Progression of distal aorta after endovascular fenestration/stenting in acute type A aortic dissection with malperfusion syndrome

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ABSTRACT

Objective: The study objective was to evaluate the progression of dissected distal aorta in patients with acute type A aortic dissection with malperfusion syndrome treated with endovascular fenestration/stenting and delayed open aortic repair.

Methods: From 1996 to 2021, 927 patients presented with acute type A aortic dissection. Of these, 534 had DeBakey I dissection with no malperfusion syndrome and underwent emergency open aortic repair (no malperfusion syndrome group), whereas 97 patients with malperfusion syndrome underwent fenestration/stenting and delayed open aortic repair (malperfusion syndrome group). Sixty-three patients with malperfusion syndrome treated with fenestration/stenting were excluded due to no open aortic repair, including death from organ failure (n = 31), death from aortic rupture (n = 16), and discharged alive (n = 16).

Results: Compared with the no malperfusion syndrome group, the malperfusion syndrome group had more patients with acute renal failure (60% vs 4.3%, $P < .001$). Both groups had similar aortic root and arch procedures. Postoperatively, the malperfusion syndrome group had similar operative mortality (5.2% vs 7.9%, $P = .35$) and permanent dialysis (4.7% vs 2.9%, $P = .50$), but more new-onset dialysis (22% vs 7.7%, $P < .001$) and prolonged ventilation (72% vs 49%, $P < .001$). The growth rate of the aortic arch (0.38 vs 0.35 mm/year, $P = .81$) was similar between the malperfusion syndrome and no malperfusion syndrome groups. The descending thoracic aorta growth rate (1.03 vs 0.68 mm/year, $P = .001$) and abdominal aorta growth rate (0.76 vs 0.59 mm/year, $P = .02$) were significantly higher in the malperfusion syndrome group. The cumulative incidence of reoperation over 10 years (18% vs 18%, $P = .81$) and 15-year survival outcome (50% vs 48%, $P = .43$) were similar between the malperfusion syndrome and no malperfusion syndrome groups.

Conclusions: Endovascular fenestration/stenting followed by delayed open aortic repair was a valid approach for patients with malperfusion syndrome. (JTCVS Open 2023;14:1-13)
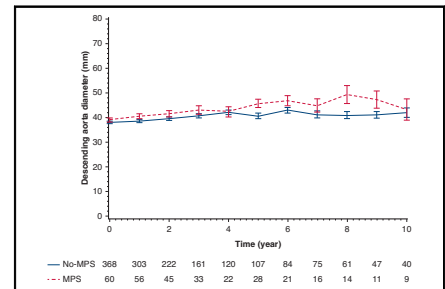
Descending thoracic aortic growth in patients with ATAAD with or without MPS.

CENTRAL MESSAGE

After endovascular fenestration/stenting and delayed open aortic repair, patients with MPS had faster aortic growth, similar re-operation, and long-term survival versus patients without.

PERSPECTIVE

Up-front aortic fenestration/stenting followed by delayed open aortic repair was a valid approach in treating patients with acute type A dissection with MPS based on the comparable short- and long-term survival, aortic growth, and cumulative incidence of reoperation to patients without any MPS.

▶ Video clip is available online.

Acute type A aortic dissection (ATAAD) is a surgical emergency with a high operative mortality between 17% and 25%.[1,2] Approximately 40% of patients with ATAAD have associated malperfusion syndrome (MPS), which

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contributes to a high perioperative morbidity and mortality between 29% and 89%.[3,4] Therefore, at our institution, since 1996, we have developed an up-front endovascular fenestration/stenting followed by a delayed open aortic repair approach for stable patients with ATAAD with MPS and have achieved improved perioperative outcomes.[5-7] Patients with ATAAD frequently have a dissected distal aorta with a persistent patent false lumen after aortic fenestration/stenting in the thoracic aorta and its branch vessels, which could predispose them to aortic false lumen dilatation. It is unknown how the distal dissected aorta progresses in patients with ATAAD with MPS after an up-front treatment with fenestration/stenting followed by open repair. In this study, we focused on the progression and reoperation of the distal aorta with residual dissection in patients with MPS after endovascular fenestration/stenting. We hypothesized there was no significant difference in the growth and reoperation of the residual dissected distal aorta in patients with MPS treated with fenestration/stenting and delayed open aortic repair compared with patients without MPS treated with emergency open aortic repair only.

MATERIALS AND METHODS

This study was approved by the Institutional Review Board at Michigan Medicine (HUM00133791, 12/3/2017). A waiver of informed consent was obtained and follows the Health Insurance Portability and Accountability Act regulations.

Data Collection

Data from January 1996 to March 2021 were obtained from the Society of Thoracic Surgeons Data Warehouse in the department of Cardiac Surgery at the University of Michigan. All the patients with ATAAD operated or nonoperated were enrolled into the ATAAD database at the University of Michigan. Imaging data were input and collected into the ATAAD database from medical record review. The reoperations included open aortic repair, thoracic endovascular aneurysm repair (TEVAR), or endovascular aneurysm repair for distal aortic aneurysm after initial ATAAD repair, including repairs of the remaining aortic arch, descending thoracic aorta, or abdominal aorta. The data of reoperations were collected through surveys, medical chart review, and the Society of Thoracic Surgeons data warehouse. Long-term survival data were obtained from the National Death Index through December 2018, the Michigan Death Index through December 12, 2021,[8] and medical chart review.

Patient Selection

From January 1996 to March 2021, 927 patients presented with an ATAAD at our institution. Of the 160 patients with ATAAD who received immediate endovascular fenestration/stenting for visceral or limb MPS, 63 patients did not receive subsequent open aortic repair due to death from multiorgan failure (n = 31) and aortic rupture (n = 16) or were discharged alive (n = 16). Therefore, the patients with ATAAD MPS (MPS group, n = 97) who all had DeBakey type I dissection and underwent up-front fenestration/stenting followed by delayed open aortic repair were used as the study group, including patients who had cerebral malperfusion (4) or spinal cord malperfusion (7) in addition to visceral or lower-extremity malperfusion. A total of 699 patients received immediate ATAAD open repair. Of the 699 patients, 87 were excluded if they had cerebral MPS (n = 46) or coronary MPS only (26), or visceral/limb MPS with cardiac tamponade on presentation (n = 15). An additional 78 patients were excluded from the study due to having DeBakey II dissection because all patients with visceral and limb MPS had DeBakey type I dissection. All the patients with DeBakey I dissection without any MPS (no MPS group, n = 534) underwent immediate open aortic repair and were used as the control group. Patients with ATAAD MPS who presented with unstable hemodynamics due to cardiac tamponade underwent immediate emergency central aortic repair. Patients with MPS who presented with shock or unstable hemodynamics due to any other etiologies, such as MPS (tissue necrosis) or chronic heart failure, still received endovascular fenestration/stenting first and medical management during recovery. The strategy was to perform open aortic repair if patients were dying of cardiac tamponade; otherwise, fenestration/stenting first was performed for any unstable patients with MPS.

Last, patients with ATAAD who were not surgical candidates or not willing to have surgery were medically managed (n = 58) or underwent TEVAR (n = 10) and thus were also excluded from the study (Figure 1).

