned after resolution of malperfusion and its associated reperfusion syndrome. It is important to note that the decision to delay operative therapy for acute type A dissection for the reasons of malperfusion was only made after full evaluation of the entire clinical picture, incorporating information from the patient's history, physical examination results, and laboratory and imaging data. The mere presence of imaging data suggesting branch vessel compromise in the absence of either symptomatic or physical findings and abnormal laboratory evaluation results did not lead to a delay in operation. The details of the initial clinical scenario prompting delay in aortic repair are listed in Table 1. Presentation in cardiogenic shock was also an indication to proceed directly for operative repair of the type A dissection, regardless of the presence of potential branch vessel compromise. The subsequent intraoperative strategy for the entire group of patients who underwent a delay strategy, including the need for root or extended arch aorta resection or use of deep hypothermic arrest, was similar to that used in the UC group. An outcomes analysis on an intent-to-treat basis was performed, comparing patients presenting with uncomplicated (UC, $n = 126$) versus suspected malperfusion (MP, $n = 70$) acute dissection. Follow-up was 100% complete at a mean of 39 ± 39 months.

Statistical Analysis

Early outcomes included 30-day or in-hospital rates of mortality, stroke, renal failure needing dialysis, and the need for tracheostomy. The primary late outcome of interest was survival time and vital status. Early mortality was defined as that occurring within 30 days of admission or in-hospital death. Late mortality was defined as that occurring thereafter.

Data were analyzed using the Statistical Package for the Social Sciences (SPSS Inc, Chicago, Ill). All data are expressed as mean $\pm$ standard deviation where applicable. Dichotomous variables were evaluated using chi-square analysis; continuous variables were evaluated using analysis of variance (1-way analysis of variance). Multivariate models (logistic regression for dichotomous variables) were constructed using a backward conditional process to

TABLE 1. Initial indications for operative delay strategy^a

Clinical and radiographic criteria	No. affected
Neurologic malperfusion (stroke)	7
Mesenteric malperfusion (all had evidence of visceral vessel involvement on CT scan)	
Acute abdomen	11
Hematochezia or hematemesis	5
Elevated transaminases, amylase, or lipase	3
Severe abdominal pain, nausea, or vomiting	21
Renal malperfusion	
Elevated creatinine and renal ischemia/infarction on CT scan	25
Documented oliguria/anuria and renal ischemia/infarction on CT scan	5
Limb malperfusion	
Loss of pulses with sensorimotor changes	23

CT, Computed tomography. ^aMore than 1 indication may be present per patient. If evidence of multiple malperfused beds were present, only those data prompting angiography were included in this table (eg, in a patient with an acute abdomen and diminished limb pulses without sensorimotor changes, malperfusion of the mesenteric bed was identified as the reason to proceed with interventional study).

identify factors that were independently associated with each of the outcomes of interest. The factors used in multivariate analysis for both the entire cohort and the operated subgroup included using those with $P \leq .1$ significance on univariate analysis. Survival analysis was analyzed by Kaplan–Meier methods.

Results

The mean age of the study cohort was 57.1 ± 14.2 years (72.4% were male). The comorbidities are listed in Table 2 and were similar between groups. Nine patients (5.2%) presented in cardiogenic shock from tamponade, and 22 patients

(11.2%) had previous cardiac surgery. Of the 70 patients presenting with suspected malperfusion and undergoing an initial percutaneous approach, 23 died before attempted operative repair. While awaiting resolution of the malperfusion syndrome, 12 of these patients had sudden hemodynamic collapse and death, consistent with aortic false lumen rupture. The remaining 11 patients died before operation from complications from malperfusion syndrome (multisystem organ failure [$n = 5$] and dense neurologic deficit without recovery [$n = 6$]). The remaining 47 patients underwent operative repair.

The overall early mortality rate was lower for the uncomplicated subgroup (UC $n = 12$ UC [9.5%] vs MP $n = 27$ [38.6%]; $P < .0001$). For univariate and multivariate analyses, an early composite end point of stroke, renal failure needing dialysis, need for tracheostomy, or early mortality was generated. By univariate analysis, the composite end point was significantly associated with a history of renal failure ($P = .023$) or presentation with cardiogenic shock ($P = .009$) or peripheral malperfusion ($P < .0001$). The only variables on multivariate analysis that correlated independently with the composite end point were the history of renal failure ($P = .014$) or cardiogenic shock ($P = .008$).

