Mesenteric Malperfusion in Acute Aortic Dissection: Challenges and Frontiers

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Malperfusion syndrome results from end-organ ischemia in the setting of an aortic dissection. Malperfusion syndrome can affect any vascular bed with mesenteric malperfusion (MMP) being the most challenging associated with a 3- to 4-fold increase in mortality in both acute type A and B aortic dissections. The incidence MMP is between 66% and 100% in different literature. The insidious onset of MMP, among the different ischemic end-organ complications, makes it a challenge for diagnosis and management. The management of MMP is still a polemic, as to whether initially the aortic repair to be done or to restore the mesenteric perfusion. The approach for acute type A aortic dissection with MMP includes initial central repair, endovascular repair followed by central repair or simultaneous repair. Endovascular remains the main mode of treatment for acute type B aortic dissection with MMP. With respect to the variation in presentation and degree of ischemia, a patient-specific approach is required for treating this condition.

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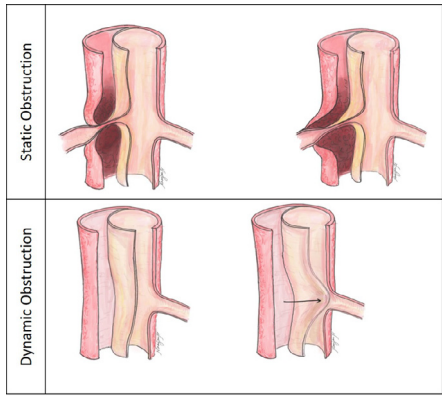

The mechanism to depict dynamic and static obstruction.

Central Message

Malperfusion syndrome resulting from end-organ ischemia in the setting of aortic dissection can be lethal. Mesentric malperfusion increases the mortality by 3 to 4 folds. The insidious onset and varying clinical presentation makes the diagnosis and management difficult. There is no clear data to suggest the exact mode of treatment. Th approach to Acute Type A aortic dissection include central aortic repair, endovascular repair followed by central repair or simultaneous repair. Endovascular remains the main mode of treatment for acute type B aortic dissection. A patient specific approach is required in treatment for this condition.

INTRODUCTION

Malperfusion syndrome results from end-organ ischemia in the setting of an aortic dissection. Malperfusion syndrome can affect any vascular bed with mesenteric malperfusion (MMP) being the most challenging associated with a 3- to 4-fold increase in mortality in both acute type A and B aortic dissections.[1–4] Complete obstruction might present with apparent symptoms, but it is equally important to identify subtotal or partial vessel occlusion which may produce intermittent symptoms of variable intensity.

INCIDENCE

In the initial analysis of the International Registry of acute Aortic Dissection (IRAD) which consisted of 12 international referral centers and 464 patients of type A aortic dissection (TAAD), the second most common cause of death was mesenteric ischemia, next only to rupture of aorta.[5] In a recent analysis of 3099 consecutive patients with TAAD from the IRAD, the incidence of MMP was found to be 3.8%. The in-hospital mortality was 63.2% with MMP as against 23.8% in patients without mesenteric malperfusion.[1] In 502 patients with acute TAAD who underwent immediate surgery, 12 had MMP. The in-hospital mortality was 15% without malperfusion and 70% for patients with MMP.[6] Yagdi et al in their series of 118 patients who underwent immediate surgery with acute TAAD presented a mortality rate of 100% with MMP.[7]

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SIGNS AND SYMPTOMS

The symptoms correspond to the degree of obstruction and vascular distribution which is involved. Further, an incomplete or subtotal vessel occlusion may produce intermittent symptoms of variable intensity. Furthermore, symptoms can occur over the course of days or weeks, complicating the diagnosis and management. Abdominal pain is the most common symptom of MMP. Careful examination reveals only tenderness, and bowel sounds are often misleading. Guarding and/or rebound tenderness might indicate a necrotic intestine with peritonitis needing a bowel resection. The symptoms are elusive, and the sequelae of vascular obstruction may become apparent only after the aortic repair.