Endovascular Fenestration/Stenting

Our approach to endovascular fenestration/stenting has been extensively described in our previous study.[5] Percutaneous fenestration/stenting was performed in the hybrid or angiography suite at our institution. Treatable malperfusion with fenestration/stenting was confirmed with angiography with a significant pressure gradient (>15 mm Hg) between the ascending aorta true lumen and a branch artery. Fenestration was performed percutaneously by creating a tear in the dissection flap to equalize the blood pressure and permit flow between the true and false lumens.[5,6] MPS was characterized by tissue necrosis and end-organ dysfunction/failure due to insufficient blood flow to end organs and dissection-related aortic branch vessel obstruction.[5,9]

Imaging Data Collection

Imaging up to 30 days before the date of operation was considered the patient's baseline. The protocol for follow-up computed tomography (CT) imaging at our aorta clinic was 3 months after the initial ATAAD repair and then every year after surgery for 3 years. After 3 years, if the distal aorta was stable, then the patient would receive imaging every 2 years. However, if the distal aorta was growing 2 to 4 mm/year, then we would perform annual CT imaging for that patient. During follow-up, the systolic blood pressure goal after surgery was less than 120 mm Hg and antihypertensives were managed by the primary care physician or the cardiologist. If patients had open repair or TEVAR of the distal aorta during follow-up after initial ATAAD repair, then data of the replaced aortic segment were not included for the analysis of the growth for that specific segment of the aorta after the date of reintervention. This excluded the following: arch measurements after a total arch replacement, descending aorta measurements after open or endovascular repair of the descending aorta, and abdominal aorta measurements after open or endovascular abdominal aortic repair. This ensured that only native aorta measurements were included for the growth analysis and not any grafts. Measurements of the aortic arch and
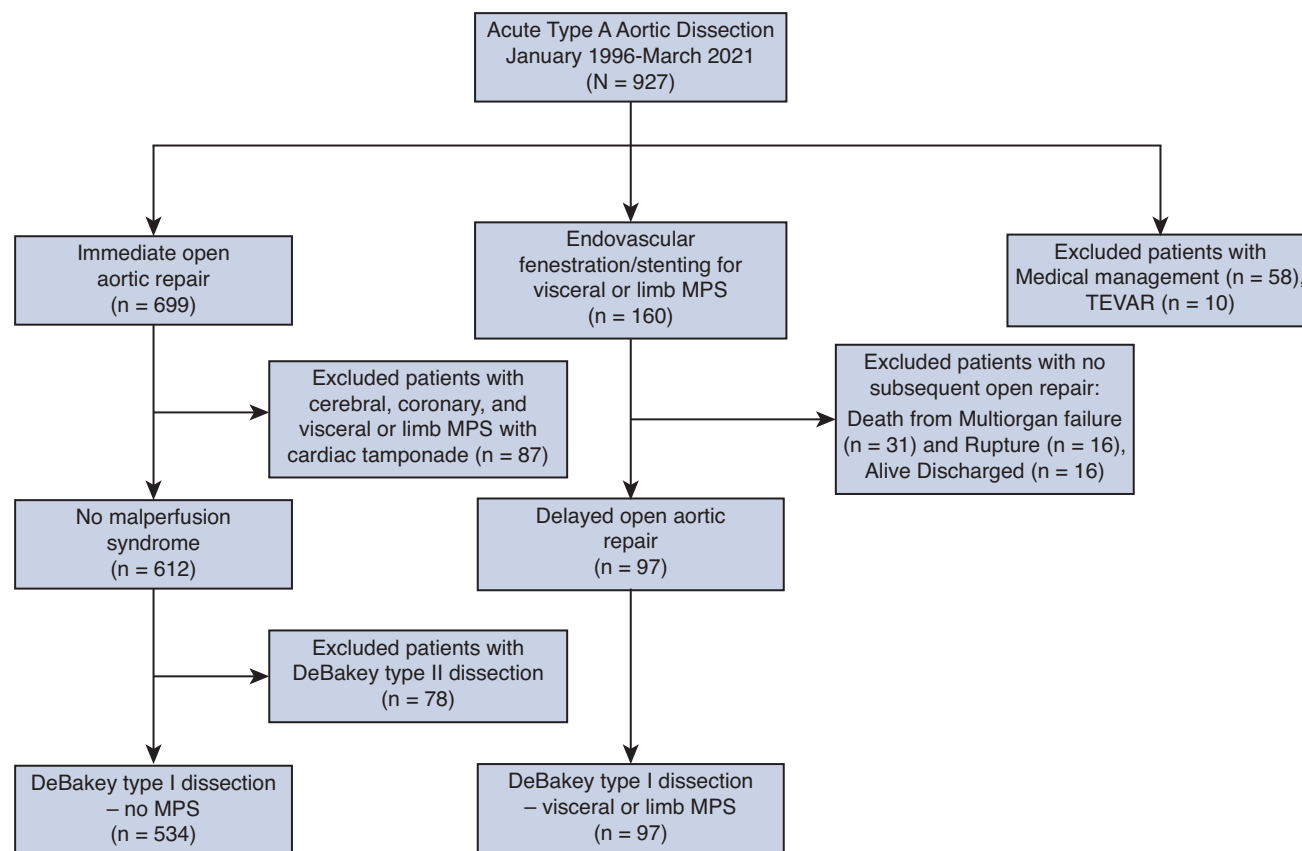
FIGURE 1. CONSORT diagram of selection and distribution of study population.

descending thoracic and abdominal aorta were taken transversely at the level of maximum segmental diameter, including both the true and false lumens, if present. Different patients may have had the maximum diameter at different levels. The radiology report includes the maximum diameter at each segment.

Statistical Analysis

Data were presented as median (25%, 75%) for continuous data and n (%) for categorical data. Univariate comparisons between the groups were performed using Wilcoxon rank-sum tests for continuous data and chi-square tests for categorical data. Because all sample sizes were greater than 50, the Kolmogorov-Smirnov test was used to check for the normality of continuous data. Variables were chosen on the basis of our previous studies and their clinical relevance.[5,7] We conducted an intent-to-treat analysis for the overall in-hospital mortality of all-comers with MPS who underwent fenestration/stenting with or without delayed open aortic repair. Cox proportional hazard regression models were used to calculate the hazard ratio of risk factors for long-term mortality adjusting for age, sex, MPS, peripheral vascular disease, previous cardiac surgery, and history of renal failure. Cardiogenic shock was set as strata because of its violation of the proportional hazard assumption. Also, risk factors for reoperation were analyzed using a Cox regression model with death as the competing risk, and adjusted for age, sex, MPS, false lumen patency of the descending thoracic aorta, aortic fenestration/stenting, and connective tissue diseases. The Kaplan–Meier method with log-rank testing was used to calculate long-term survival. Gray's test was used to calculate any statistical difference in the cumulative incidence of reoperation for distal aortic pathology between the 2 groups, adjusting for death as a competing factor. Linear mixed effect univariate models with aorta sizes as repeated measurements were used to quantify the rates

of aorta growth over time in each group. Statistical calculations were performed using SAS 9.4 (SAS Institute, Inc).

RESULTS

Preoperative Demographic Data

Compared with the no MPS group, the MPS group had a significantly higher body mass index (30 vs 28 kg/m^2, $P = .006$), higher proportion of patients with hypertension (89% vs 73%, $P < .001$), history of renal failure (9.3% vs 3.6%, $P = .03$), peripheral vascular disease (31% vs 22%, $P = .05$), previous cardiac surgery (17% vs 6.4%, $P < .001$), acute stroke (4.1% vs 0.6%, $P = .01$), acute renal failure (60% vs 4.3%, $P < .001$), acute paralysis (9.3% vs 0%, $P < .001$), and preoperative creatinine level (1.4 vs 1.0 mg/dL, $P < .001$). The MPS group had fewer patients with cardiac tamponade (2.1% vs 10%, $P = .01$) compared with the no MPS group (Table 1).

