ORIGINAL

Impact of persistent malperfusion syndrome following central repair of acute type A aortic dissection on early outcomes

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Abstract : We investigated impact of persistent malperfusion syndrome (MPS) following central repair of acute type A aortic dissection (ATAAD) on outcomes. Thirty patients who underwent central repair for ATAAD with MPS were included. Patients were divided into two groups : 23 patients without MPS following central repair (No-MPS group) and 7 with MPS (Persistent-MPS group). The mean age was 66.8 ± 9.6 and 59.4 ± 13.4 years in the No-MPS and Persistent-MPS groups, respectively (P = 0.176). Preoperative MPS included the left coronary artery (n = 3), brain (n = 3), abdomen (n = 7), and extremities (n = 11) in the No-MPS group. In the Persistent-MPS group, the right coronary (n = 1), brain (n = 2), abdomen (n = 3), and extremities (n = 5) were observed. In the No-MPS group, one patient died of extensive cerebral infarction (4.3%). In the Persistent-MPS group, 2 patients died of sepsis and multi-organ failure, respectively (28.6%) (P = 0.061). The Persistent-MPS group had more patients requiring hemodialysis than the No-MPS group (P = 0.009). Three patients underwent intestinal resection due to persistent MPS (P < 0.001). Persistent MPS following central repair for ATAAD significantly contributed to outcomes. J. Med. Invest. 71 : 158-161, February, 2024

Keywords **:** *persistent, malperfusion syndrome, acute type A aortic dissection*

INTRODUCTION

Acute type A aortic dissection (ATAAD) is a life-threatening condition. It typically requires emergency surgery to save lives. The International Registry of Acute Aortic Dissection reported a 23.9% in-hospital mortality rate (1) ; however, in Japan, surgical outcomes in ATAAD repair have been improving over the last decades with a recent in-hospital mortality rate of 11% (2).

Organ necrosis and failure due to malperfusion syndrome (MPS) in ATAAD showed the worse outcomes even after a successful central repair, with an approximately 20% operative mortality rate (3-5). It was because acute disruption of blood supply to each organ leads to irreversible organ damage (6, 7). Furthermore, mortality rates increased as the number of affected organ systems due to MPS increased (5).

Generally, to prevent aortic rupture and save lives, ATAAD with MPS should be immediately operated, with the expectation of resolving MPS (3). However, cases wherein MPS persisted were noted, and revascularization for MPS was required immediately following central aortic repair (5). How persistent MPS following central aortic repair affects surgical outcomes has not been elucidated. In this study, we aimed to investigate the impact of persistent MPS following central aortic repair on early outcomes in ATAAD.

MATERIALS AND METHODS

The institutional review board approved this study on 15, March, 2023 (No 4-194).

Of 150 patients who underwent central aortic repair for ATAAD between 2006 and 2020, 30 patients with preoperative MPS were included. Patients with connective tissue disorders, chronic dissection, and traumatic aortic dissection were excluded from this study.

We defined malperfusion as inadequate blood flow to the vital organs due to ATAAD-related obstruction of the aorta and the main branches, and MPS as tissue necrosis and functional failure of vital organs secondary to malperfusion (3). MPS diagnosis includes both clinical and laboratory findings as well as imaging findings on computed tomography (CT) revealing the static or dynamic obstruction of the aorta or the main branches. The diagnosis or suspicion of MPS was made at the time of ATAAD diagnosis preoperatively.

Persistent MPS was defined as an additional treatment for organ ischemia following central aortic repair or symptom fixation from the preoperative period. Indications of additional treatment for persistent MPS following central repair included absent arterial pulse, laboratory abnormalities, ongoing (suspected) signs of mesenteric ischemia including unexplained lactic acidosis and abdominal pain/distension, or abnormal cardiac function on intraoperative transesophageal echocardiography or on gross during surgery, and imaging findings including on radiography, CT, or selective angiography.

CT, particularly contrast-enhanced CT in patients with sufficient renal function to tolerate venous contrast, was postoperatively performed to assess the thoracic aorta for which surgical repair was performed. Furthermore, CT was repeatedly performed whenever there was suspicion of persistent or ongoing ischemia due to ATAAD even following central aortic repair.

Patients were divided into the following two groups : 23 patients without MPS following central repair (No-MPS group) and 7 patients with MPS following central aortic repair (Persistent-MPS group), and the clinical outcomes were compared.

The mean follow-up period was 4.3 ± 2.7 years, and the follow-up rate was 100%.

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Central aortic repair for ATAAD

Emergency central aortic repair with limited graft replacement and entry resection was our strategy for treating ATAAD. In cases wherein MPS persisted following central aortic repair, surgery or intervention to revascularize the blood supply to the affected organs was added.

