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CURRENT TOPICS REVIEW ARTICLE

Acute medical management of aortic dissection

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Abstract
Acute aortic dissection is a life-threatening disease. Current therapeutic guidelines recommend medical therapy with aggressive blood pressure lowering for patients with acute aortic dissection, when they are not indicated for emergency surgery. In particular, patients with aortic dissection without ascending aorta involvement (Stanford type B) are treated medically, unless they have fatal complications. Patients with type B aortic dissection who have critical complications have higher early mortality than that in patients without complications. However, recent advances in thoracic endovascular aortic repair can improve the clinical outcomes in such patients. Accordingly, current guidelines recommend thoracic endovascular aortic repair for patients with complicated type B aortic dissection. However, patients with visceral ischemia still have a poor prognosis, even when they are treated with thoracic endovascular aortic repair; an early diagnosis and intervention is crucial to prevent mortality. Understanding the pathophysiological anatomy that can induce organ malperfusion might be important for an early diagnosis and intervention. This review summarizes the current state of acute medical management in patients with acute aortic dissection, based on current evidence and expert consensus, focusing on patients with type B aortic dissection.

Keywords Acute aortic dissection · Management · Medical therapy · Surgery · Thoracic endovascular aortic repair

Introduction

Acute aortic dissection (AD) is a life-threatening disease, and its prompt and precise diagnosis is essential for proper management. Current therapeutic guidelines for AD recommend that patients with acute AD with ascending aorta involvement, known as Stanford type A, should be treated surgically [1–3]. In contrast, patients with AD without ascending aorta involvement (Stanford type B) are treated medically, unless they have fatal complications. Most uncomplicated patients with type B AD (TBAD) have a favorable short-term prognosis with medical therapy. Although medical management can be initially applied to selected patients with type A AD [4], it is mainly indicated for patients with TBAD. Thus, in this review, we focused on TBAD and summarized the present recommended acute medical management for patients with TBAD, based on the current evidence and expert consensus [5, 6].

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Medical management for acute AD

In acute medical treatment, the reduction of hemodynamic stress to the aortic wall and avoidance of fatal complications are essential. In particular, blood pressure lowering is crucially important to avoid both acute adverse events and chronic aortic dilatation. Intravenous calcium-channel blockers, nitroglycerin, and beta-blocking agents should be started in the super-acute phase to lower the systolic blood pressure to 100–120 mmHg. Beta-blocking agents are highly recommended to reduce the heart rate and dP/dt. However, since excessive lowering of the blood pressure and heart rate may change the hemodynamics and possibly worsen organ perfusion, conditions (e.g. symptoms, vital signs, and urine volume) should be monitored closely.

During the chronic phase, current guidelines recommend that blood pressure should be controlled below 140/90 mmHg (US and European guidelines) [1, 3] with lifestyle changes and an adequate use of antihypertensive drugs. However, limited evidence is available regarding which drugs are beneficial for patients with chronic AD. Previous studies have suggested that beta-blocker therapy improves clinical outcomes in patients with TBAD [7, 8]. However, observational data from the International Registry

of Aortic Dissection (IRAD) suggest that beta-blocker use has no significant clinical benefit, whereas calcium-channel blocker use is associated with improved outcomes in patients with TBAD [9, 10]. Although several studies failed to demonstrate the efficacy of beta-blocker therapy, one observational study revealed that tight heart rate control improves clinical outcomes in patients with TBAD [11]. Thus, the importance of heart rate control, rather than beta-blocker use, is suggested. Further studies are required to clarify the optimal medical therapy in patients with acute and chronic TBAD.

