Review

Medical Management of Acute Type A Aortic Dissection

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Introduction

The time-honored dictum is that type A aortic dissection requires urgent surgery. Are there any times when medical management of aortic dissection is more appropriate?

Certainly. Medical management is part of the initial stabilization of any patient with type A dissection, during clinical and radiographic evaluation and en route to the operating room.

There are, however, situations where the patient's treatment stops with medical management: Patients with completed stroke, comorbid conditions (e.g., cancer, advanced multiple organ dysfunction, age), prior aortic valve replacement (AVR), and presentation to the hospital beyond 48–72 hours of the onset of aortic dissection.

Stroke in the Setting of Acute Type A Aortic Dissection

The introduction of stroke into an already complicated picture of acute type A dissection results in a less favorable short- or long-term survival. The reestablishment of blood flow into the infarcted area of the brain and the administration of high-dose heparin for extracorporeal circulation may induce hemorrhagic infarcts and result in intractable brain edema.[1] Many experienced cardiac surgeons have had the misfortune of performing an impeccable aortic procedure in this setting, only to see a brain-dead patient with massive intracranial hemorrhage and brain stem herniation from severe mass effects returned to the intensive care unit (ICU). Piccione and colleagues have reported on the usefulness of intentionally delaying surgery in a patient with Marfan syndrome.[2] Deeb and associates reported good results with a combination of early percutaneous reperfusion and delay of surgery until the reperfusion injury is resolved.[3] Intentional delay of surgery and observation with medical treatment is useful for patients who have acute type A aortic dissection with cerebral infarction[4] (Fig. 1).

Stroke in patients with acute type A aortic dissection should constitute only a relative contraindication to operation, because full neurological recovery and acceptable outcomes are possible.[5] A coma may not represent an absolute contraindication for resuscitative surgery with modern techniques in hemodynamically stable patients with acute type A aortic dissection, provided that surgery is performed expeditiously after the onset of brain malperfusion.[6] Surgical repair of acute type A aortic dissection with acceptable mortality in the setting of acute stroke was demonstrated in one recent study, without a worsening of neurological condition after surgical repair.[7]

Although additional clinical studies are needed to draw definitive conclusions, we believe that if a patient with acute type A aortic dissection presents with stroke that is in progress, i.e., the stroke is evolving, immediate surgical repair will produce suitable results. In a completed stroke, however, acute type A aortic dissection should be medically managed because of the risk of heparin-induced hemorrhagic infarcts intraoperatively. If the infarct has been realized for four hours or more, or if a CT scan shows a sizable acute infarction, surgery should be avoided.

Advanced age and comorbidities in the setting of acute type A aortic dissection

It is important to consider whether it is acceptable to leave uncorrected substantive comorbidities in the setting of emergency surgery, or if treating them at the cost of deferred or denied surgery is more appropriate. Mehta and associates have shown that the risk of mortality from surgery for acute type A aortic dissection is 45% for patients 80 to 84 years of age and 50% for those 85 or older.[8] These are formidable levels of operative risk that

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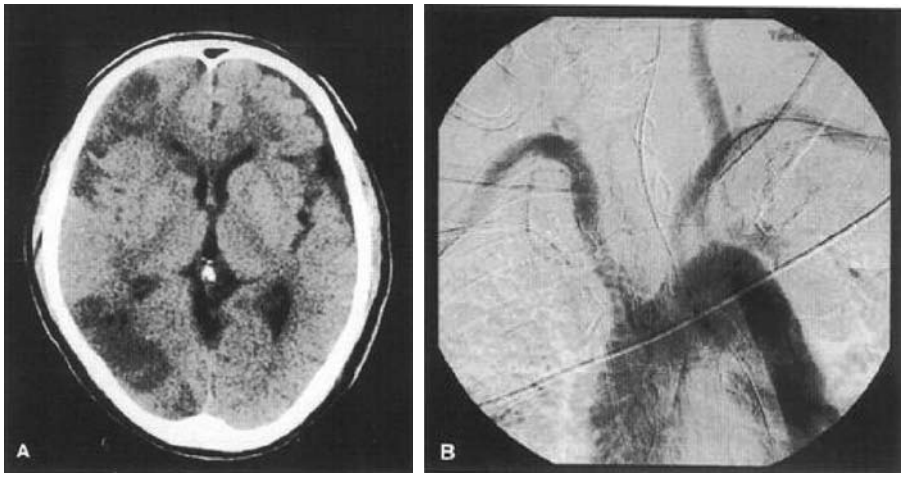

Fig. 1.
A: A brain CT demonstrating multiple low-density infarctions in the right hemisphere, with moderate cerebral edema.
B: An arch angiogram of the same patient, demonstrating impaired flow through the right carotid artery as a result of the dissection process. It was felt that immediate surgical intervention was inappropriate in the acute phase of the dissection. Interval medical management was undertaken, with eventual aortic replacement three months after initial presentation.[4]

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beg the question of whether nonoperative management can produce similar results in patients with advanced age.