MECHANISMS OF MALPERFUSION

The relationship between the true lumen and the mobile intimo-medial septum is complex. The pressure difference between both lumens will allow the mobile septum to bulge and cause static obliteration of branch vessel ostia (Fig. 1). This will subsequently lead to thrombosis of the branch vessel impairing the perfusion.[29] Dynamic dissection will have protrusion into the ostium of a branch vessel, which is the most common cause of malperfusion syndrome (80%) and results in variable symptoms given the dynamic nature of the occlusion.[30]

CHALLENGES IN MMP

The insidious onset of MMP, among the different ischemic end-organ complications, makes it a challenge for diagnosis and management. The difficulty in making a definitive diagnosis is responsible for delayed referral from primary care physicians to tertiary hospitals. Interestingly, 40% of the patients with MMP do not have any abdominal pain and 20% of the patients with abdominal pain did not have MMP.[8,9] On analyzing the signs and symptoms of different end-organ ischemia, the signs and symptoms of MMP are very vague as compared to stroke, anuria, and loss of pulses in the limbs. Not all centers across the globe have the experts or facility to determine whether the malperfusion is due to dynamic or static obstruction.

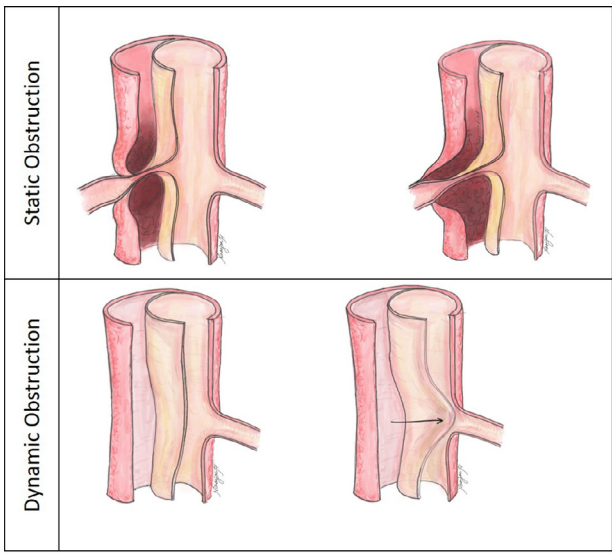

Figure 1. The mechanism to depict dynamic and static obstruction. Dynamic obstruction is more common than static obstruction.

The management of MMP is still a polemic, as to whether initially the aortic repair to be done or to restore the mesenteric perfusion. Organ malperfusion can develop at any of the following stages: (1) at the onset of dissection, (2) during false lumen thrombosis, occluding the branch vessel (static mechanism), (3) at initiation of cardiopulmonary bypass, (4) after aortic cross clamp, and (5) after the aortic repair.[10] There are reports of visceral ischemia occurring 8 days after central aortic repair.[11] Malperfusion syndrome itself perpetuates an inflammatory cascade emanating from end-organ ischemia which may significantly impair operative success.[12] Further, it is a well-known fact that intestinal ischemia leads to disruption of the gut mucosal barrier releasing the endotoxins into the portal system. Hepatic macrophages produce tumor necrosis factor, which is a critical mediator in reperfusion injury.[13] Further, this reperfusion injury is easily exasperated by the highly invasive aortic surgery in the setting of aortic dissection. Hence, it is no exaggeration to say that even after complete revascularization and central aortic repair we do not have a control on the reperfusion injury, which is responsible for the high mortality. Most of the patients die within the first 24 hours despite the fact that adequate mesenteric perfusion is established.

MANAGEMENT IN TAAD

The key issues associated with the management of this condition include (1) to determine which lesion is to be treated first (aorta vs visceral organs), (2) the manner in which the compromised arteries is to be perfused, and (3) combating the reperfusion injury (Table 1).

Immediate Central Aortic Repair Approach

Conventionally, surgical doctrines have emphasized on the emergent surgery to restore blood to the true lumen — identifying the primary tear and replacing the ascending aorta with or without aortic arch.[14] Even with diligent surgical repair of ascending aorta in TAAD, branch vessel ischemia persists in 25% of the patients.[15,16] The reasons include (1) distal re-entry tears, (2) persistence of false lumen flow, and (3) branch vessel involvement. Three different groups retrospectively analyzed TAAD patients who underwent immediate central aortic repair.[6,7,17] The mortality rate in patients with MMP in these studies was 70–100%. The authors concluded that immediate central aortic repair in patients with MMP had dismal prognosis, and hence these patients should be managed with percutaneous interventional procedures followed by delayed surgery.

