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Management Strategies for Acute Type A Aortic Dissection Complicated By Limb Malperfusion

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ABSTRACT

Background: Acute type A aortic dissection complicated by limb malperfusion presents a risk of mortality to the patients. Debates exist regarding management, whether focused on reperfusion first or immediate repair. Here, we aimed to describe our experience with the management of acute type A aortic dissection (ATAAD) complicated by limb malperfusion.

Methods: From January 1, 2020 to December 31, 2021, 22 consecutive patients were admitted to Xiamen Cardiovascular Hospital, due to acute type A aortic dissection complicated by limb malperfusion. All perioperative variables were recorded and analyzed. Limb malperfusion was diagnosed, according to the clinical symptoms, computed tomography angiography, and laboratory test. We adopted the clinical categories of acute limb ischemia to stratify severity of limb ischemia. Surgery strategies are as follows: Reperfusion first followed by central repair, immediate central repair, and immediate central repair followed by stenting.

Results: There were 21 males and one female with an average of 53.3±11.7 years. Management strategies were as follows: immediate central repair using total arch replacement with frozen elephant trunk in 15 patients, endovascular stenting followed by central repair in four patients, and endovascular stenting after central repair in two patients. The average extracorporeal circulation time was 258.8 ± 70.5 min; the average aortic cross-clamp time was 177.9 ± 54.2 min; and the average circulatory arrest time was 45.5 ± 13.1 min. The early mortality rate was 13.6% (3/22). Two patients left the hospital voluntarily, due to cerebral infarction and bleeding. One patient underwent fasciotomy for osteofascial compartment syndrome and uneventfully was discharged. Six patients underwent continuous renal replacement therapy and hemoperfusion.

Conclusion: Central repair is safe and feasible for ATAAD complicated with limb malperfusion. For serious limb malperfusion, endovascular stenting followed by central repair is a good choice with continuous renal replacement therapy (CRRT) and hemoperfusion. Hospital mortality rate is high in cases with multiple organ malperfusion.

INTRODUCTION

Acute type A aortic dissection is a lethal catastrophe that generally requires salvage surgery to prevent rupture. However, some cases may be complicated by organ malperfusion, from cerebral, coronary, visceral, renal, or iliofemoral artery ischemia, due to a dissection flap or compression from the false lumen. Preoperative organ malperfusion has been reported to be strongly associated with early mortality and worse survival [Czerny 2015; Immer 2006; Yagdi 2010]. Extremity ischemia caused by malperfusion affects 15%-40% of patients with acute aortic dissection [Arnar 2007].

The management of acute type A aortic dissection complicated by limb ischemia remains controversial. Tear-oriented surgery traditionally has been performed to eliminate the risk of rupture. However, in some cases with severe malperfusion, the mortality from limb ischemia exceeds the mortality risk of rupture. With good control of blood pressure and heart rate, reperfusion should be considered as the initial procedure.

Reperfusion results in local and systemic cascade action of inflammatory mediators, including complement, interleukins, thromboxane and platelet-activating factor, resulting in cellular and endothelial injury, and ultimately leading to tissue edema [Blaisdell 2002]. Finally, reperfusion of the ischemic limb may cause extremity compartment syndrome, which may necessitate amputation. Additionally, the muscle ischemic time is 4 h. Professor Robert B. Rutherford stratified the severity levels of acute limb ischemia into three categories [Rutherford 1997]: I, "viable"- not immediately threatened; II, "threatened"- implies reversible ischemia in a limb that is salvageable without major amputation if arterial obstruction is relieved quickly; IIa marginally threatened and IIb immediately threatened; and III, "irreversible"- permanent nerve damage inevitable.

Reperfusion of the ischemic limb can be performed by three surgical methods: (1) central repair using a frozen elephant trunk to expand the true lumen and decompress the false lumen, thus restoring blood flow to the malperfused limb; (2) percutaneous endovascular stent for treating obliteration of the aortic true lumen; and (3) extra-anatomic bypass, such

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Table 1. Characteristics of patients with aortic dissection complicated with malperfusion

Characteristics	
Patients (n)	22
Age (years)	53.3±11.7
Sex (female/male)	1/22
Leg site	
Ischemic left leg	10
Ischemic right leg	11
Bilateral ischemic leg	1
Hypertension	18
Chronic renal failure	6
Current smokers	12
Visceral malperfusion	5
Cerebral malperfusion	3
Pericardium effusion/tamponade	4/0
Previous cardiac surgery	1
Moderate or severe aortic valve insufficiency	4
Mechanisms of the obstruction	
True lumen compressed by the false lumen	16
Thrombosis	6
Categories of clinical acute limb ischemia	
I, IIa	15
IIb	7
Interval time from the onset of symptom to hospital (h)	9.27±19.5

as femoral-femoral bypass and axillofemoral bypass, wherein a bypass graft reperfuses the occluded vessel. According to our protocol, the management strategies for aortic dissection complicated by limb ischemia are as follows: (1) percutaneous stent implantation to reperfuse the ischemic limb followed by central repair; and (2) immediate central repair and evaluation of the pulse of the occluded arteries after repair.¬¬¬

This article describes our management strategies for treating acute type A aortic dissection complicated by limb malperfusion at our cardiovascular center. Additionally, we sought to establish an algorithm for patients presenting with peripheral vascular malperfusion.