Intraoperative Outcomes

Among the 97 patients in the MPS group, 79 (81%) had branch vessel fenestration/stenting, including 11 patients (11%) who had endovascular stenting of their branch vessels only before open repair. Intraoperatively, compared with the no MPS group, the MPS group had significantly fewer concomitant coronary artery bypass grafts (0% vs

TABLE 1. Demographics and preoperative comorbidities

	No MPS (n = 534)	MPS (n = 97)	P value
Patient age (y)	60 (49-68)	56 (50-65)	.22
Sex, male	364 (68)	74 (76)	.11
BMI (kg/m²)	28 (25-32)	30 (26-34)	**.006**
Preexisting comorbidities			
Hypertension	387 (73)	86 (89)	**<.001**
Diabetes	36 (6.7)	10 (10)	.21
Smoking status			
Never	226 (42)	39 (40)	.70
Former	149 (28)	26 (27)	.82
Current	159 (30)	32 (33)	.53
CAD	87 (16)	14 (14)	.64
COPD	57 (11)	8 (8.2)	.47
History of MI	30 (5.6)	6 (6.2)	.82
History of renal failure	19 (3.6)	9 (9.3)	**.03**
History of CVA	17 (3.2)	4 (4.1)	.55
PVD	117 (22)	30 (31)	**.05**
Connective tissue disease	26 (4.9)	2 (2.1)	.29
Previous cardiac surgery	34 (6.4)	16 (17)	**<.001**
Preoperative aortic insufficiency			
None	138 (27)	29 (30)	.59
Trace	54 (11)	10 (10)	.92
Mild	109 (21)	20 (21)	.84
Moderate	87 (17)	16 (17)	.87
Severe	119 (24)	22 (23)	.87
Ejection fraction	55 (55, 60)	55 (55, 65)	.37
Acute MI	1 (0.2)	1 (1.0)	.28
Acute stroke	3 (0.6)	4 (4.1)	**.01**
Acute renal failure*	23 (4.3)	58 (60)	**<.001**
Acute paralysis	0 (0)	9 (9.3)	**<.001**
Cardiogenic shock	51 (9.6)	2 (2.1)†	**.01**
Cardiac tamponade	54 (10)	2 (2.1)†	**.01**
Preoperative creatinine (mg/dL)	1 (0.8, 1.3)	1.4 (1.0, 2.4)	**<.001**
MPS	0 (0)	97 (100)	**<.001**
Coronary	0 (0)	0 (0)	1
Cerebral	0 (0)	4 (4.1)	**<.001**
Spinal cord	0 (0)	7 (7.2)	**<.001**
Celiac	0 (0)	15 (16)	**<.001**
Mesenteric	0 (0)	68 (70)	**<.001**
Renal	0 (0)	60 (62)	**<.001**
Lower extremity	0 (0)	64 (66)	**<.001**
Time from intervention radiology to open repair (d)	-	3 (1, 12)	-

Data presented as median (25%, 75%) for continuous data and n (%) for categorical data. *P* value indicates the difference between no malperfusion no MPS and MPS groups. *P* value less than or equal to .05 was considered statistically significant. *MPS*, Malperfusion syndrome; *BMI*, body mass index; *CAD*, coronary artery disease; *COPD*, chronic obstructive pulmonary disease; *MI*, myocardial infarction; *CVA*, cerebrovascular accident; *PVD*, peripheral vascular disease. *Preoperative acute renal failure is defined as abnormal creatinine if available in patients who did not have a history of renal failure. †Two patients in the MPS group developed cardiogenic shock and cardiac tamponade at the conclusion of their interventional radiology repair and were taken directly to the operating room. Patients with visceral and extremity MPS who were unstable due to cardiac tamponade on presentation were treated with emergency open aortic repair and excluded from the study.

6.2%, *P* = .01). Both groups had similar aortic root and arch procedures with similar cardiopulmonary bypass time (221 vs 216 minutes, *P* = .78), crossclamp time (151 vs 153 minutes, *P* = 1.0), and hypothermic circulatory arrest time (36 vs 34 minutes, *P* = .22). The MPS group had significantly more intraoperative transfusion of packed red blood cells (5 units vs 3 units, *P* < .001). All other intraoperative outcomes were similar between groups (Table 2).

Postoperative Outcomes

Compared with the no MPS group, the MPS group had a significantly higher proportion of patients with new-onset acute renal failure (34% vs 16%, *P* < .001) and acute renal failure requiring dialysis (22% vs 7.7%, *P* < .001) but similar permanent dialysis (4.7% vs 2.9%, *P* = .50), which was defined as being on dialysis at discharge. The MPS group had a higher rate of gastrointestinal complications (14% vs 7.7%, *P* = .03), pneumonia (26% vs 16%, *P* = .02), prolonged ventilation (72% vs 49%, *P* < .001), and total length of stay (21 vs 10 days, *P* < .001). The operative mortality was similar between the MPS and no MPS groups (5.2% vs 7.9%, *P* = .35). All other postoperative outcomes were similar between groups (Table 3). With an intent-to-treat analysis, the overall in-hospital mortality of all-comers with MPS who underwent fenestration/stenting with or without delayed open aortic repair was significantly higher than in the no MPS group (33% vs 7.9%, *P* < .001).

Long-term Outcomes
Imaging follow-up and growth rate of distal aorta after endovascular fenestration/stenting or open ATAAD repair. CT imaging over a 23-year period between the MPS versus no MPS group compared the progression of the aortic arch (470 measurements vs 1978 measurements), descending aorta (394 measurements vs 2034 measurements), and abdominal aorta (405 measurements vs 2063 measurements). Of patients who survived the operative period, 84 patients (91%) from the MPS group had CT imaging after their surgery date and 426 patients (87%) from the no MPS group had CT imaging after their surgery date. The median follow-up imaging (CT) time was 3.5 years (interquartile range, 2-6) for the MPS group and 3.1 years (interquartile range, 1.2-7.4) for the no MPS group. The average amount of imaging for patients was 4 scans in the MPS group and 4 scans in the no MPS group over the 10-year window. Of the 84 patients in the MPS group with adequate follow-up CT imaging, we found 68 patients (81%) had a patent false lumen of the descending thoracic aorta during their most recent CT imaging versus 258 (62%) of 417 patients in the no MPS group (*P* = .001). In both the MPS and no MPS groups, the growth rate of all 3 segments of the distal aorta over time were

TABLE 2. Intraoperative data

	No MPS (n = 534)	MPS (n = 97)	P value
Aortic root procedure			
None	5 (0.9)	3 (3.1)	.11
Root repair	317 (59)	54 (56)	.50
Root replacement	167 (31)	29 (30)	.79
Aortic valve replacement	9 (1.7)	0 (0)	.37
Aortic valve repair	36 (6.7)	11 (11)	.11
Arch replacement			
None	11 (2.1)	1 (1.0)	.70
Hemiarch	326 (61)	58 (60)	.82
Zone 1 Arch	47 (8.8)	5 (5.2)	.23
Zone 2 Arch	101 (19)	23 (24)	.27
Zone 3 Arch	49 (9.2)	10 (10)	.72
Frozen elephant trunk	84 (16)	10 (10)	.17
Concomitant procedures			
CABG	33 (6.2)	0 (0)	**.01**
Mitral valve	4 (0.7)	0 (0)	1
Tricuspid valve	3 (0.6)	0 (0)	1
CPB time (min)	216 (175-273)	221 (184-261)	.78
Crossclamp time (min)	153 (114-199)	151 (118-191)	1
HCA	525 (99)	96 (99)	1
HCA time (min)	34 (25-45)	36 (29-48)	.22
Cerebral perfusion			
None	3 (0.5)	1 (1)	.46
Antegrade	261 (45)	37 (39)	.23
Retrograde	195 (34)	30 (31)	.64
Both antegrade and retrograde	120 (21)	28 (29)	.06
Lowest temperature (°C)	18 (18-24)	18 (16-20)	**.002**
Blood (PRBCs), units	3 (0-6)	5 (1-8)	**<.001**