We have shown that in patients presenting two or three days from symptom onset, correcting comorbidities prior to surgery or avoiding surgery can result in acceptable outcomes. Our patients presenting with acute type A aortic dissection who were denied surgery because of their advanced age and/or comorbidities achieved a 30-day survival rate of 42%.[9]

Delayed presentation of acute type A aortic dissection for 48–72 hours

Immediate surgical therapy is still recommended for acceptable operative candidates with acute type A aortic dissection who seek immediate treatment.[10,11] However, patients with type A aortic dissection who are referred from outside facilities and patients whose conditions are diagnosed several days after presentation and have survived the initial perilous period can safely undergo semielective surgery.[9,11] Delayed repair after optimization of the clinical condition and detailed evaluation of concomitant diseases result in outstanding long-term results.[9] If such late-presenting patients are not considered operable candidates, they may be treated with aggressive anti-impulse therapy and accomplish suitable early and short-term outcomes with in-hospital mortality of 12.5%.[11] Specifically, if a patient has presented beyond 48 to 72 hours after onset of pain, he or she will not be taken to the operating room in the middle of the night; rather, we will operate during the next daytime slot with our full specialized team available.

Prior aortic valve replacement

At the present time, aortic resection is considered appropriate for patients undergoing AVR for valvular disease who have coexisting moderate aortic enlargement. However, many patients in the past underwent AVR without concomitant resection of a moderately dilated ascending aorta. In a retrospective study, 18 out of 330 patients with previous AVR had an ascending aorta with a diameter of more than 5 cm. Aortic dissection occurred in 4 (22%) of these 18 patients, and three of the 18 underwent elective replacement of the ascending aorta.[12] In another study, 8 of 2,202 patients who underwent AVR were subsequently reoperated on because of ascending aortic dissection, 5 with acute and 3 with chronic ascending aortic dissection.[13] In acknowledgment of this observed risk of late events, we have recommended replacement of the ascending aorta during aortic valve replacement when its diameter is greater than 4.5 cm.[14]

Thus patients who have had aortic valve surgery present not infrequently with type A dissection. We usually do not operate on these patients acutely; rather, we pursue medical therapy with the anti-impulse paradigm. We take this approach because we feel that prior AVR provides substantial protection from the complications that make type A dissection lethal in other circumstances. Specifically, aortic insufficiency cannot occur as a consequence of type A dissection in the presence of a prosthetic aortic valve. Furthermore, dissection cannot cross a suture line, and the right coronary artery is protected by the suture line made previously for the AVR. Lastly, the periaortic adhesions from the prior operation are very likely to discourage free rupture of the later acute type A dissection

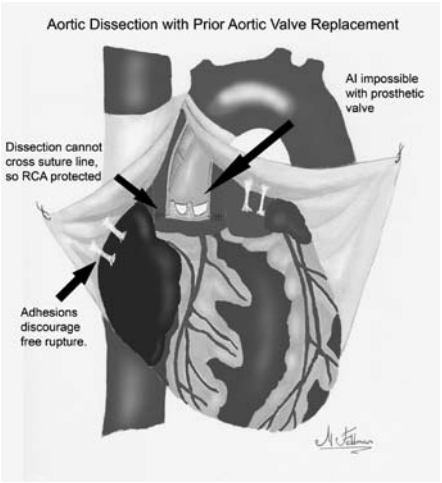
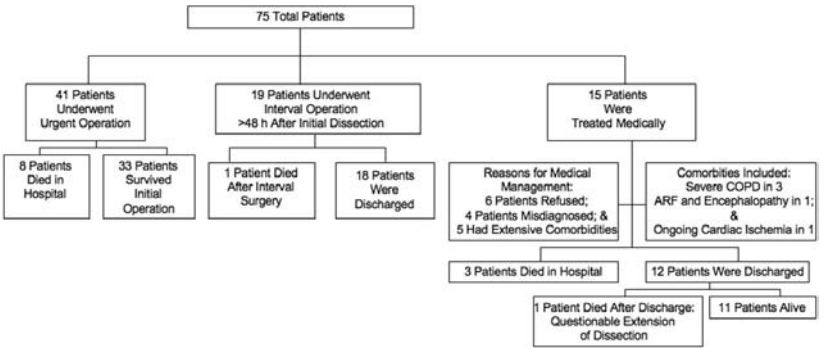


Fig. 2. A type A dissection is less virulent if there has been a prior aortic valve replacement (AVR).
Dissection cannot cross a suture line, so the right coronary artery is protected. Aortic insufficiency is impossible due to the prosthetic valve in place. Adhesions discourage free rupture into the pericardial sac.
RCA, right coronary artery.