The overall late mortality rate was also significantly lower for the uncomplicated group (UC $n = 31$ [24.6%] vs MP $n = 36$ [51.4%]; $P < .0001$). By univariate analysis, vital status at last follow-up correlated with age ($P = .01$), preoperative ejection fraction ($P = .004$), a history of stroke ($P = .004$), presentation in cardiogenic shock ($P = .009$), or suspected peripheral malperfusion syndrome ($P < .0001$). However, on multivariate analysis, only age ($P = .009$), preoperative ejection fraction ($P = .041$), or presentation in cardiogenic shock ($P = .023$) were independently associated with long-term mortality. Although there was no independent effect

TABLE 2. Demographics and univariate analysis of the entire study cohort

	Uncomplicated dissection (n = 126)	Dissection with ischemic end-organ dysfunction (n = 70)	P value
Demographics			
Age (y)	57.1 $\pm$ 15.5	57.3 $\pm$ 11.7	.92
Male sex	91 (72.2%)	51 (72.8%)	1.0
Comorbidities			
Previous MI	8 (6.3%)	7 (10%)	.39
Previous cardiac surgery	9 (7.1%)	13 (18.6%)	.02
Preoperative EF (%)	50.7 $\pm$ 11.7	49.7 $\pm$ 9.6	.61
History of tobacco abuse	70 (55.6%)	34 (48.5%)	.87
COPD	11 (8.7%)	4 (5.7%)	.58
Diabetes	5 (3.9%)	4 (5.7%)	.27
Hypertension	91 (72.2%)	46 (65.7%)	.87
Preoperative creatinine (mg/dL)	1.23 $\pm$ 1.57	1.51 $\pm$ 0.72	.19
Marfan's syndrome	6 (4.8%)	2 (2.9%)	.71
PVOD	11 (8.7%)	10 (14.3%)	.24

MI, Myocardial infarction; COPD, chronic obstructive pulmonary disease; PVOD, peripheral vascular occlusive disease; EF, ejection fraction.

Figure 1. Entire cohort survival distribution function. This graph demonstrates that presentation with acute dissection with malperfusion and ischemic end-organ dysfunction is an important adverse risk factor for long-term survival. Mean survival times were higher in the uncomplicated group (UC 95.9 months vs MP 53.7 months; $P < .001$). Note that these curves are relatively parallel beyond the first 3 months, thus emphasizing the predominant early effects on survival in patients with malperfusion.

of suspected peripheral malperfusion on the overall long-term mortality rate, a survival curve analysis demonstrated important time-dependent effects of malperfusion syndrome. This survival analysis is displayed in Figure 1 and demonstrates a significant decrease in survival for the suspected malperfusion group ($P < .0001$). As is evident from the curves, the predominant difference in mortality is in the early time period (< 3 months). The curves remain relatively parallel thereafter.

Effects of Malperfusion of Different Vascular Beds on Mortality

An analysis was conducted to determine the importance of malperfusion of different vascular beds on both early and late mortality. This is detailed in Table 3. Of the 70 patients diagnosed with end-organ ischemia, 9 did not have angiographic evidence of peripheral vascular compromise at the time of the study. All patients but one had findings consistent with mesenteric ischemia on clinical examination (ie, severe abdominal pain or tenderness, elevated liver or pancreatic enzymes, diarrhea, or lactic acidosis.). These patients likely underwent spontaneous reentry between the time of injury and angiography. On resolution of the reperfusion injury, 8 patients underwent operative repair a median of 2 days after the interventional study. This shorter time span compared with those undergoing fenestration and stenting likely corresponds to the degree and duration of end-organ ischemia and its associated resolution of reperfusion injury. The remaining patient found to have fibromuscular dysplasia of the hepatic and renal arteries on angiography had recently been diagnosed with multiple myeloma and had sustained a dense stroke. On request of the family, care was withdrawn.

Notably, although 26 patients were initially thought to have end-organ ischemia of multiple vascular beds on clinical grounds, 40 (57.1%) were found to have angiographic evidence of malperfusion of multiple vascular beds. As is seen in Table 3, all types of malperfusion correlated with early mortality on univariate analysis. However, the prognostic independent importance of mesenteric malperfusion should be noted, because this was the only vascular bed significantly associated with both early ($P = .01$) and late mortality ($P = .04$).