Data presented as median (25%, 75%) for continuous data and n (%) for categorical data. *P* value indicates the difference between no MPS and MPS groups. *P* value less than or equal to .05 was considered statistically significant. *MPS*, Malperfusion syndrome; *CABG*, coronary artery bypass graft; *CPB*, cardiopulmonary bypass; *HCA*, hypothermic circulatory arrest; *PRBCs*, packed red blood cells.

TABLE 3. Postoperative outcomes

	No MPS (n = 534)	MPS (n = 97)	P value
Reoperation for bleeding	42 (7.9)	9 (9.3)	.64
Tamponade	12 (2.3)	1 (1.0)	.70
Deep sternal wound infection	14 (2.6)	1 (1.0)	.49
Sepsis	13 (2.4)	4 (4.1)	.31
Postoperative MI	6 (1.1)	0 (0)	.60
Atrial fibrillation	171 (32)	37 (38)	.24
Cerebrovascular accident	41 (7.7)	6 (6.2)	.61
Transient ischemic attack	1 (0.2)	0 (0)	1
New-onset paraplegia	3 (0.5)	0 (0)	1
Acute renal failure*	83 (16)	33 (34)	**<.001**
Requiring dialysis	41 (7.7)	21 (22)	**<.001**
Permanent	14 (2.9)	4 (4.7)	.50
Gastrointestinal complications	41 (7.7)	14 (14)	**.03**
Pneumonia	85 (16)	25 (26)	**.02**
Prolonged ventilation (>24 h)	260 (49)	70 (72)	**<.001**
Hours intubated	35 (20, 85)	83 (38, 130)	**<.001**
Reintubation	30 (5.6)	10 (10)	.08
Tracheostomy	18 (3.4)	3 (3.1)	1
Postoperative LOS (d)	10 (7, 16)	16 (10, 21)	**<.001**
Total LOS (d)	10 (7, 16)	21 (12, 29)	**<.001**
Intraoperative mortality	8 (1.5)	0 (0)	.62
In-hospital mortality	40 (7.5)	4 (4.1)	.23
30-d mortality	33 (6.2)	4 (4.1)	.43
Operative mortality†	42 (7.9)	5 (5.2)	.35

Data presented as median (25%, 75%) for continuous data and n (%) for categorical data. *P* value indicates the difference between no MPS and MPS groups. *P* value less than or equal to .05 was considered statistically significant. *MPS*, Malperfusion syndrome; *MI*, myocardial infarction; *LOS*, length of stay. *Acute renal failure defined using the Society of Thoracic Surgeons definition: (1) an increase in serum creatinine level 3× greater than baseline, or serum creatinine level ≥4 mg/dL, with an acute increase being at least 0.5 mg/dL or (2) a new requirement for dialysis postoperatively. †Operative mortality includes 30-d mortality or in-hospital mortality.

significant. There was no significant difference between the MPS and no MPS groups in the growth rate of aortic arch (0.38 vs 0.35 mm/year). However, the growth rate of both the descending (1.03 mm/year vs 0.68 mm/year, *P* = .001) and abdominal aorta (0.76 mm/year vs 0.59 mm/year, *P* = .02) was significantly higher in the MPS group compared with the no MPS group (Figure 2, *A-C*).

Cumulative Incidence of Reoperations

The overall 15-year cumulative incidence of reoperation for distal aortic aneurysm in all patients who had initial open aortic repair for ATAAD (n = 796) was 23% (95% confidence interval [CI], 18-27) (Figure 3, *A*). The 10-year cumulative incidence of reoperation was similar between the MPS and no MPS groups (18%; 95% CI, 10-28) versus 18% (95% CI, 14-22) (Figure 3, *B*). In the