Endovascular First With Delayed Aortic Repair

With the advent of endovascular techniques, many centers have adopted a strategy of central aortic operation after

Table 1. Management of Mesenteric Malperfusion

Yagdi et al, Turkey, 2006[7]	• 118 patients with acute TAAD were immediately operated • 100% mortality in patients with MMP	• New strategies to be investigated — Surgical delay with interventional procedures to reduce mortality in MMP
Girdauskas et al, Germany, 2008[17]	• 276 patients underwent surgery for acute type A dissection • 75% mortality in patients with MMP	• Percutaneous interventional reperfusion and a delayed surgical strategy in clinically apparent MMP • Immediate proximal aortic repair in malperfusion syndromes (except coma/MMP)
Pacini et al, Italy, 2012[6]	• 502 patients underwent immediate surgery • 70% mortality in patients with MMP	• Immediate proximal aortic repair may be suboptimal • Alternative management strategies should be considered
	Endovascular first with delayed aortic repair	
Patel et al, USA, 2008[18]	• 70 of the 196 patients with ischemic end-organ dysfunction underwent percutaneous fenestration or branch vessel stenting as an initial procedure • 33% died before attempting operative repair • 8.5% early mortality rate in patients that reached operative treatment	• Patients who survive the initial malperfusion and undergo repair have a similar operative and late survival when compared to those patients presenting with uncomplicated dissection
Yang, USA, 2018[31]	• 135 of 597 patients were treated upfront endovascular reperfusion followed by delayed open repair (OR) • 96% of patients either survived to discharge or underwent delayed OR (69.5%) or died from end-organ failure (26.5%) before delayed OR.	• Relatively stable (no rupture, no tamponade) patients with MPS benefit from a staged approach
	Simultaneous approach	
Okada et al, Japan, 2007[20]	• Case report: Laparotomy — Selective SMA perfusion — Central correction — Saphenous vein bypass grafting to the SMA	• Emergent direct inspection of the bowel concurrently with proximal aortic repair. If the intestines are moribund, a temporary perfusion is effective
Totsugawa et al, Japan, 2010[23]	• Case report: Laparotomy — Saphenous vein graft from common iliac to SMA — Central correction — Endotoxin absorption using column of polymyxin B-immobilized fiber	• Intraoperative endotoxin adsorption could be a new therapeutic option that can lower the high mortality of visceral malperfusion complicating aortic dissection helping to combat reperfusion injury
Ferlan et al, Italy, 2011[22]	• Case report: Abdominal symptoms — Central correction — Laparoscopic — Laparotomy — Bowel resection	• Laparoscopic exploration is indicated every time the integrity of the abdominal viscera has to be verified to avoid delay in its treatment
Kato et al, Japan, 2014[21]	• Case report: CPB — Laparotomy with temporary mesenteric perfusion — central correction — SMA plasty with/without thrombectomy	• Simultaneous correction of MMP and dissection with temporary perfusion of the mesentery and SMA plasty
	Mechanism-specific approach	
Shiiya et al, Japan, 2007[32]	• 38 of 135 (28%) patients with acute dissection presented with organ malperfusion • 6 of 38 had celiac and superior mesenteric malperfusion	• Central aortic operation or fenestration is effective for aortic-type malperfusion, whereas the branch-type may require stenting or bypass grafting

(*continued*)

Concept of hybrid OR		
Tsagakis et al, Germany, 2013[24]	• 124 patients with acute type A dissections were treated in a hybrid operating room • Visceral malperfusion syndromes detected in 23% patients	• The hybrid OR concept enables the exact diagnosis of coronary status and downstream malperfusion sites and influences the design of surgical and/or endovascular treatment, without time delay and at negligible risk to the patient

percutaneous end-organ blood flow restoration in patients presenting with significant mesenteric malperfusion. The Michigan group presented the long-term follow-up of patients who initially had a percutaneous intervention to restore end-organ perfusion and delayed operative repair after resolution of the malperfusion syndrome.[18] In the 47 patients who survived to delayed central aortic repair, operative therapy was delayed by a median of 4 days, and mortality (8.5%) was similar to that of patients presenting without malperfusion. The same group has recently published their 20 years' experience with this strategy.[31] From 1996 to 2017, among 597 patients who presented with acute TAAD, 135 patients with malperfusion syndrome were treated with upfront endovascular reperfusion (fenestration/stenting) followed by delayed open repair. Ninety-six percent of patients either survived to discharge or underwent delayed open repair (69.5%) or died from end-organ failure (26.5%) before delayed open repair. This suggested that even after the branch arterial obstruction was resolved with fenestration/stenting, the risk (hazard ratio) of dying from end-organ failure was ≈7 times higher than the risk of aortic rupture.