PATIENTS AND METHODS

The ethics committee of Xiamen Cardiovascular Hospital of Xiamen University approved this retrospective study, and all patients or relatives provided informed consent.

Patients diagnosed with acute type A aortic dissection between 2020 and 2021 at our center retrospectively were examined. As a cardiovascular center in Fujian province, we accepted cases of acute aortic emergency referred from areas

Figure 1. Slogan of our center: Life-saving circle with 4 hours

in the Minnan District. The perioperative characteristics of the 22 patients are presented in Table 1. (Table 1)

Although contrast increases the risk of nephropathy, prompt diagnosis is essential for appropriate management of aortic events. Therefore, patients with suspected type A acute aortic dissection underwent contrast-enhanced computed tomography angiography (CTA) and transthoracic echocardiography for assessment of intimal tear, evidence of pericardial effusion and aortic regurgitation, and blood supply to the aortic branch vessel. Limb malperfusion was defined as follows: (1) clinical signs and symptoms, such as pedal pulse deficit, pain, and cyanotic skin, and (2) evidence from CTA, showing little contrast in the distal aortic branches or thrombus-occluded iliac or femoral vessels.

Management strategies: According to our single-center protocol, the surgical strategies were as follows: (1) percutaneous stent implantation to reperfuse ischemic limb, followed by central repair; and (2) immediate central repair and evaluation of the pulse of the occluded arteries after repair¬¬, and stent implantation, if necessary. (Figure 2) The results are shown in Figure 1. (Figure 1) The decision to perform aortic dissection was made by a cardiac surgeon, vascular surgeon and anesthetist, depending on the symptoms, laboratory tests, and CT scanning analysis.

Stent implantation was considered if the limb ischemia degree belonged to IIb and III, and there was access to the true lumen. The stenting procedure previously has been described. Briefly, the vascular surgeon introduced a guidewire into the sheath, and angiography was performed to confirm the true lumen. A balloon was inserted to expand the true lumen, and a stent was inserted. After the procedure, angiography was performed again to confirm the vessel flow. Additionally, we examined the pulse of the pedal artery and the temperature of the skin to confirm reflow in the impaired artery.

All stenting procedures were performed percutaneously in the angiography suite. The common femoral artery was accessed under ultrasound guidance, and a sheath introducer

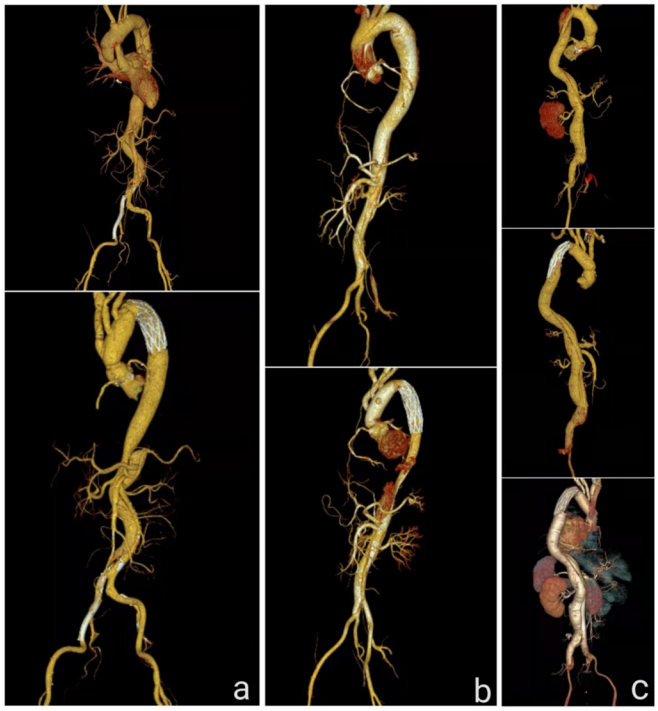

Figure 2. The algorithm for acute type A aortic dissection complicated by limb malperfusion. A) Percutaneous stent implantation followed by central repair; B) immediate central repair; C) percutaneous stent implantation after central repair

was placed. We used a coaxial guide wire-catheter technique to insert a guide wire (RF*GA35153M, RADIFOCUS®) and a VER 135°(Cordis®) catheter into the abdominal aorta. Only when the branch artery, such as lumbar artery, and visceral and spinal cord artery are visualized can we confirm that the true lumen is identified.