Operated Subgroup Analysis

A separate analysis was conducted comparing outcomes for all those who underwent operative repair. This cohort consisted of the 126 patients undergoing immediate repair, as well as the 47 (of 70 total) patients presenting with suspected malperfusion

TABLE 3. Details regarding malperfusion syndromes

Affected vascular bed	No. of patients affected	Mortality in affected	Mortality in unaffected	Univariate <i>P</i> value
Early mortality				
Renal	40	14 (35%)	25 (16%)	.01
Mesenteric	37	15 (40.5%)	24 (15.1%)	.001
Limb	41	14 (34.1%)	25 (16.1%)	.01
Neurologic	7	4 (57.1%)	35 (18.5%)	.03
Multiple	40	13 (32.5%)	26 (16.7%)	.04
Late mortality				
Renal	40	17 (42.5%)	50 (32.1%)	.26
Mesenteric	37	19 (51.4%)	48 (30.4%)	.02
Limb	41	19 (46.3%)	48 (31%)	.095
Neurologic	7	5 (71.4%)	62 (32.8%)	.047
Multiple	40	17 (42.5%)	50 (32.1%)	.26

TABLE 4. Demographics, procedural details, and postoperative outcomes in operated group

	Uncomplicated dissection (n = 126)	Dissection with ischemic end-organ dysfunction (n = 47)	P value
Demographics			
Age (y)	57.1 ± 15.5	57.9 ± 11.1	.76
Male sex	91 (72.2%)	34 (72.3%)	1.0
Comorbidities			
Previous MI	8 (6.3%)	5 (10.6%)	.33
Previous cardiac surgery	9 (7.1%)	9 (19.1%)	.05
Preoperative EF (%)	50.7 ± 11.7	49.7 ± 9.6	.66
History of tobacco abuse	70 (55.6%)	28 (59.6%)	.73
COPD	11 (8.7%)	3 (6.4%)	.76
Diabetes	5 (3.9%)	4 (8.5%)	.26
Hypertension	91 (72.2%)	37 (78.7%)	.44
Preoperative creatinine (mg/dL)	1.23 ± 1.57	1.42 ± 0.72	.42
Marfan's syndrome	6 (4.8%)	2 (4.3%)	1.0
PVOD	11 (8.7%)	10 (14.3%)	.04
Procedural details			
Aortic valve resuspension	64 (66.7%)	25 (53.2%)	.86
Aortic root replacement	51 (40.4%)	17 (36.1%)	.73
Proximal hemiarch replacement	77 (61.1%)	24 (51.1%)	.3
Extended arch replacement	44 (34.9%)	23 (48.9%)	.12
CABG	11 (8.7%)	2 (4.3%)	.52
Need for hypothermic circulatory arrest	117 (92.8%)	45 (95.7%)	.73
Use of antegrade cerebral perfusion	55 (43.7%)	26 (55.3%)	.22
Cardiopulmonary bypass time (min)	236.6 ± 76	246.4 ± 93.4	.48
Aortic crossclamp time (min)	176 ± 64.6	181.7 ± 64.3	.61
Cerebral ischemic time (min)	24.7 ± 21	23.1 ± 19.9	.7
Lower body hypothermic circulatory arrest time (min)	41.2 ± 17.4	46.3 ± 19.1	.11
Postoperative morbidity			
Operative mortality	12 (9.5%)	4 (8.5%)	1.0
Reoperation for bleeding	14 (11.1%)	4 (8.5%)	.78
Deep sternal infection	10 (7.9%)	0 (0%)	.06
Stroke	10 (7.9%)	2 (4.3%)	.52
Need for dialysis	11 (8.7%)	9 (19.1%)	.07
Pneumonia	26 (20.6%)	9 (19.1%)	1.0
Need for tracheostomy	9 (7.1%)	2 (4.3%)	.73
Composite outcome	30 (23.8%)	14 (29.8%)	.44
Total length of stay (d)	16.8 ± 14.6	31.6 ± 41.2	.001

MI, Myocardial infarction; COPD, chronic obstructive pulmonary disease; PVOD, peripheral vascular occlusive disease; EF, ejection fraction.

who survived to operation. Operative therapy was delayed by a median of 4 days for the operated MP subgroup. The preoperative comorbidities, procedural details, and postoperative complications are listed in Table 4. Of note, 4 patients were thought to have renal malperfusion postoperatively and underwent intervention. Of this group, 3 patients required dialysis, and 1 patient (with a prolonged postoperative course) died of upper gastrointestinal hemorrhage.