Differentiation of patients with malperfusion (ischemic but not necrotic) and malperfusion syndrome (necrotic bowel) is of paramount importance. Malperfusion with dynamic obstruction that is medically corrected with no end-organ damage or patients with subclinical malperfusion is not an indication for delayed operative repair. Only patients with concomitant relative hemodynamic stability (no tamponade, no rupture) and MMP can be approached by this method.[31]

Endovascular treatment includes stenting of the superior mesenteric artery (SMA) to restore the blood flow, fenestration of the intimal flap in the aorta for depressurizing the false lumen and guiding the blood to the branch vessels, placing an uncovered stent in the descending thoracic aorta

Simultaneous Approach

Few authors have supported the concept of simultaneous approach. If the intestine is necrotic, an urgent laparotomy accompanied with intestinal resection will be required. Central aortic repair is undertaken later. During cardiopulmonary bypass, the mesenteric artery was temporarily perfused using a side graft or via a separate cannula through the ostium. Later, a bypass graft from the common iliac artery to the SMA or SMA plasty is performed.[19–21] Immediately after the completion of the central repair and when the integrity of the abdominal viscera is suspected, few authors have suggested laparoscopic exploration to avoid delay in treatment.[22] To combat reperfusion injury, Totsugawa et al have used a column of polymyxin B-immobilized fiber (PMX-DHP) during cardiopulmonary bypass facilitating early removal of endotoxins.[23] It is also advised to delay definitive abdominal closure in these situations to provide an opportunity for a second look to ensure the remaining bowel is viable.

Mechanism-Specific Approach

Shiiya and et al[32] proposed a mechanism-specific approach in patients with vital organ malperfusion, which included central aortic surgery for aortic-type malperfusion and percutaneous interventions for branch-type malperfusion (Fig. 2). Further, if the aortic lumen is compromised by the pressure in the false lumen, a balloon fenestration of the intimal flap with or without aortic stent is performed. If the true lumen is compressed by the false lumen within the branch vessel, the vessel is stented or bypass grafting is performed.

Concept of Hybrid Operating Room

The classical concept to operate quickly in TAAD to reinstate peripheral true lumen perfusion and addressing branch vessel

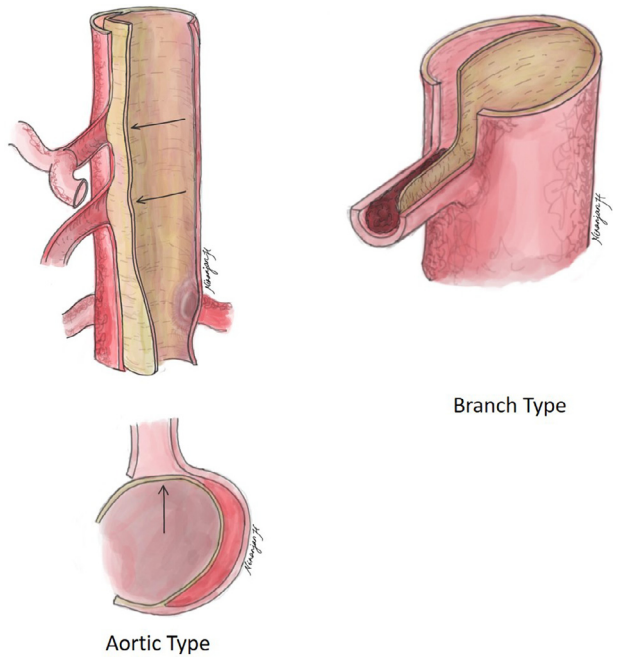

Figure 2. Aortic type is due the pressure in the true lumen, while the branch type is occlusion at the level of the branch vessel.