Treatment for patients with complicated TBAD

Several previous studies have reported the natural history of TBAD [12–15]. Furthermore, IRAD investigators reported the in-hospital mortality rates of patients with TBAD who were treated medically (9.6%), surgically (32.1%), or with endovascular therapy (6.5%) [12]. A considerable number of patients with TBAD suffer from fatal complications, including aortic rupture, persistent or recurrent pain, uncontrolled hypertension despite full medication, early aortic expansion and malperfusion in cerebral, spinal, visceral, renal, or peripheral vascular territories. These complications are considered to be a major cause of early mortality in patients with TBAD. Afifi et al. reported that the early mortality rate of patients with complicated TBAD is significantly higher than that of patients with uncomplicated TBAD [15]. Thoracic endovascular aortic repair (TEVAR) is considered effective for the treatment of fatal complications. Several studies have confirmed an improvement in clinical outcomes with TEVAR in patients with complicated TBAD [16–20]. Furthermore, several recent meta-analyses have reported favorable short- and mid-term results in patients with complicated TBAD who were treated by TEVAR [21–23]. Given these results, current guidelines recommend TEVAR for patients with TBAD and complications that are Class I indications [1–3]. However, patients complicated with visceral malperfusion have a poorer prognosis than that in patients with other complications [24, 25]. Patients with visceral ischemia have been reported to have a high risk of mortality, with a similar mortality rate after surgical and endovascular management [25]. Thus, an early diagnosis and intervention for visceral ischemia seem to be crucial.

Pathophysiology of complications in acute AD

It is crucial to understand the association between the pathological anatomy caused by AD and fatal complications. Additionally, it is clinically important to recognize patients at high-risk for fatal complications. Below, we review the pathophysiology associated with visceral ischemia and acute respiratory failure, which are common complications in acute AD.

Visceral ischemia

Visceral ischemia, a type of branch-vessel obstruction, is considered to be one of the most serious and critical complications, and is generally caused by obstruction of the superior mesenteric artery (SMA). Williams et al. reported that there are two types of branch-vessel obstruction, static and dynamic obstruction [26]. In static obstruction, the dissection flap enters the branch-vessel origin. In dynamic obstruction, the dissection flap spares the branch-vessel wall, but is compressed across the branch-vessel origin, covering it like a curtain. A mixed type of static and dynamic obstruction also exists (Fig. 1). Understanding the type of

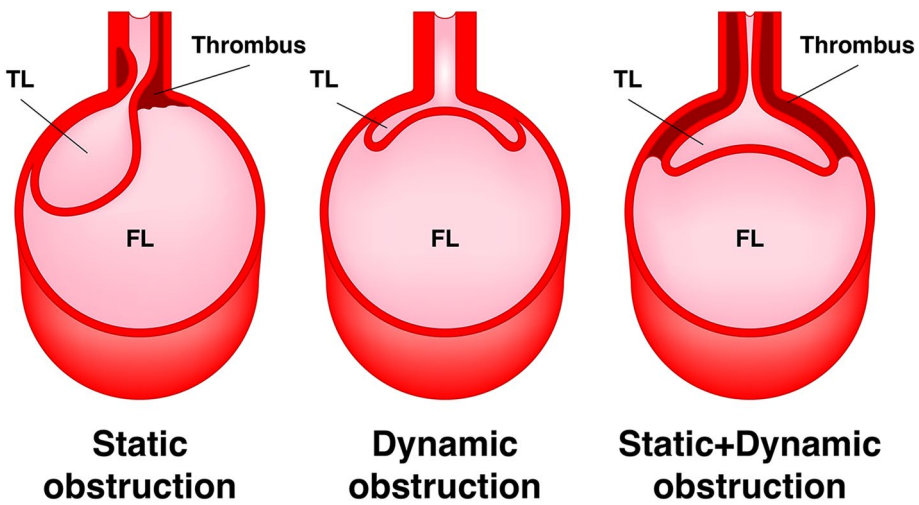

Fig. 1 Types of branch-vessel obstruction in patients with aortic dissection. Left panel: in static obstruction, the dissection flap intersects or enters the branch-vessel origin. Middle panel: in dynamic obstruction, the dissection flap spares the branch-vessel wall, but is compressed to the branch-vessel origin. Right panel: mixed type of static and dynamic obstruction. TL, true lumen; FL, false lumen. Adapted with permission from ref. [26]. Copyright 1997 by The Radiological Society of North America