MPS group, 17 patients had reintervention to the distal aorta. This included 2 median sternotomies for arch aneurysm, 7 open repairs of the descending thoracic or thoracoabdominal aneurysm, and 8 TEVARs. In the no MPS group, 75 patients had reintervention to distal aorta. This included 7 median sternotomies for arch aneurysm, 37 open repairs of the descending thoracic or thoracoabdominal aneurysm, 1 open repair of an abdominal aortic aneurysm, 28 TEVARs, 1 endovascular aneurysm repair, and 1 unknown repair of the distal aorta at an outside hospital. The presence of MPS, patent false lumen in the descending thoracic aorta, aortic endovascular fenestration/stenting, and connective tissue diseases were not significant risk factors for reoperation (Table 4).
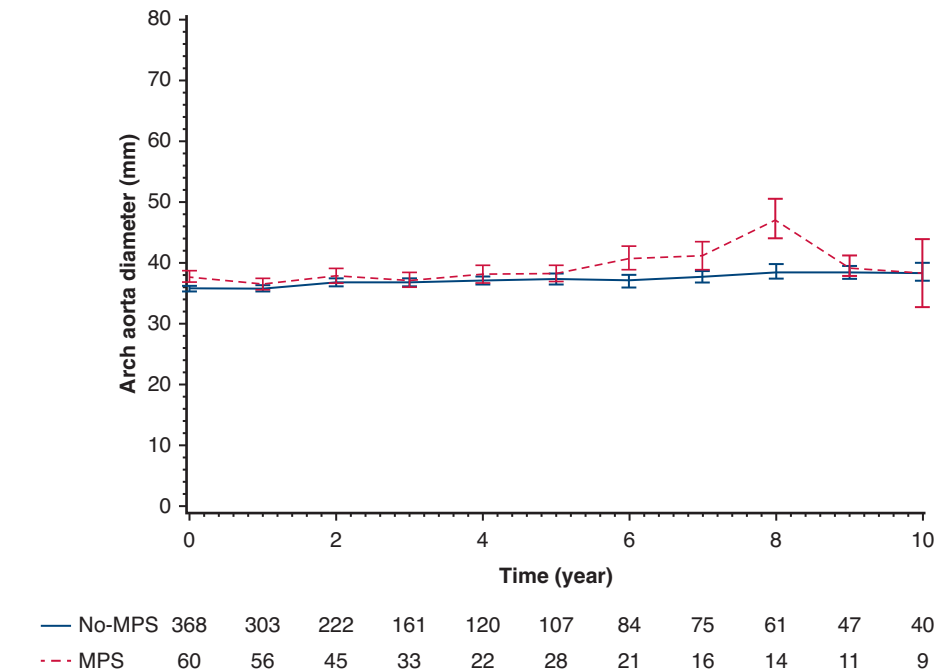
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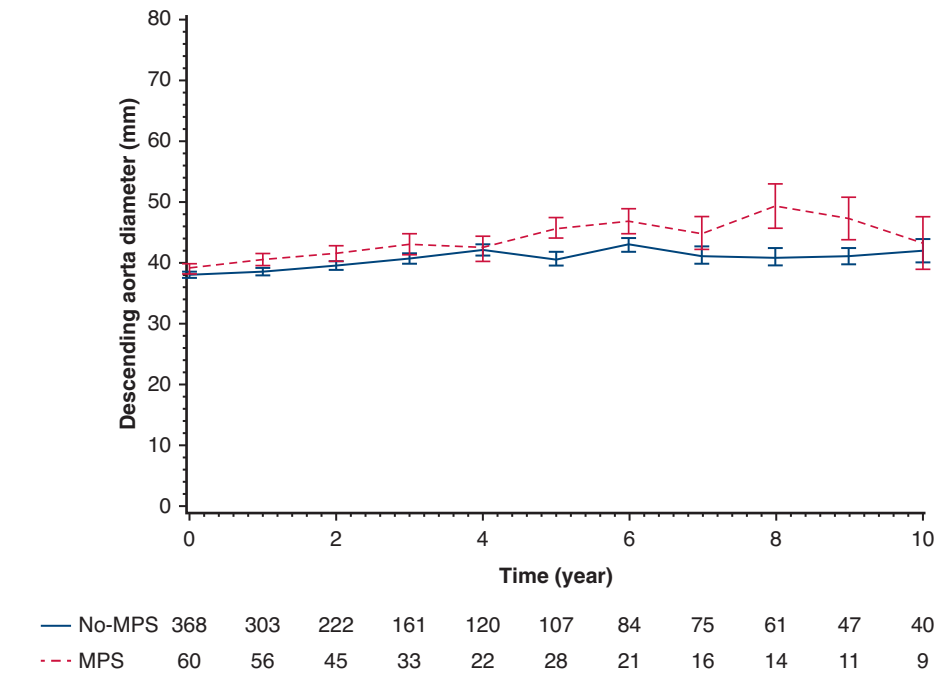
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FIGURE 2. A, There was no difference in aortic arch growth rate over 10 years between the MPS and no MPS groups (0.38 mm/y vs 0.35 mm/y, $P = .81$). B, The growth rate of the descending thoracic aorta over 10 years was significantly higher in the MPS group compared with the no MPS group (1.03 mm/y vs 0.68 mm/y, $P = .001$). C, The growth of the abdominal aorta over 10 years was significantly higher in the MPS group compared with the no MPS group (0.76 mm/y vs, 0.59 mm/y, $P = .02$). *MPS*, Malperfusion syndrome.
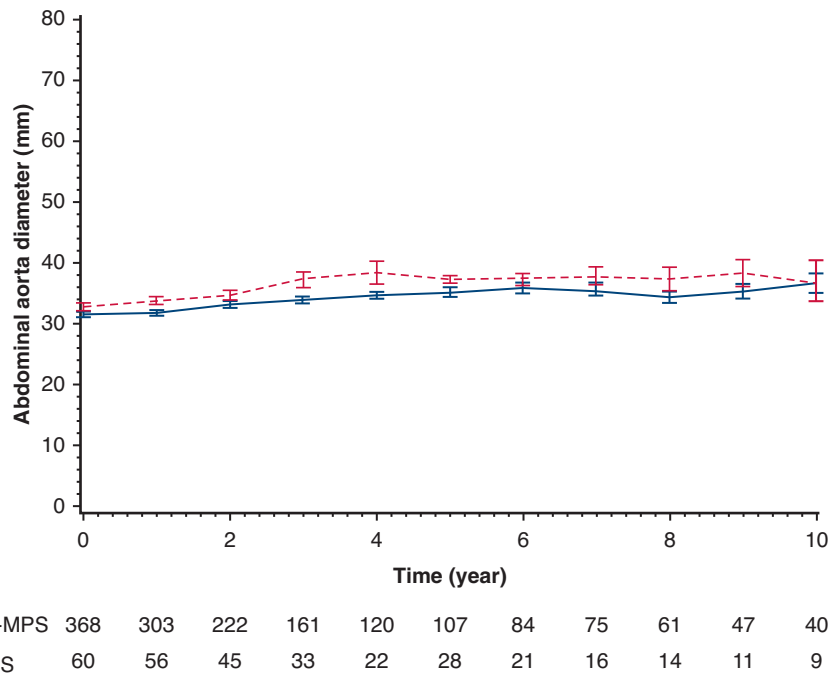
FIGURE 2. (*continued*).

Long-term Survival

The median follow-up time for survival was 6.1 years, and there was 100% completeness to follow-up with the end of study date on December 12, 2021. The 15-year survival in all patients after initial open aortic repair for ATAAD (n = 796) was 51% (95% CI, 46-56) (Figure 4, *A*). The 15-year survival was similar between the MPS and no MPS groups (50%; 95% CI, 36-63 vs 48%; 95% CI, 42-55) (Figure 4, *B*). Age and history of
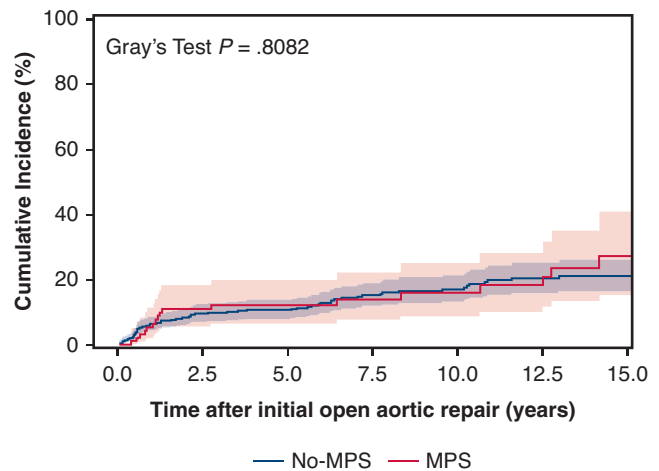
renal failure were significant risk factors for long-term mortality (hazards ratio, 1.03; 95% CI, 1.02-1.05, *P* < .0001 and hazards ratio, 2.28, 95% CI, 1.35-3.85, *P* = .002), respectively (Table 4).

DISCUSSION

In this study, we found that short- and long-term outcomes were similar between patients with ATAAD with MPS after endovascular fenestration/stenting followed
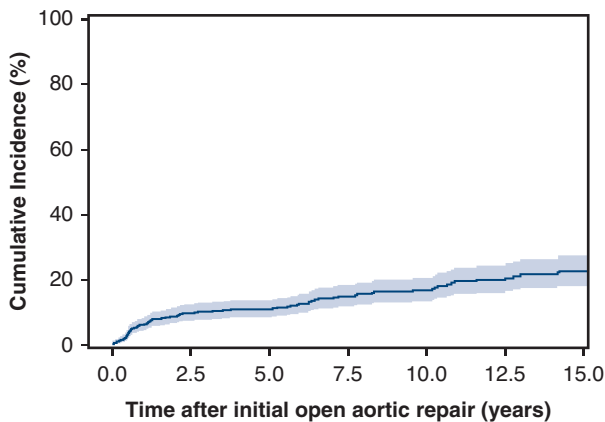
FIGURE 3. A, The overall 15-year cumulative incidence of reoperation for distal aortic aneurysm in all patients who had initial open aortic repair for ATAAD (n = 796) was 23% (95% CI, 18-27). B, The 10-year cumulative incidence of reoperation was similar between the MPS and no MPS groups (18%; 95% CI, 10-28) versus 18% (95% CI, 14-22, *P* = .81). *MPS*, Malperfusion syndrome.