Our surgical technique was described in detail (8).

In most cases, emergency surgery is performed following a diagnosis of ATAAD is confirmed on CT. Cardiologists assess cardiac function, the degree of aortic regurgitation, or pericardial effusion with/without cardiac tamponade using transthoracic echocardiography at the emergency department. We select the arterial cannulation site on the basis of site of entry and extent of dissection involving peripheral arteries. Intraoperatively, cardiopulmonary bypass is established via arterial and right atrial cannulations, and patients are gradually cooled down to bladder temperatures of 25℃ and 28℃ for total and non-total arch replacement, respectively. Circulatory arrest is achieved with the initiation of retrograde or selective perfusion of cold blood cardioplegia. The ascending aorta is opened and transected. Each neck vessel is cannulated with a balloon-tipped cannula for antegrade cerebral perfusion. Distal aortic anastomosis is performed under circulatory arrest. Lower body circulation is resumed via a side branch, and whole-body rewarming is initiated. Subsequently, proximal aortic repair and anatomical reconstruction of the neck vessels are performed. Finally, patients are weaned from cardiopulmonary bypass.

Statistical analysis

All statistical analyses were conducted with StatView version 5.0 software (SAS Institute, Cary, NC, USA). Categorical variables were analyzed using the χ^2 test and are expressed as percentages. Continuous variables were analyzed using Wilcoxon signed-rank test and are expressed as the mean ± standard deviation (SD). The Kaplan-Meier method was applied to calculate estimates of survival. The Log-rank test was used to compare the statistical level. P value < 0.05 was considered statistically significant.

RESULTS

Preoperative conditions

The mean age was 66.8 ± 9.6 and 59.4 ± 13.4 years in the No-MPS and Persistent-MPS groups, respectively (P = 0.176). Preoperative shock status was observed in 7 and 2 patients in the No-MPS and Persistent-MPS groups, respectively (P = 0.925). In the No-MPS group, preoperative MPS included the left coronary artery (n = 3), brain (n = 3), abdomen (n = 7), and extremities (n = 11). Preoperative stenting of the left coronary artery was performed in cases with the left coronary artery malperfusion, and extracorporeal membrane oxygenation support was provided in one of the cases. In the Persistent-MPS group, the right coronary (n = 1), brain (n = 2), abdomen (n = 3), and extremities (n = 5) were observed preoperatively. No statistically significant difference was noted in the proportion of preoperative MPS between groups. Preoperative characteristics are summarized in Table 1.

Early outcomes

Intraoperative data are summarized in Table 2. The proportion of the type of central aortic repair and arterial cannulation site was similar between the groups. Circulatory arrest duration that was shorter in the No-MPS group than in the Persistent MPS group (P = 0.046), was the only difference observed in

Table 1. Preoperative patients' profile (n = 30)

Variables	No-MPS (n = 23)	Perst-MPS (n = 7)	P value
Age	66.8+/-9.6	59.4+/-13.4	0.176
Male	20 (87.0)	5 (71.4)	0.334
BSA	1.74+/-0.17	1.71+/-0.21	0.273
Hypertension	13 (56.5)	5 (71.4)	0.481
Diabetes mellitus	0 (0)	1 (14.3)	0.065
Dyslipidemia	5 (21.7)	0 (0)	0.177
CAD	1 (4.3)	0 (0)	0.575
Stroke	3 (13.0)	2 (28.6)	0.334
COPD	1 (4.3)	0 (0)	0.575
PAD	1 (4.3)	1 (14.3)	0.356
Creatinine > 1.5mg/dL	1 (4.3)	0 (0)	0.575
Reoperation	0 (0)	1 (14.3)	0.065
Shock status	7 (30.4)	2 (28.6)	0.925
Preope MPS			
Brain	3 (13.0)	2 (28.6)	0.195
Coronary	3 (13.0)	1 (14.3)	0.933
Abdomen	7 (30.4)	3 (42.9)	0.542
Extremities	11 (47.8)	5 (71.4)	0.273

BSA ; body surface area, CAD ; coronary artery disease, COPD ; chronic obstructive pulmonary disease, PAD ; peripheral artery disease, MPS ; malperfusion syndrome, Perst ; persistent

Table 2. Intraoperative details (n = 30)