branch obstruction is essential in managing branch ischemia, especially for visceral ischemia. If a patient has a dynamic obstruction, local intervention to a side branch is ineffective, and central repair, including entry closure with TEVAR, or open surgery is required. In addition, they proposed that benign and ischemic configurations of the dissection flap might exist (Fig. 2) [26]. Although it has not been validated in other studies, identification of an ischemic configuration is very useful in clinical settings. The ischemic configuration has a true lumen that resembles a concave lens at some level between the branch arteries and entry tear, which indicates that the true lumen was compressed by false lumen expansion. The benign configuration has a true lumen that resembles a convex lens, appears hemodynamically adequate, and is between the branch arteries and entry tear of the dissection. A better understanding of both ischemic and benign configurations of the dissection flap may be helpful in predicting and managing visceral ischemia. However, since the dissection flap is moving dynamically during the super-acute phase, it may be difficult to determine whether or not a patient has the ischemic configuration by snap-shot images with multidetector computed tomography in some cases. In such cases, transesophageal or abdominal echocardiography might aid in elucidating the anatomy. Figure 3 shows the representative CT images of patients with visceral ischemia.

Acute respiratory failure

Acute AD is frequently accompanied by acute respiratory failure (ARF), which often prolongs the hospital-stay and could be fatal, if patients are complicated with acute respiratory distress and acute lung injury. It has been suggested that ARF is associated with the activation of systemic inflammatory reactions in acute AD. Kurabayashi et al. reported that the impairment of oxygenation in patients with acute AD is closely correlated with the amount of aortic injury (i.e. the extent of the AD), which might be mediated by

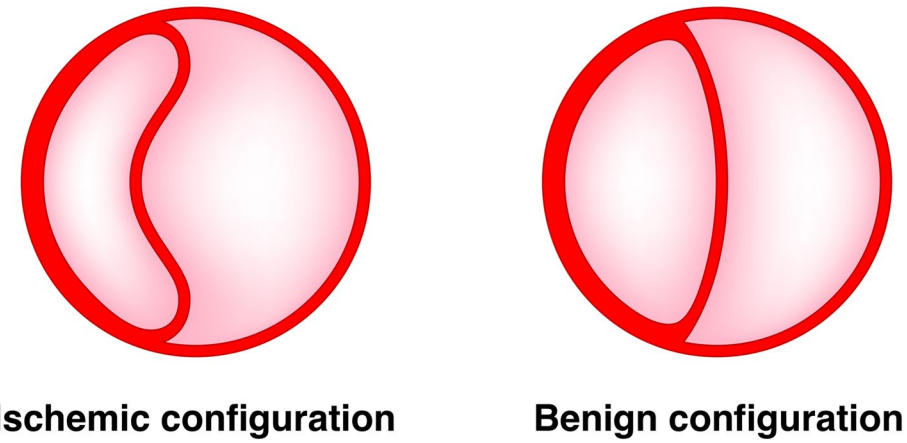

Fig. 2 Two types of the predominant configuration of the dissecting flap. Left panel: the ischemic configuration of the dissection flap, in which the true lumen resembles a concave lens. Right panel: the benign configuration of the dissection flap, in which the true lumen resembles a convex lens. Adapted with permission from ref. [26]. Copyright 1997 by The Radiological Society of North America