After evaluation by a multidisciplinary team, total arch replacement was performed using the frozen elephant trunk -Sun's procedure [Ma 2013]. Limbs were reassessed immediately after aortic repair, and revascularization procedures urgently were performed, if any uncorrected persistent limb ischemia persisted.

All patients closely were observed in the intensive care unit, particularly for kidney and liver function. The biomarker creatine kinase (ck), myohemoglobin (myo), creatinine (crea), and mediators play pivotal role in ischemia-reperfusion damage. If osteofascial compartment syndrome is highly suspected, early fasciotomy is recommended to actively relieve pressure.

RESULTS

The main preoperative, intraoperative, and postoperative data for the global population are summarized in Tables 1 and 2. (Table 2)

The early mortality rate was 13.6%. Seventeen patients were diagnosed with acute type A aortic dissection complicated by limb malperfusion in our study; of those, five patients had visceral malperfusion, whereas three patients had cerebral malperfusion. All the patients showed hypertension and uncontrolled blood pressure. The mean age of the patients was 53.3 years, with a predominance of men (95.4%). Four patients had pericardial effusion, and none had tamponade. In total, immediate central repair procedure was performed in 68.1% of the cases; four patients underwent restoration of blood flow by stenting followed by central repair; and two patients immediately were sent to the operative room for central repair, after which we assessed the pulse of the artery and restored the flow supply by stenting. Most patients underwent aortic valve plasty, and one patient underwent Wheat's procedure. The mean cross-clamp time was 177.9 minutes; 14 patients underwent unilateral antegrade cerebral perfusion, and six patients had bilateral antegrade cerebral perfusion based on cerebral oxygen saturation. Six patients, who were highly suspected to show hyperinflammation, received continuous renal replacement therapy (CRRT) combined with HA380 (a hemoperfusion device in China) and uneventfully recovered. One patient, who underwent the Bentall procedure and hemi-arch replacement due to DeBakey II aortic dissection, had previously undergone immediate total arch replacement followed by remedial stent implantation. However, he required early fasciotomy because of osteofascial compartment syndrome. Three patients died after central repair, with continuously elevated levels of lactate and unstable hemodynamics. One patient died after stent implantation at the proximal iliofemoral site, which revealed that more proximal iliofemoral malperfusion was correlated with high mortality rates than distal malperfusion [Salameh 2016]. Two patients who showed complications of multiple

Table 2. Intraoperative and postoperative outcomes

Characteristics (*N* = 22)	
CPB time (min)	258.8±70.5
Clamp time (min)	177.9±54.2
Circulatory arrest time (min)	45.5±13.1
Femoral cannulation	
Right	13
Left	5
CRRT + Hemoperfusion	6
ICU stay (days)	10.03±6.34
Central repair	15
Reperfusion followed by central repair	4
Central repair followed by reperfusion	2
Fasciotomy	1
Tracheotomy	1
Amputation	0
Outcome	
In-hospital mortality	13.6%

organ malperfusion (cerebral, visceral, and limb) were discharged on request. No patients required amputation because of ischemic necrosis. Examples of patients with acute type A aortic dissection complicated by limb malperfusion, who were treated with different management strategies (immediate central repair or stent implantation followed by central repair), are shown in Figure 1.

At follow up, all the surviving patients showed good outcomes, including those who initially underwent stenting first followed by central repair, and one patient with fasciotomy still is undergoing rehabilitation training.

DISCUSSION

Pericardial effusion, aortic regurgitation, a ruptured flap, and impaired perfusion are critical problems that urgently should be addressed. Most studies have reported poor outcomes of aortic dissection presenting with organ malperfusion [Czerny 2015; Yagdi 2010; Norton 2019]. However, although different studies have reported their own experiences and yielded multiple insights into this issue, the optimal management for acute type A aortic dissection with concomitant malperfusion has not yet been established to be date.