TABLE 4. Cox model of risk factors for reoperation and long-term mortality

	Hazard ratio (95% CI)	P value
Reoperation		
Age	0.99 (0.97-1.00)	.11
Sex, female	0.56 (0.31-0.99)	**.05**
MPS	0.36 (0.05-2.63)	.32
Aortic fenestration/stenting	2.84 (0.38-21.5)	.31
CTD	0.92 (0.40-2.12)	.85
Patent false lumen in the descending thoracic aorta	1.31 (0.84-2.04)	.24
Long-term mortality		
Age	1.03 (1.02-1.04)	**<.0001**
Sex, female	0.86 (0.64-1.17)	.35
MPS	0.74 (0.49-1.09)	.13
PVD	1.15 (0.80-1.64)	.45
Previous cardiac surgery	0.84 (0.52-1.34)	.46
History of renal failure	2.28 (1.35-3.85)	**.002**

$P \leq .05$ is significant. *CI*, Confidence interval; *MPS*, malperfusion syndrome; *CTD*, connective tissue diseases; *PVD*, peripheral vascular disease.

by delayed open aortic repair compared with patients with ATAAD DeBakey I without MPS, including the operative mortality, growth of the residual dissected aortic arch, cumulative rate of reoperation for aneurysm of the distal residual dissected aorta, and long-term survival. The MPS group had a significantly higher growth rate of the residual descending aorta and abdominal aorta compared with the no MPS group, although this was minimal (Figure 5, Video 1, and Video Abstract).

Previously, we reported the operative outcomes of patients with ATAAD with MPS managed with endovascular fenestration/stenting followed by delayed open aortic repair.[5,7] In this study with more patients, we furthermore confirmed that the operative mortality of patients with ATAAD with MPS who underwent fenestration/stenting and delayed open aortic repair compared with patients without MPS was similar. Because of MPS, it was not surprising that the MPS group had a higher proportion of acute renal failure requiring dialysis, prolonged ventilation, and total length of hospital stay compared with the no MPS group. The short-term outcomes supported that our approach for patients with MPS was a valid approach. This concept was also supported by the outcomes from another group using endovascular stent graft to treat malperfusion first for patients with MPS followed by delayed open aortic repair.[10]

It is unknown how the distal aorta progresses in patients with ATAAD with MPS after fenestration/stenting followed by open repair, that is, the remaining dissected aortic arch, descending thoracic, and abdominal aorta. In this study, we found the overall growth rate of all segments of the distal aorta was slow, with the descending thoracic aorta growth fastest, similar to reports in the literature.[11] The reason was unknown for the higher growth rate of the residual descending thoracic aorta and abdominal aorta in the MPS compared with the no MPS group. We speculated the MPS group may have had more aortopathy or vasculopathy that resulted in aortic branch vessel dissection and static malperfusion, which eventually led to MPS. In the MPS group, 81% had aortic branch vessel dissection and stenting, which was higher than in the no MPS group.
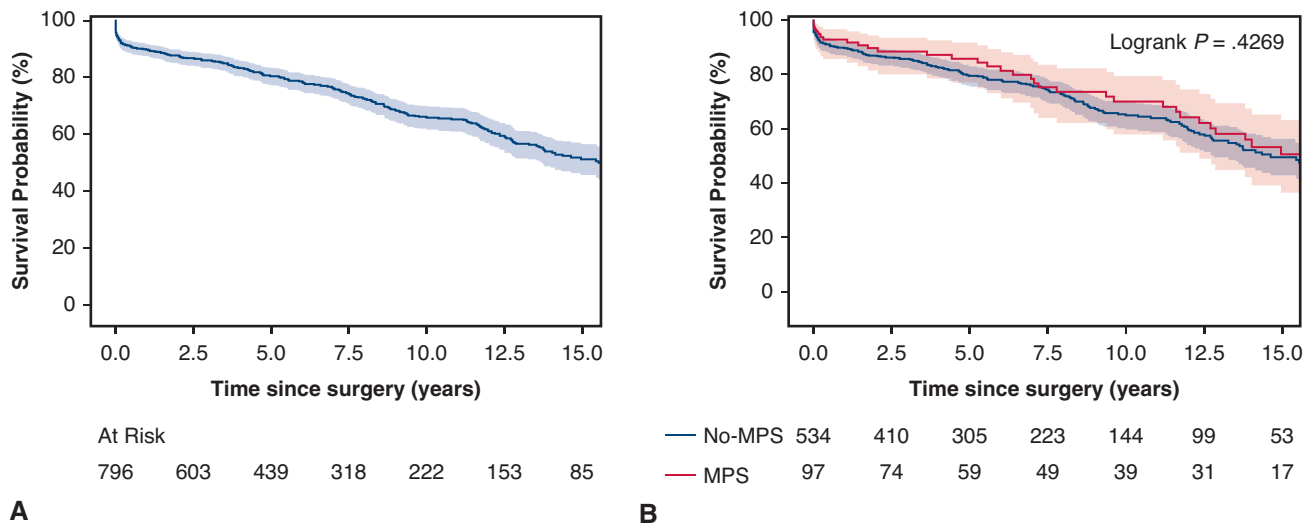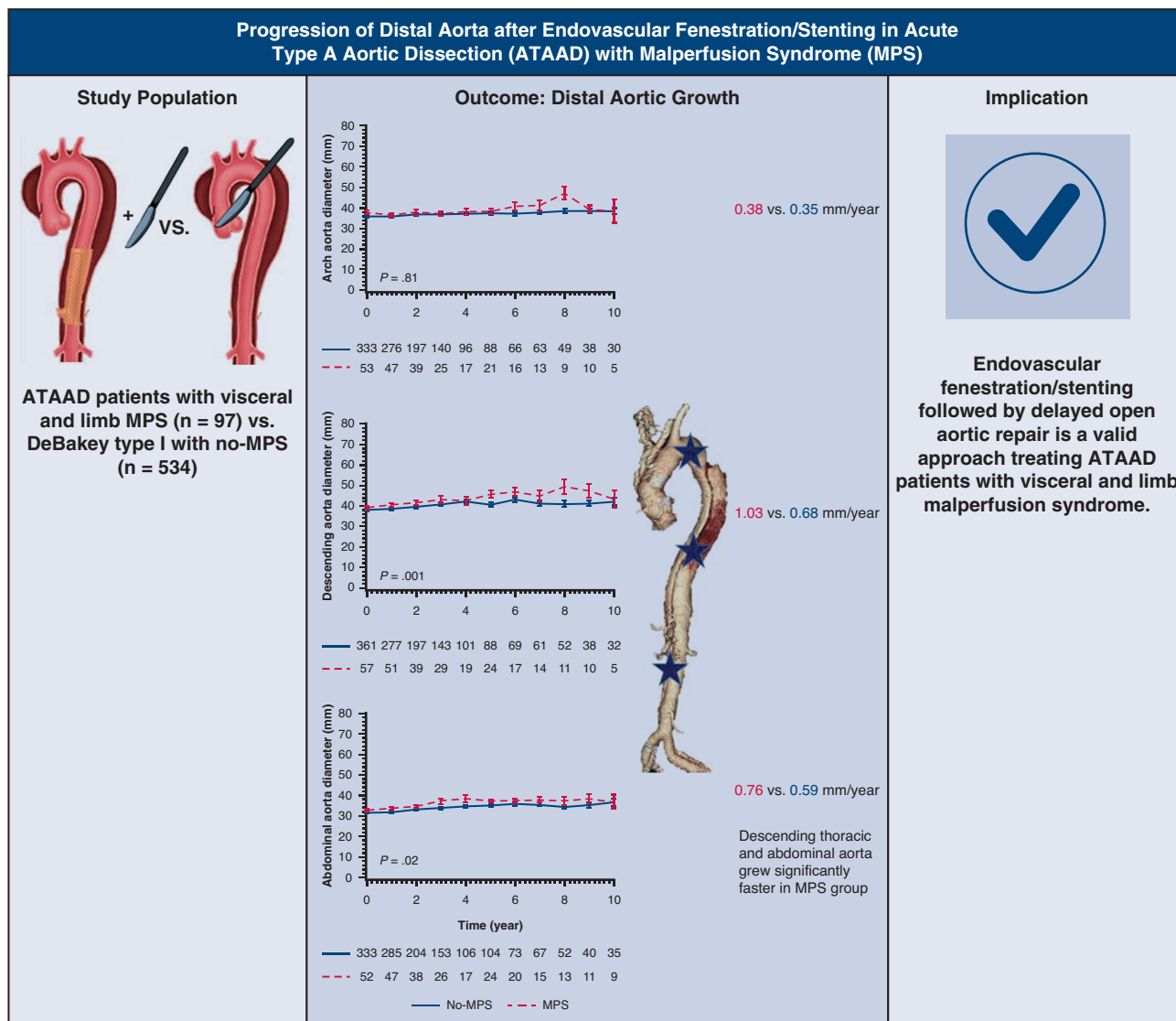