©1999 American Medical Association. All rights reserved. Scholl FG, Coady MA, Davies R, Rizzo JA, Hammond GL, et al. Interval or permanent nonoperative management of acute type A aortic dissection. Arch Surg 1999; 134: Fig. 1, 402–6.

Fig. 3. Outcome of all patients treated for acute type A aortic dissection.
The three main branch points respectively represent patients treated with urgent surgery, patients undergoing delayed operation, and patients undergoing exclusively medical management.[11]
COPD, chronic obstructive pulmonary disease; ARF, acute renal failure.

(Fig. 2). This protection from dissection was confirmed in a study by Gillinov and associates.[15] Organ ischemia may still occur downstream and is not impacted by the prior AVR.

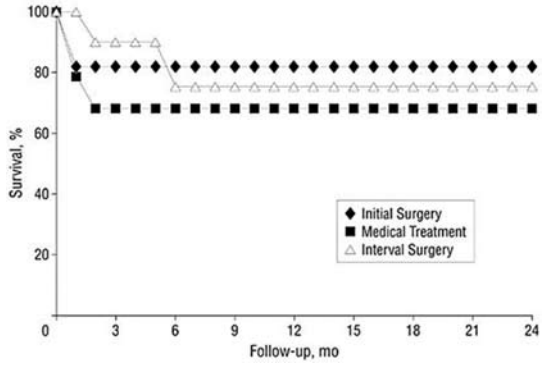
Thus in our view, type A dissection in the setting of prior AVR behaves more like type B dissection, and we treat it as such,[16–20] at least early on after dissection. Later, we undertake semielective or elective resection when the patient is more stable and the aorta is no longer acutely dissected. The Cleveland Clinic experience in patients with acute type A dissection in the face of prior cardiac surgery also generally supports a nonemergent approach to these patients (with angiography to identify coronary graft status), finding that rupture, tamponade, and hemodynamic instability occur infrequently.[15] Evidence from Europe also suggests that prior cardiac surgery is protective against rupture in acute type A aortic dissection, and that interval or sole medical therapy may be considered.[21]

Permanent nonoperative management

It has always been maintained that without surgical therapy, acute type A aortic dissection was nearly invariably lethal, with a stated mortality of 1% per hour and an expected 90-day mortality of 70 to 90%.[20,21] With modern ICU care, anti-impulse therapy, and medical management, it is becoming apparent that survival rates are greater than previously thought.

Our own studies found that in patients with absolute contraindications to surgery, we were able to produce a better survival with medical management than anticipated from prior (often quite old) studies.[9] In Fig. 3 we can see the flow patterns in three groups of patients: those treated with immediate surgery, those treated with delayed surgery, and those treated entirely nonoperatively. We were able to achieve a hospital survival rate of 88% in patients who underwent interval or permanent nonoperative management and 80% in patients who underwent entirely nonoperative management. Figure 4 indicates that the survival was essentially equivalent in the immediate surgery, delayed surgery, and exclusively medical groups. We hasten to point out that this data did not deter our enthusiasm for urgent surgery as a general principle for acute aortic dissection. Rather, we only wish to indicate that when necessary, interval or exclusive medical management can produce better results than previously expected.

In patients presenting later than 48 hours after the initial onset of pain, a 10-year follow-up study by our group has shown that medical and surgical treatment modalities have resulted in no significant difference in survival ($P = 0.10$) (Fig. 4). There is a trend, however, toward better survival in the surgical group. These conclusions have been reached in other studies: Chan and associates were able to achieve a survival of about 50% with medical management alone[22] and Masuda and associates also reported



©1999 American Medical Association. All rights reserved. Scholl FG, Coady MA, Davies R, Rizzo JA, Hammond GL, et al. Interval or permanent nonoperative management of acute type A aortic Dissection. Arch Surg 1999; 134: Fig. 2, 402–6.