Variables	No-MPS (n = 23)	Perst-MPS (n = 7)	P value
CA (min)	59.9+/-11.3	69.1+/-15.2	0.046
AoX (min)	153.4+/-41.9	162.0+/-21.0	0.311
CPB (min)	238.7+/-51.1	261.3+/-27.2	0.237
Min Tm (℃)	25.9+/-1.4	25.4+/-0.8	0.106
Arterial cannulation			
Ascending aorta	5 (21.7)	2 (28.6)	0.708
Axillary artery	4 (17.4)	2 (28.6)	0.517
FA	10 (43.5)	3 (42.9)	0.977
Combined	4 (17.4)	0 (0)	0.236
Procedures			
AAR	12 (52.2)	3 (42.9)	0.666
PAR	5 (21.7)	1 (14.3)	0.666
TAR	6 (26.1)	3 (42.9)	0.397
Concomitant			
Bentall	1 (4.3)	0 (0)	0.575
Root remodeling	1 (4.3)	0 (0)	0.575

AAR ; ascending aortic replacement, AoX ; aortic cross clamp, CA ; circulatory arrest, CPB ; cardiopulmonary bypass, Min Tm ; minimal temperature, MPS ; malperfusion syndrome, PAR ; partial aortic arch replacement, Perst ; persistent, TAR ; total arch replacement

intraoperative data.

Early outcomes between groups are summarized in Table 3.

In the Persistent-MPS group, additional procedures for addressing persistent MPS following central aortic repair were observed (Table 4).

Two patients (No 3 and 4) in the Persistent-MPS group underwent the superior mesenteric artery (SMA) stenting following central repair for ATAAD at a hybrid operating theater. Laparotomy was added in a patient (No 4) to further investigate ischemia in abdomen. At that time, blood supply was confirmed in both patients. However, they required intestinal resection on postoperative day (POD) 12 and 60, respectively. Three patients (No 1, 6 and 7) underwent femoro-femoral crossover bypass following central aortic repair. One patient (No 5) required femoral artery fenestration following central repair due to persistent MPS in the lower extremity. Although the patient developed preoperative MPS in SMA, there was no evidence of abdominal ischemia following central repair from the perspective of laboratory examination. However, additional intestinal resection due to persistent MPS in SMA was performed on POD 4. A patient (No 2) with extensive cerebral infarction due to preoperative occlusion of the left carotid artery underwent cranial decompression on POD 3.

In the No-MPS group, one patient who required preoperative cardiopulmonary resuscitation died of extensive cerebral infarction (4.3%). In the Persistent-MPS group, one patient who underwent femoro-femoral crossover bypass for persistent leg ischemia died of sepsis, and the other who underwent femoral artery fenestration and intestinal resection due to persistent abdominal ischemia died of multi-organ failure (28.6%) (P = 0.061). The Persistent-MPS group had more patients who required hemodialysis than the No-MPS group (P = 0.009). The three patients who required hemodialysis did not develop preoperative MPS in the renal arteries. The hemodialysis was temporarily required due to acute kidney injury.

Table 3. Early outcomes (n = 30)

Variables	No-MPS (n = 23)	Perst-MPS (n = 7)	P value
Hospital death	1 (4.3)	2 (28.6)	0.061
Permanent ND	6 (26.1)	3 (42.9)	0.400
Chest reopening for bleeding	0 (0)	0 (0)	---
Hemodialysis	1 (4.3)	3 (42.9)	0.009
Tracheostomy	3 (13.0)	2 (28.6)	0.334
Mediastinitis	1 (4.3)	0 (0)	0.575
Afib	4 (17.4)	0 (0)	0.236

Afib ; atrial fibrillation, MPS ; malperfusion syndrome, ND ; neurological deficit, Perst ; persistent

DISCUSSION

We have demonstrated the negative impact of persistent MPS following central repair for ATAAD on early outcomes. However, patients after the index admission in both groups were able to survive without statistically significant difference.

Outcomes following ATAAD repair accompanied by MPS have been significantly poor despite successful central aortic repair (3-5). Central aortic repair for ATAAD is a standard of care for ATAAD management to avoid aortic rupture and improve true lumen flow and restore the artery patency in MPS cases. Thus, addressing MPS before central aortic repair has been a rare occurrence. In contrast, we have to be aware that there were cases wherein MPS persisted and revascularization for MPS was required immediately following central aortic repair. Of 77 coronary malperfusion cases, 53 (69%) required coronary artery bypass grafting following central aortic repair. Moreover, 14 (11%) of 124 patients with leg malperfusion underwent peripheral bypass surgery. Regarding mesenteric ischemia, mesenteric bypass surgery and bowel resection were performed in 8% and 5% of the patients following central aortic repair (5). In our study, the incidence rate of persistent MPS following central aortic repair was 23.3% (7/30 patients). Almost one fourth of ATAAD cases with preoperative MPS developed persistent MPS following central aortic repair. As shown in Table 4, to address persistent MPS following central aortic repair, various types of surgery were added.