Acute type A aortic dissection with extremity ischemia presents an interesting clinical problem, regarding whether immediate central repair or limb reperfusion should take precedence. Central aortic repair, prevention of rupture, and direct revascularization of the affected arteries restores blood flow into the true lumen by entry resection, after which a frozen elephant trunk can be used to expand the false lumen and solve malperfusion. In a retrospective study of 335 patients with acute type A aortic dissection with or without coexisting limb ischemia, Charlton-Ouw et al. adopted a strategy of immediate central repair followed by intraoperative or postoperative assessment to correct any limb ischemia. Malperfusion was resolved in 78.4% of these patients through expeditious central repair, and excellent results were achieved in the remaining patients after timely assessment and intervention. Girardi et al. concluded that vascular malperfusion in the setting of acute type A dissection should be treated with immediate aortic reconstruction, and timely and active early postoperative intervention is critical [Girardi 2004]. Orihashi et al. claimed that to solve the practical problems associated with the treatment of acute type A dissection with organ ischemia, real-time information on ischemia organs is very crucial in detecting changes, which is consistent with the beliefs of Girardi et al. [Orihashi 2011]. In contrast, in a study of 1026 patients, Kawahito et al. concluded that the effects of central repair were limited to severe or complex malperfusion, and emergency reperfusion of affected organs followed by central repair is recommended [Kawahito 2019]. Fujita et al. reported stenting for acute aortic dissection with malperfusion as a bridge therapy [Fujita 2009]. Several large-scale studies have emphasized the importance of early reperfusion first, followed by central repair, because in certain cases of severe malperfusion, the mortality from organ failure exceeds the mortality risk associated with rupture [Kawahito 2019; Goldberg 2017; Patel 2008; Yang 2018; Uchida 2018; Berretta 2018; Ahmed 2021; Jaffar-Karballai 2021; Rteil 2019].

As mentioned above, our algorithm was based on physical examination, imaging examinations, laboratory testing, categorization of acute limb ischemia, and evaluation by the cardiac surgeon, interventional cardiologist, and anesthetist. We performed Sun's procedure-total arch replacement, using a tetrafurcated graft with stented elephant trunk implantation. Our results showed that most patients achieved good outcomes with central repair.

For the "Southwest of Min Province" district, we have popularized our slogan "Life-saving Circle with 4 hours, which means "fast diagnosis and fast transport" that shorten the time from symptom to surgery, as shown in Figure 1. Patients with suspected aortic dissection in this area can seek first aid at our center because of the importance of prompt treatment in aortic dissection, particularly for aortic dissection complicated by malperfusion. It's a tough truth that the internet facilitates the process: Once aortic angiography is performed and uploaded, we can see the image online, and immediate operation of the patient is started, if it is with intention to perform emergency surgery. Physiological and anatomical studies have shown that irreversible muscle cell damage begins after 3 h of ischemia and is nearly complete at 6 h [Blaisdell 2002]. Transportation and confirmation of diagnosis is a time-consuming process; hence the mean time to restore blood flow in ischemic vessel can be as high as 14 h, which exceeds the muscle cell damage time limit and poses a great challenge to treatment.

The inflammatory responses following limb reperfusion syndrome, which present as hyperinflammation, can result in multiple-organ failure and death [Blaisdell 2002]. Common therapeutic approaches, such as fluid infusion, can decrease the inflammatory response; however, it can further aggravate tissue damage and lead to high mortality [Napp 2019]. Extracorporeal hemoperfusion increasingly is being being used for the management of severe inflammation. A reduction in the levels of inflammatory mediators can result in good clinical outcomes [Supady 2021]. In 2010, Totsugawa et al. reported successful intraoperative endotoxin adsorption for visceral malperfusion complicating acute type A aortic dissection. Totsugawa thought that mesenteric reperfusion could be exacerbated by systemic metabolic abnormalities and that hemoperfusion enables removal of circulating endotoxins before initiation of the inflammatory cascade [Totsugawa 2010]. We recommend routine adsorption combined with continuous renal replacement therapy to remove inflammatory mediators and myoglobin, which will have beneficial therapeutic effects.

Acute type A aortic dissection with organ malperfusion is associated with higher postoperative mortality and morbidity rates [Yagdi 2010]. The GERAADA study revealed that the influence of the number of organs involved on the outcome substantially differs. Organ malperfusion involves cerebral and simultaneous visceral or limb malperfusion, which is challenging for surgeons. In our study, three patients died because of visceral and limb malperfusion manifesting as unstable hemodynamics. Two patients with multiple organ

malperfusion were discharged on the basis of their relatives' accord due to cerebral events, including bleeding and infarction.

This study had several limitations that were inherent to its retrospective design. First, because of the small sample size and limited clinical observation in our study, well-designed prospective clinical trials are required to confirm the efficacy of our algorithm. Second, we recognize that acute type A aortic dissection always involves dynamic obstruction by the dissection flap and static obstruction by the thrombosis, or both. Our protocol primarily was based on the clinical categorization of acute limb ischemia, physical examination and laboratory tests, regardless of the morphological state. We firmly believe that a morphological study of the complex extent of the aortic dissection process is crucial for treatment planning, and that the procedure we presented can achieve good results.

CONCLUSION

Central repair is safe and feasible for ATAAD complicated with limb malperfusion. For serious limb malperfusion, endovascular stenting followed by central repair is a good choice with continuous renal replacement therapy (CRRT) and hemoperfusion. Hospital mortality rates are high in cases with multiple organ malperfusion.

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