FIGURE 4. A, The 15-year survival in all patients after initial open aortic repair for ATAAD (n = 796) was 51% (95% CI, 46-56). B, The 15-year survival was similar between the MPS and no MPS groups [50% (95% CI, 36-63) versus 48% (95% CI, 42-55), P = .43]. *MPS*, Malperfusion syndrome.

FIGURE 5. Patients with ATAAD and MPS treated with endovascular fenestration/stenting followed by delayed open aortic repair had overall minimal growth of their distal residual dissected aorta and similar cumulative rate of reoperation and long-term survival compared with patients without any MPS. The up-front endovascular fenestration/stenting followed by delayed open aortic repair is a valid approach for patients with ATAAD with MPS.

The goal of fenestration and stenting at the dissected distal descending thoracic aorta was to create a reentry tear to decompress the false lumen of the aorta and decrease the strain. Previously, we reported that patients with a large distal reentry tear of the false lumen have a slower growth of their distal dissected aorta.[12] Other studies have shown that lack of distal tear increases aortic false lumen pressure and subsequent growth.[13,14] When patients presented with malperfusion and MPS, the aortic true lumen was compressed by the false lumen. After aortic fenestration/stenting, the true lumen compression was resolved and false

lumen was decompressed, just as in patients without MPS. This could be the reason for the slow growth rate in all segments of the distal aorta in MPS groups after ATAAD repair. It is likely that the distal aorta could have grown even faster if the patients had not received endovascular fenestration/stenting to decompress the aortic false lumen and open the dissected aortic branch vessels.

As one of the consequences of the slow growth of the distal aorta after initial ATAAD repair, we found that the 10-year cumulative incidence of reoperation for the aortic aneurysm of the distal aorta with death as a competing

VIDEO 1. Discussion of the long-term distal aorta progression for patients with ATAAD MPS who underwent endovascular fenestration before open aortic repair. Video available at: https://www.jtcvs.org/article/S2666-2736(23)00074-8/fulltext.

factor was similar between the MPS and no MPS groups (18% vs 18%), which was among the range of reoperation rate reported in the literature.[15-17] We need to keep in mind that at 10 years, 30% of the patients in the MPS group and 35% of the patients in no MPS group had died after initial ATAAD repair (Figure 4, *A* and *B*). We did not know if there was any aortic-related late mortality because the National Death Index and Michigan Death Index data did not report the cause of death. The association of patent false lumen and reoperation is controversial.[15,16] A meta-analysis showed complete false thrombosis does not significantly correlate with lower aortic reoperation of the distal aorta.[18] Likewise, our study did not find that a patent false lumen of the descending aorta was a significant risk factor for late reoperation of the residual dissected distal aorta (Table 4). Although the false lumen of the dissected distal aorta was patent after endovascular fenestration and stenting, the reentry tear created by fenestration and stenting was able to decompress the aortic false lumen. It could potentially decrease the distal aortic growth rate and the need for reoperation.

Finally, our study showed that the 10-year and 15-year survival outcomes of patients with ATAAD with MPS was favorable (70% and 50%, respectively) after up-front fenestration/stenting followed by delayed open aortic repair and similar to patients without MPS (65% and 48% respectively) treated with emergency open aortic repair (Figure 4, *B*). Only patients who recovered from MPS had open aortic repair. When they eventually had open aortic repair, they did not have any malperfusion or MPS. Those patients were supposed to have similar outcomes as those who did not have MPS at the presentation. The favorable short- and long-term outcomes in patients with MPS in our study were likely due to patients' selection for open aortic repair. Some patients did not recover from multiorgan failure after the malperfusion was resolved with endovascular fenestration/stenting. Those patients were

not surgical candidates and did not have open aortic repair, or they did not need surgery because the dissection became subacute and the ascending aorta did not grow significantly. They died of organ failure or aortic ruptures, or were discharged alive without an operation.[5] The patients who died of organ failure after malperfusion was resolved endovascularly likely would not have survived open aortic repair. No matter what we had done, their outcomes likely would have been the same. Ten percent of patients (16/160) with MPS treated with endovascular fenestration/stenting died of aortic rupture (Figure 1). Most of the aortic ruptures (13/16 patients) happened in the first decade (1996-2007). In the second decade, only 4% of patients died of aortic rupture while they were recovering from MPS.[5] The operative mortality for those patients with MPS ranges from 29% to 89%.[3,4]

In summary, with up-front endovascular fenestration/stenting followed by delayed open aortic repair, patients with MPS had slow growth of the distal aorta and similar short- and long-term outcomes compared with patients without MPS, including operative mortality, long-term survival, and reoperation rate for the aneurysm of the residual dissected distal aorta. The endovascular fenestration/stenting followed by open aortic repair was a valid approach for patients with ATAAD with MPS.

Study Limitations

This study is limited by being a single-center, retrospective study. The sample size of the fenestration/stenting group was relatively small and could affect the power of the study. There was a selection bias. This study only included the patients who survived MPS after endovascular fenestration/stenting and had delayed open aortic repair because this study was designed to determine the progression of dissected distal aorta after open aortic repair in patients with or without MPS. The follow-up of image studies and reoperations was not 100% complete. We could underestimate the cumulative incidence of reoperation. We created an aortic database, and all the patients with ATAAD have been followed by our aortic clinic. Patients who missed follow-ups were identified by our dedicated clinical coordinators and contacted appropriately.

CONCLUSIONS

Endovascular fenestration/stenting followed by open aortic repair in patients with ATAAD with visceral or limb MPS had favorable short- and long-term outcomes compared with patients without MPS. Our findings supported that up-front endovascular fenestration/stenting followed by delayed open aortic repair was a valid approach for patients with ATAAD with visceral and limb MPS.