Univariate analysis of the occurrence of the early composite outcome is listed in Table 5. Multivariate logistic regression, including those variables from Table 5, demonstrated that only preoperative creatinine ($P = .02$), presentation in cardiogenic shock ($P = .02$), and duration of cardiopulmo-

nary bypass ($P = .002$) correlated independently with the composite outcome.

Finally, long-term mortality was seen in 44 (25.4%) of the 173 patients undergoing operative repair (UC $n = 31$ [24.6%] vs operated MP $n = 13$ [27.6%]; $P = .7$). Univariate analysis of factors used in multivariate analysis for long-term mortality is shown in Table 5. Logistic regression demonstrated that only duration of cerebral ischemic time ($P = .005$) correlated independently with long-term mortality. In this analysis, suspected preoperative malperfusion was not correlated with a higher long-term mortality rate (UC 24.6% vs MP 27.6%), $P = .7$ and did not affect survival times ($P = .45$; Figure 2).

TABLE 5. Univariate analysis for group undergoing operative repair

Variable	P value
Early composite outcome	
Age	.073
Preoperative creatinine	.004
PVOD	.06
Cardiogenic shock	.009
Need for CABG	.02
Need for hypothermic circulatory arrest	.066
Cardiopulmonary bypass time	<.0001
Aortic crossclamp time	.015
Lower body circulatory arrest time	.001
Late mortality	
Age	.001
Ejection fraction	.002
Cardiogenic shock	.009
Presentation with renal malperfusion	.06
Cardiopulmonary bypass time	.001
Aortic crossclamp time	.046
Lower body circulatory arrest time	.002
Cerebral ischemic time	<.0001
Need for CABG	.097
Use of antegrade cerebral perfusion	.078
Postoperative stroke	.078

PVOD, Peripheral vascular occlusive disease; CABG, coronary artery bypass grafting.

Discussion

Mortality in acute type A dissection results not only from the rupture of a dissected ascending aorta but also from the associated ischemic end-organ dysfunction from malperfusion. Our group and others have described the pathophysiology of peripheral malperfusion secondary to aortic dissection.^{4,5} This work suggests that end-organ ischemia can result from a static obstruction (flap enters and narrows branch vessel lumen), dynamic obstruction (flap covers orifice of branch vessel), or a combination of these 2 mechanisms. As we and others have demonstrated, either mechanism is amenable to percutaneous therapy, with subsequent rapid restoration of end-organ perfusion.^{4,10}

Traditional therapy for acute type A dissection entails immediate operative repair to prevent rupture and death. Cambria and colleagues⁵ and Lauterbach and colleagues⁶ called to attention the high rates of morbidity and mortality associated with malperfusion syndrome, particularly for the subgroups with renal or mesenteric malperfusion. They suggested that the optimal approach in that setting consisted of initial operative revascularization with subsequent central aortic repair. In contrast, Fann and colleagues⁷ have suggested that immediate aortic repair with proximal false lumen obliteration and reestablishment of true lumen flow may restore peripheral arterial perfusion without the need for associated peripheral arterial revascularization. This group also

Figure 2. Survival distribution function for operated subgroup. For those patients surviving to operative repair, survival is similar for both patients initially presenting with uncomplicated acute dissection and those initially presenting with malperfusion and end-organ ischemia syndrome (UC 95.9 months vs MP 80.5 months; $P = .45$).

noted the incidence of mortality to be significantly elevated (>50%) in those subgroups with renal and mesenteric ischemia. Others have also suggested similar outcomes with preferential aortic repair.⁸