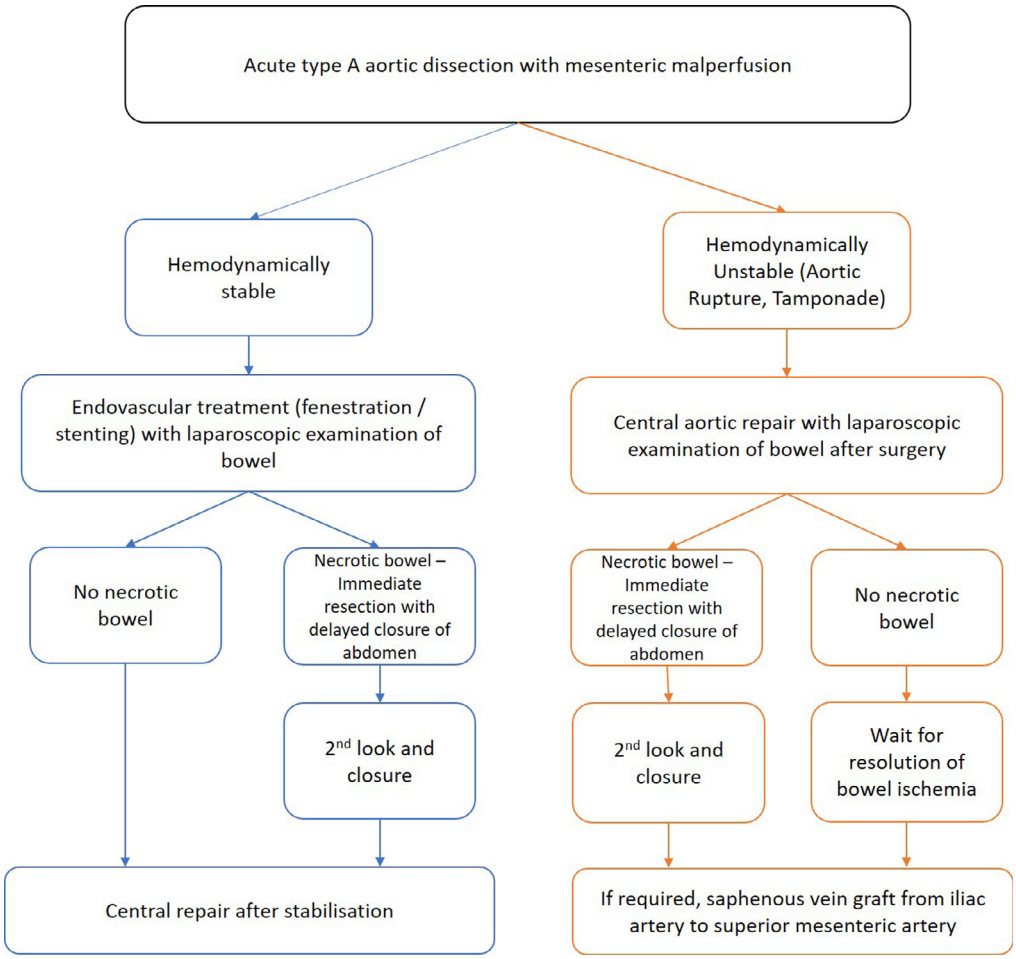

Figure 3. "ICAD" protocol for patients with TAAD mesenteric malperfusion.

ischemia can be accomplished using hybrid OR.[24] The potential malperfusion sites are studied for strategic planning. In case of severe static obstruction, endovascular revascularization is performed prior to central repair. In cases with dynamic malperfusion, the decision is based on hemodynamic stability of the patient. In cases of tamponade, following a sternotomy a controlled drainage is carried out. In 124 patients with acute TAAD, MMP was detected in 23% of patients. In-hospital mortality with MMP was 25% after preoperative endovascular repair as against 75% without preoperative endovascular repair.

The Institute of Cardiac and Aortic Disorders has adopted a paradigm of care for patients with TAAD with mesenteric malperfusion (Fig. 3).

MANAGEMENT IN TYPE B AORTIC DISSECTION

Ever since the inception of the thoracic endovascular aortic repair (TEVAR), it has emerged as a viable treatment in the management of type B aortic dissection.

Studies had demonstrated superior outcome with TEVAR as compared to open surgical repair.[25,26] Identification of true and false lumen is of paramount importance in type B aortic dissection. Intravascular ultrasound is a preferred method of distinguishing true and false lumens and delineating the relationship between the intimal flap and the ostia of branch vessel arteries.[27] Techniques to alleviate MAP include central aortic fenestration and/or branch artery stenting. In the setting of static obstruction, a self-expanding bare stent or a balloon expandable stent graft.[28] Often endovascular fenestration is the first step in the management of dynamic obstruction. Even after a successful endovascular procedure, ischemia can progress to necrosis. In such situations, surgical intervention including resection of the devitalized intestine is necessary.

CONCLUSION

It is not an exaggeration to say that not every untreated TAAD will rupture, but every untreated MMP will result in death. It would be easier to advocate for either an aortic centric or peripheral centric approach. But with respect to the variation in presentation and degree of ischemia, a patient-specific approach is required. This mandates shift in the management of such patients to the concept of hybrid operating room.

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