Typically, peripheral perfusion is restored when central aortic repair is performed. However, as previously described, when persistent MPS develops, surgeons must consider how to assess persistent MPS and how to address it immediately following central repair. As we can assess cardiac function using transesophageal echocardiography or take peripheral pulse, assessing perfusion impairment in visible areas including leg or coronary malperfusion is straightforward. However, intraoperative assessment of non-visible organs, particularly abdominal organs, is more challenging. Delays in intervening abdominal organ malperfusion are critical and life-threatening.

Early intervention of MPS before central aortic repair has been reported with excellent outcomes. Authors described that aortic rupture that is a life-threatening situation in ATAAD repair, was not common in reality (3, 4).

Table 4. Details of patients with persistent malperfusion syndrome (n = 7)

No	Age	Sex	Perst-MPS organs	Procedures*	Outcomes	Survival
1	40	Male	LE	FF bypass	None	No
2	71	Male	Brain	---	Craniotomy	Yes
3	54	Male	Abdomen	SMA stenting	IR (POD60)	Yes
4	56	Male	Coronary/Abdomen	CABG/SMA stenting/Laparotomy	IR (POD12)	Yes
5	74	Female	Abdomen/LE	FA fenestration	IR (POD4)	No
6	48	Male	LE	FF bypass	None	Yes
7	73	Female	LE	FF bypass	None	Yes

CABG ; coronary artery bypass grafting, FA ; femoral artery, FF ; femora-femoral, IR ; intestinal resection, LE ; lower extremity, MPS ; malperfusion syndrome, Perst ; persistent, POD ; postoperative day, SMA ; superior mesenteric artery

Procedures* mean that they were performed following the central aortic repair.

Uchida, *et al*. described their results of early reperfusion strategy for ATAAD with MPS. The mortality rate from early reperfusion followed by central aortic repair in ATAAD with MPS was 3.6%, whereas that from central aortic repair without early reperfusion was 18% (4). In their 20-year experience with ATAAD repair, Yang, *et al*. concluded that relatively stable patients with ATAAD and MPS benefit from upfront endovascular reperfusion followed by delayed open repair. The 30-day operative mortality using the approach for the patients was 3.7%. Furthermore, they reported that the risk of dying from organ failure due to MPS was higher than the risk of dying from aortic rupture (3). This indicated the significance of early reperfusion strategy for relatively stable patients with ATAAD and MPS.

We had two cases of SMA stenting for persistent MPS following central aortic repair. However, both patients required intestinal resection despite blood flow restoration during stenting. Both survived and were discharged. We retrospectively analyzed that the blood supply was insufficient for all abdominal organs with SMA stenting. We had another patient who required intestinal resection due to MPS on POD 4. Initially, the patient did not show signs of visceral malperfusion ; therefore, additional procedures were not planned. However, the patient developed MPS. We believed that restoring the true lumen flow by utilizing endovascular aortic repair in the descending aorta was the priority. SMA stenting would be an additional measurement of endovascular aortic repair. Direct perfusion of SMA in patients with ATAAD and MPS was reported (4). It required laparotomy that took a while. Endovascular repair is easy to perform quickly. Measuring the superior mesenteric arterial pressure following central aortic repair would be effective considering our experience ; however, the measurement requires laparotomy as well (4).

Regarding brain malperfusion following central aortic repair, we did not perform any specific strategy, such as direct surgical fenestration of the carotid artery. Intraoperatively, differentiating reversible brain ischemia from irreversible is challenging. The utility of preoperative CT perfusion for brain malperfusion has been reported. CT perfusion can detect irreversible ischemic areas (9). In patients with preoperative brain malperfusion secondary to ATAAD, CT perfusion might be effective for assessing reversible areas immediately after central aortic repair. Based on preoperative CT findings, surgeons can decide whether to perform ATAAD repair or not.

This study had some limitations. First, this was a retrospective, single-institute study. Second, a small number of patients was included ; therefore, drawing a definitive conclusion was difficult. Third, changes in operative techniques and perioperative management during the study period might have affected the outcomes presented in this study. Despite the limitations, our study re-confirmed the negative impact of persistent MPS following central aortic repair of ATAAD on early outcomes.

In conclusion, persistent MPS following central aortic repair for ATAAD significantly contributed to poor postoperative mortality and morbidity. Moreover, persistent MPS to SMA had a severe postoperative course requiring intestinal resection. Early revascularization by utilizing SMA stenting before central repair may have spared intestinal resection, thereby leading to improved early outcomes.

CONFLICT OF INTEREST

None

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