In our first study in 1997, we described a comparative analysis of patients treated with immediate operation regardless of peripheral vascular involvement and patients treated with a selective operative delay.⁴ That study suggested that there was a significantly higher risk of mortality (89% vs delay 25%, $P = .003$) with immediate central aortic repair in those patients with malperfusion syndrome and ischemic end-organ dysfunction. On the basis of this previous work, our algorithm during the last decade for managing patients with acute type A dissection is to proceed with immediate operative repair unless there is evidence of ischemic end-organ dysfunction and malperfusion. This group includes those with 1) no CT angiographic evidence of malperfusion; 2) CT angiographic malperfusion without severe end-organ dysfunction; 3) absent peripheral pulses with intact sensation and motor function of the affected limb; 4) evidence of elevated creatinine without CT evidence of malperfusion; and 5) evidence of a compromised true lumen and no clinical evidence of end-organ ischemia and dysfunction. In contrast, those patients who presented with evidence of neurologic, visceral, renal, or limb malperfusion with end-organ damage proceeded directly for percutaneous intervention with aortic

fenestration, true lumen, or branch vessel stenting where appropriate. The purpose of this report was not to ascertain the more suitable strategy for patients presenting with malperfusion (ie, immediate repair for all vs selective operative delay). We believe that early operative repair is indicated in the majority of patients to decrease the risk of dissection-related mortality. Rather, this study was undertaken to describe long-term results associated with a consistent application of a selective operative delay approach in those patients presenting with significant ischemic end-organ dysfunction as a consequence of prolonged branch vessel compromise. In doing so, we assessed the outcomes for the largest group of patients with type A dissection with malperfusion and ischemic end-organ dysfunction reported in the literature. In addition, although most previous studies have focused on early complication rates, few have determined the long-term outcomes for this cohort.¹¹

The long-term results from this study suggest that malperfusion syndrome is an important adverse risk factor for long-term survival. The importance of mesenteric malperfusion syndrome as an independent adverse risk factor for early and late mortality has been noted in this study and by others.⁴⁻⁸ The early mortality rate of 40.5% for patients with mesenteric malperfusion in our report is consistent with the contemporary results reported by Lauterbach and colleagues,⁶ who also espouse operative delay for this subset of patients with acute type A dissection.

In contrast, the long-term results in our study differ when the analysis is conducted on those who underwent operative repair. In this subgroup, the survival curves of patients with malperfusion who eventually proceeded to operative repair were restored to the level of those who presented with uncomplicated dissection. Although this is admittedly a highly selected group, it suggests the effects of malperfusion syndrome are primarily seen early. Indeed, in the survival analysis of the entire cohort, the predominant difference in survival is seen in the first 3 months with relatively parallel survival curves thereafter, further supporting the notion of predominantly early effects of malperfusion.

The recent report by Geirsson and colleagues¹¹ from the University of Pennsylvania deserves mention. They suggested that although an approach espousing early repair is associated with a higher in-hospital mortality for the group with malperfusion (30.5% vs 6.2% in non-malperfusion), long-term survival may be similar between groups. Although their data suggest an early mortality similar to that of our strategy of operative delay for malperfusion (38.7% for all malperfusion in this report), their group had a significantly different profile than in our study. In particular, although the prevalence of both renal and mesenteric malperfusion with end-organ dysfunction was high in our study (57.1% and 52.1%, respectively), their report had a significantly lower incidence of malperfusion of these beds (renal = 4.1%; mesenteric = 1.4%). Because we and others have suggested a lower sur-

vival for these groups, the results from their study may not be suitable for comparison with our data.

A final important point should be noted. Because of our previous work with acute dissection and malperfusion, we have noted a dramatic increase in referrals of patients presenting with this complication. Geographic considerations and referral patterns often result in patients presenting to other institutions (≥ 1) before transfer to the University of Michigan. These transfers increase the time interval between the onset of dissection with malperfusion to the time of definitive treatment and worsen the degree of ischemic end-organ dysfunction. These considerations may explain some differences between other series and ours, and may also account for the relatively high proportion of patients with malperfusion seen in our study compared with others.

Limitations of this study include the lack of a comparison group (ie, a cohort undergoing immediate operation regardless of malperfusion status). However, this was not the intent of our study; rather, the focus was to analyze the long-term results of an adopted strategy of operative delay for acute dissection and ischemic end-organ dysfunction. Operative delay while awaiting resolution of the malperfusion syndrome in these patients is associated with a significant risk for early mortality from either aortic false lumen rupture or complications of the malperfusion syndrome. A future study could therefore evaluate whether earlier operative therapy (ie, operation immediately after fenestration and stenting) could improve results by ameliorating the risk for early rupture and subsequent mortality. It is possible that the beneficial effects of avoidance of rupture may be offset by a higher operative mortality in the setting of significant ischemia-reperfusion injury and its deleterious consequences.⁴

Conclusions

Presentation with acute dissection, malperfusion, and ischemic end-organ dysfunction is an important adverse risk factor for survival, particularly in the setting of mesenteric ischemia. A strategy of immediate percutaneous reperfusion and delayed operative repair to allow resolution of malperfusion and associated reperfusion injury still carries a significant risk for early mortality. However, in those patients who undergo operative repair with this approach, survival times are restored to those who present without evidence of ischemic end-organ dysfunction.