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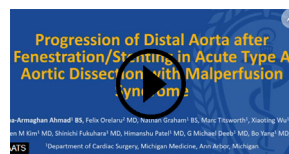
Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Discussion
Presenter: Rana-Armaghan Ahmad

Dr Bradley Leshnower *(Atlanta, Ga)*. Thanks to Dr Kelly and the Association for the invitation to discuss this article. Great job, Armi, and thank you to Dr Yang for providing a well-written manuscript. Again, you guys are shedding light on this concept of a delayed central aortic repair and a vascular treatment of MPS followed by delayed aortic repair in selected MPS to improve outcomes. Certainly, I've adopted this slightly different approach for mesenteric malperfusion, but in this article, you address it with both visceral and iliac malperfusion. Essentially, what you've done is take a control group and compare it with an MPS group that you have converted to non-MPS and showed the safety of that and that there's no difference in short- and long-term mortality reintervention, and slightly increased growth in the descending abdominal aorta, but fantastic work.

When I looked at the manuscript I extracted a couple of other important data points. This is another large series of type A dissections to Dr Girardi's point that he eloquently made, only a 21% need for reintervention over the long term for distal reintervention, so that should be noted. Second, certainly, the delayed aortic repair concept is controversial. It's always a big discussion when we talk about it. I want to point out that in your big algorithm, you did lose 10% of patients with aortic rupture when you delayed them, but that those patients likely would have died had you operated on them emergently, we'll never know. I want to point out the safety of the delayed aortic approach, as Himanshu Patel actually put it the other day, that the Michigan group believes the bigger threat to life is the

MPS, not the risk of rupture. Although you showed that the mortality short term was about 5% in your MPS, you do have to consider those with aortic ruptures, it's a strategy of an intent to treat, and when I did the numbers, the mortality was 33%. But again, if you're dealing with mesenteric malperfusion, those patients have a 60% to 70% mortality, so it's still better.

On to my questions. First, in your arch measurement, you showed the descending and abdominal group, but in the arch measurements, I think it's skewed because 40% of your malperfusion patients actually received a zone 1, 2, or 3 arch. Did you think about just looking at the hemiarches? Because when you sew a completely circular anastomosis, we all know you have a better chance of closing the false lumen, which will reduce it. Did you look at just the hemiarches in each group and compare measurements?

Rana-Armaghan Ahmad *(Ann Arbor, Mich)*. For this study, we didn't just exclude the hemiarch, but we do think that's a great further follow-up. The main limitation right now is just the limited data, right? We already have only 97 patients in that group. We take out 40%. So eventually, over the next several years, that is definitely a possibility, but yes.

Dr Leshnower. Okay. If the MPS was resolved, why did you add TEVARs to 10% of the MPS groups?

Dr Ahmad. Are you saying the patients who didn't receive open aortic repair?

Dr Leshnower. No. In your data, in the MPS group, 10% of those, when I looked at the operative data, received frozen elephant trunks.

Dr Ahmad. Okay.

Dr Leshnower. What was the need for that?

Dr Ahmad. So, that was not to treat the MPS, but more so to treat the proximal tear and prevent downstream aortic pathology. Maybe Dr Yang can further clarify that.

Dr Leshnower. This gets into a bit of deeper thought; 89% of your MPS cases had both aortic and branch vessel stenting. Now, when I do a TEVAR first for a mesenteric malperfusion, the malperfusion is usually dynamic, so a TEVAR will completely resolve it. But you're saying in almost 90% of patients, you're also having to do branch vessel stenting, which would mean it's static. So can you comment on the reason why and the differences you perceive?

Dr Ahmad. So, with the Michigan Protocol, once they go to interventional radiology for that, the way it's done is that Dr Williams, the interventional radiologist, measures the difference in the systolic blood pressure between the aorta and each branch vessel. If it's greater than 15, then they perform stenting.

Dr Leshnower. The way I do it is I shoot a picture in the operating room, and if there's robust filling, I don't do the physiologic measurements, so that explains it. The last

question gets to the technique. You've shown that the descending and abdominal aortic growth rates are higher in your fenestration and stenting group. In your article, you offer the hypothesis that this is likely related to the aortopathy or vasculopathy of the patient, so it's inherent to the aorta. But remember, you're creating a 16-mm fenestration, and when we look at, for instance, stenting chronic type Bs, retrograde false lumen perfusion is a big reason why aneurysms grow. So, I would submit it's not inherent to the aorta. It's inherent to your technique. You are creating a large tear in the aorta and increasing blood flow to that false lumen and probably increasing pressure. It's just something to think about. It's not necessarily a question, but it's a difference in the technique, whereas if I do a stent graft, I'm covering tears and eliminating blood flow into the false lumen. But anyways, very good job.

Dr Bo Yang *(Ann Arbor, Mich)*. Just a clarification. Number one is that the rupture, yes, when you observe those patients, there's always risk of aortic rupture. The most rupture happened in the first decade in our circulation paper. It's about 16% ruptured in the first decade. In the second decade, 4% of patients had rupture because we're gaining experience on how to manage those patients to control the blood pressure. It's really low, below 90, and on waking them up, well, you keep them in the intensive care unit tightly controlled, and intensive care units are more confident with those patients in the second decade. This is number one. Those patients, if we take them to the operating room, their mortality is probably 30% to 40% operative mortality. But yes, when we do this, there is a risk of rupture. We found out that limb malperfusion has more risk of rupture than mesentery malperfusion. Number 2 is the tear. We cover the tear with TEVAR during the open repair because we see the tear in the proximal descending aorta and we cover it. That's why it's not for malperfusion per se. Number 3, the stenting of the branch vessels. David always measured the blood pressure of branch vessels. If it is 15 mm Hg lower than the ascending aorta, he will stent it just to prevent all of these things being malperfused. That's why he does more.

Dr Marek Deja *(Katowice, Poland)*. Maybe I missed it, but can you clarify what was the time frame? I mean, in the group that you stented or stent-grafted, between the presentation and the operation on the ascending part, how long was the delay and what do you guide the delay with? This is one question. And another, you excluded the patients in the group without stent-grafting who had malperfusion. Can you give us a hint of what was the fate of those patients who directly went to aortic surgery rather than performing stent-grafting on them?

Dr Ahmad. I can answer the first question, or I guess the second question first. For the patients who had MPS and were excluded, who didn't have fenestration stenting, it was because they had cerebral, coronary, or visceral with

cardiac tamponade. We excluded them because it didn't make sense to compare them directly because they were never corrected for MPS. Our point was that we take the MPS patients, return them to the same baseline as patients who didn't have MPS, with fenestration and stenting, and then it's a direct comparison. If we included those patients, then it's not really analyzing the efficacy of fenestration and stenting before open repair.

Dr Yang. But the fate of those patients, that's a good question. We do not have the data right now. We didn't look into it, but we will. I don't think the outcome is good, but we'll look into it. Cerebral malperfusion and coronary malperfusion are treated the way of open aortic repair. I had a discussion before about this issue.

Dr Deja. And the delay of the–?

Dr Yang. Oh, delay, yeah. The delay.

Dr Deja. What was the strategy? How long do you wait?

Dr Yang. The median time used to be 4 days. Now, it's about 1 to 2 days, where it will be more active. We operate those patients earlier now. The criteria for waiting for operation are if the acidosis is corrected, a shock is corrected, they are not on multiple pressors, acute respiratory distress syndrome is better, they're not on 100% oxygen but instead just 50, and you think the patient can't tolerate the cardiopulmonary bypass and hypothermia circulatory arrest, then we'll take the patient to the operating room. Kidney function takes a long time to recover, so I don't wait for renal failure to recover.

Dr Deja. So, on average, this is what, 2 days?

Dr Yang. Yes. Maybe it's 1 to 2 days now. In the first decade, it was 4 days.