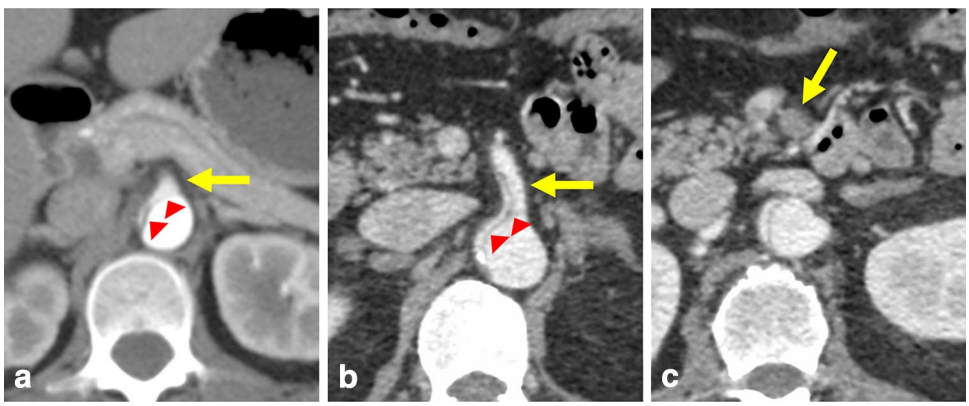

Fig. 3 Obstruction of the superior mesenteric artery in patients with visceral ischemia. **a** A 46-year-old woman with TBAD complicated with visceral ischemia. The dissection flap (red arrow heads) is compressed by the false lumen, resulting in a near occlusion of the superior mesenteric artery (yellow arrow). **b** A 50-year-old man with TBAD complicated with visceral ischemia. The dissection flap (red arrow heads) intersects the branch-vessel origin, resulting in the poor perfusion of the superior mesenteric artery (yellow arrow). **c** Caudal slice of the same patient as in **b**. The distal part of the superior mesenteric artery (yellow arrow) was occluded

the magnitude of the systemic inflammatory reaction to the aortic injury [27]. Suppression of the systemic inflammatory reaction and local reduction in the amount of aortic injury might be future targets for the prevention of ARF in acute AD.

Currently, the prevention of ARF is difficult in the acute medical management of patients with AD. Early mobilization is thought to be effective in preventing secondary pulmonary atelectasis. Furthermore, the avoidance of fluid overload might be preventive, as this can be harmful by inducing pulmonary edema, especially in patients with left ventricular dysfunction. However, no oral or intravenous drug has been proven as effective for prevention or treatment of ARF [1–3]. Recently, noninvasive positive pressure ventilation has become frequently used in patients with ARF; this is also helpful in patients with AD complicated by ARF, allowing the avoidance of intubation and mechanical ventilation.

Can biomarkers predict adverse aortic events?

Several biomarkers have been reported as predictive for adverse aortic events. First, a fibrinogen degradation product (FDP) level ≥ 20 μg/mL at admission is associated with aortic growth [28]. However, the FDP level might not be widely available because of the difficulty in obtaining measurements in emergency settings. On the other hand, several studies have shown that the peak CRP level is a strong predictor of adverse aortic events in patients with TBAD [29, 30]. The serum CRP level is widely available and may be a less-invasive marker for identifying high-risk patients. However, because CRP is a nonspecific marker, its usefulness might be limited; the CRP level reflects, not only the extent of the AD, but also concomitant inflammatory diseases, including pneumonia and urinary tract infections. Finally, recent studies revealed that D-dimer, which has been previously reported to be useful in diagnosing AD, may also have a substantial effect on prognostic pathways [31–33]. Although these biomarkers are considered to be prognostic factors, it remains unclear whether they can predict fatal complications in the acute phase.

Conclusions

Optimal medical therapy with aggressive blood pressure lowering is essential for patients with acute AD, when they are not indicated for emergency surgery. During the clinical course, TEVAR should be recommended as the first line therapy when patients have fatal complications. Although TEVAR is beneficial for complicated patients, the prognosis of patients complicated with visceral malperfusion is poorer than that for patients with other complications. Therefore, an early diagnosis and intervention is crucial for patients complicated with visceral ischemia. Furthermore, an understanding of the pathophysiological anatomy associated with the induction of organ malperfusion is important to avoid serious complications.

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Compliance with ethical standards

Conflict of interest The author has no conflict of interest to disclose.

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