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Discussion

Dr Roderick Macarthur (Edmonton, Alberta). I thank the association for the opportunity to discuss this article, and congratulations to Dr Patel and colleagues for an excellent and provocative article addressing the management of patients with acute type A aortic dissection presenting with severe coexisting malperfusion. We are reminded by this article of the challenges in dealing with this high-risk group of patients. The Michigan group's approach to this cohort of patients has been consistent with primary percutaneous fenestration followed by delayed central aortic repair once patients have stabilized and their end-organ ischemic injury has resolved. This strategy originated from a poor outcome with primary central aortic repair in this group of patients.

I think this is an important article in that it provides follow-up to a controversial article the authors published almost a decade ago. The authors should be commended for providing an updated report regarding the outcomes associated with their approach to these patients. Many times, controversial approaches are introduced in the literature but never followed up with the appropriate studies. This makes it difficult to know which approach has been proven efficacious in the long run and which has not. The authors are also clear that the purpose of the article is not to compare immediate central repair with delayed surgery but to evaluate the long-term outcomes when their delayed approach is used. The delayed approach has significantly improved the outcomes in their institution for this high-risk group of patients, and they should be congratulated.

I do believe, however, that this article challenges what many of us currently teach our trainees, that many of these malperfusion syndromes will resolve with primary central aortic repair and acute type A aortic dissection is a surgical emergency that requires immediate surgical repair.

I have 4 questions for Dr Patel. Clearly it is in the group of patients with severe malperfusion that this strategy is used in your institution. How do you define severe malperfusion? For example, are

patients with paraplegia delayed for surgical repair? How do you define renal malperfusion? What are the determinants that indicate that it is now appropriate to proceed with surgical repair and that the patient has been sufficiently delayed?

Dr Patel. Typically when a patient presents at the University of Michigan with acute type A aortic dissection, our algorithm involves precisely what I mentioned. Those patients who present with tamponade or coronary malperfusion without evidence of a dead ventricle (eg, regardless of malperfusion) will proceed directly to operation. If patients present with severe malperfusion with end-organ dysfunction, for example, those with significantly abnormal or increasing creatinine, severe abdominal pain, abnormal abdominal exam, or neurologic malperfusion with dense stroke or paraplegia, their operative procedure will be delayed until their ischemia reperfusion injury resolves. This would be evident by decreasing creatinine, restoration of urine output, or benign abdominal exam. It is important to note that a specific objective number is not targeted for us to decide on the date of operation, but rather the entire clinical picture is used to determine the optimal time of aortic repair.

Dr Macarthur. Many advances in the management of these complex cases have taken place during the past years. For example, some believe that antegrade perfusion from the outset with right axillary cannulation is beneficial, particularly in patients with malperfusion. Do you believe that strategies and other such advances will affect the outcome in this high-risk group of patients? Do you anticipate this influencing the management of your delayed strategy?

Dr Patel. I am not sure how axillary perfusion would alter perfusion to the end organs because the path of blood flow often will be similar to that seen with restoring perfusion in an antegrade fashion.

Dr Macarthur. How often did the percutaneous interventions in the malperfusion group successfully reestablish flow within a compromised branch vessel, and were there any direct complications from this procedure, for example, in the 23 patients who died while awaiting surgical repair, were any of those deaths due to complications from the fenestration procedure?

Dr Patel. We are very fortunate. We have a good interventional radiology team that we work closely with, and thankfully none of the complications, none of the mortality that was seen in those patients who were awaiting resolution of the malperfusion syndrome, were attributed directly to the results of the fenestration procedure.

Dr Macarthur. My final question is, have the authors considered the thoracoabdominal aorta in this group of patients and does a delayed approach influence a requirement for the risk and need for subsequent distal surgery? What is your follow-up imaging strategy in these patients and does it differ from patients presenting without malperfusion?

Dr Patel. Typically the thoracoabdominal aorta is dissected in these patients who present with malperfusion. Our approach of creating a flap fenestration may prevent total thrombosis of the residual dissected aorta by creating a large reentry tear, but that is uncertain and is a subject of future study. Our followup in all patients following repair of acute Type A dissection, whether malperfusion existed or not is the same. We image them with echocardiography and CT scanning only (3 and 9 months) and then annually thereafter if the aorta remains stable. Our indications for intervening on the distal dissected aorta are the standard ones, namely size, growth or symptoms.

Dr Craig Miller (Stanford, Calif). Thank you for updating the Michigan series. I will never forget in January 1996 when Mike

Deeb got up at the Society of Thoracic Surgeons meeting; he sure took a lot of flack.

Dr Patel. He still has some bullet holes I think. [laughter]

Dr Miller. It is good to see the follow-up. I am not sure, however, exactly what you have learned from the last 10 years; perhaps the most salient question I need to ask is how many patients did you actively decide to do nothing for because of irreversible infarction of the gut, kidney, brain, or some other important end organ? Are you still in the “warm autopsy” mode that Mike was accused of 11 years ago?

Dr Patel. Of the 23 patients who died, 11 expired directly as a result of malperfusion syndrome with multisystem organ failure. Half of these had dense neurologic deficits and never recovered. The remaining 12 patients ruptured while awaiting resolution of their malperfusion syndrome. In this group, evidence of severe ischemia reperfusion injury was still apparent, and included for example, patients who required laparotomy for bowel resection.

Dr Chad Hughes (*Durham, NC*). I have a couple questions for you. Maybe I just missed it, but did you break down the difference—I mean, I think dynamic malperfusion of the gut and static malperfusion of the gut are 2 different animals. If someone presents acutely with acute type A dissection, with some abdominal pain and evidence of dynamic malperfusion on CT scan, that should get better by replacing the ascending aorta, but if it is static malperfusion and the superior mesenteric artery is thrombosed, that is obviously not going to get better by reestablishing true lumen flow. In our experience, that has a much higher mortality rate, and those are the patients in whom we will typically place branched vessel grafts into the superior mesenteric artery or celiac first before we do the ascending aorta, versus if it is just dynamic malperfusion, we would expect that to get better by replacing the ascending aorta. Have you looked at the difference between those?

Dr Patel. We have not. It is an interesting point, but the intention of this analysis was to look at the outcomes on an intent-to-treat basis. You cannot always sort out the dynamic vs. static mechanism on the preoperative CT scan. We agree that dynamic obstruction will resolve with central aortic repair. However, in the group treated with

operative delay in this presentation were those that had evidence of significant end-organ ischemia with dysfunction. I think that was the biggest point that Mike had tried to make in the original presentation, namely that a difference exists between end-organ ischemia and end-organ ischemia with severe end-organ dysfunction. It was the our intent to focus on that latter group in both the first and the current study.

Dr Hughes. I think it depends on how early they present. My second question is on fenestrations. Have you tried, which we have done, just using endografts instead only in the true lumen? We have had, at least in our institution, better success with that compared with fenestration, especially for dynamic malperfusion, to open the true lumen.

In your delayed group, are any of the deaths due to rupture of the aorta or severe aortic insufficiency with heart failure rather than malperfusion syndrome?

Dr Patel. I am not sure that treating a dissected thoracabdominal aorta with a thoracic endograft is the best therapy. I think that one of the biggest issues is that in this situation, both the proximal and distal landing zones are not necessarily stable since the aorta is not normal. Secondly, you would be covering up multiple intercostals, and thus subjecting patients to a risk for paralysis. When we perform percutaneous fenestration and stenting, it is a percutaneous procedure maintaining intercostal artery patency and avoiding the need to deliver larger bore devices through a femoral cutdown.

Regarding the second question concerning cardiac causes of death, it is important to note that in contrast to the original study where there were patients with severe ventricular dysfunction and coronary malperfusion, for some reason in this study no patients with this scenario were seen during the current study period. If patients had severe aortic insufficiency and had severe ischemic end-organ dysfunction, operative delay was utilized in some. However, if they did not appear to be tolerating the AI, we proceeded to operative repair earlier. Again, what is important to note is that the clinical decision to proceed with surgery was undertaken after evaluating the entire clinical scenario.