Fig. 4. Kaplan-Meier actuarial survival curve from date of initial presentation and treatment.
Note that survivals over the first two years are equivalent.
See text for a perspective on these therapies.
Comparison made using the log-rank test (P = 0.44).[11)]

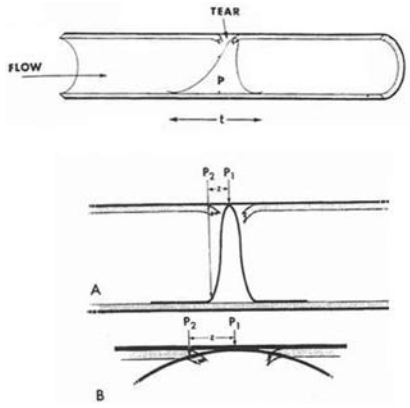


Fig. 5.
Top: This schematic demonstrates the Tygon tubing model used by Wheat in his seminal studies in the 1960s. A lining of rubber cement was placed within the Tygon tubing, and a tear was created in the rubber cement to mimic the intimal tear of aortic dissection. P represents a pressure wave (pressure over time t).[29)]
Bottom: This schematic compares the pressure gradient between the intima and the adventitia (really, rubber and Tygon) in two conditions.
The top A, a normal or increased pulse pressure; the bottom B, a pharmacologically blunted pulse wave; Z, the length of the torn intima; P_1, the pressure applied to the adventitia at point P_1; P_2, the pressure applied to the adventitia at point P_2.
Note that when the pressure curve is flattened (as with β-blockade), the pressure differential, ΔP, becomes less. The ΔP is thought to drive the process of dissection.[28)]

better-than-expected results with medical management.[23)]

A paper by Centofani group asked an intriguing question "Is surgery always mandatory for type A aortic dissection?".[24)] The authors found that age, coma, acute renal failure, shock, and redo operation constitute highly predictive surgical risk factors. They suggest that when the predicted risk level exceeds 58%, surgery should be withheld because survival with medical therapy alone will be equal. They arrive at this figure by means of International Registry of Acute Aortic Dissection (IRAD) data, which indicate that medically treated patients can achieve a survival of 42% (i.e., a mortality of 58%).[25)] Thus if predicted surgical risk exceeds this criterion, medical therapy can be considered in lieu of surgical therapy. This recommendation remains controversial and has elicited strong contrary response.[26)]

History of "Anti-Impulse" Therapy

The groundbreaking work in medical management of type A aortic dissection emerged from the classic studies by Simpson and Taylor,[27)] and Wheat and associates[28)] more than 40 years ago. Most of the modern medical management of aortic dissection is a result of an ex vivo model, the theoretical constructs by Wheat and associates on artificial "aortas" built from Tygon tubing coated internally with rubber cement[28–30)] (Fig. 5). The two primary goals of pharmacological therapy—reduction in blood pressure (BP) and diminution of left ventricular ejection force (dp/dt)—were established by Wheat's experiments[28–30)] (Fig. 6). Some of the theories were also tested on the isolated canine aortas, but the many decades of medical management of aortic dissection were established without human models for testing.

The thrust of the studies by Wheat and associates[28–30)] was that the contractile force of the myocardium, expressed as the change in pressure over time (dp/dt), plays a major role in the initiation and propagation of acute aortic dissection. The dp/dt is expressed in the initial upstroke of the arterial pressure curve. In Wheat's in vitro studies,[28–30)] neither high pressure alone nor high blood flow alone caused aortic dissection to progress; rather, it was the strength of pulsation that led to progression of the aortic dissection.

Historically, the most effective animal model for aortic dissection is a broad-breasted white turkey. Although it is not generally appreciated, these birds are quite prone to aortic dissection. Whole populations of turkeys can be rendered exceptionally dissection prone via iatrogenic induction of lathyrism, so that most of the birds die from acute aortic dissection. B-aminopropionitrile, an inhibitor of

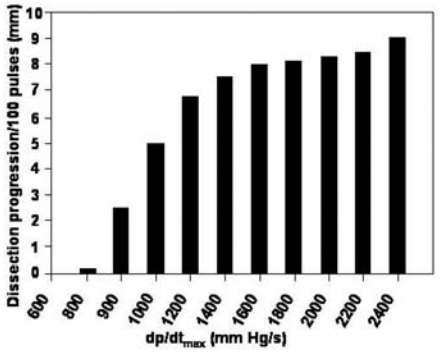


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Fig. 6. Exacerbated progression of aortic dissection in relation to increasing dp/dt.
In this experimental setting, no progression occurs until a threshold level of dp/dt is exceeded.[32]

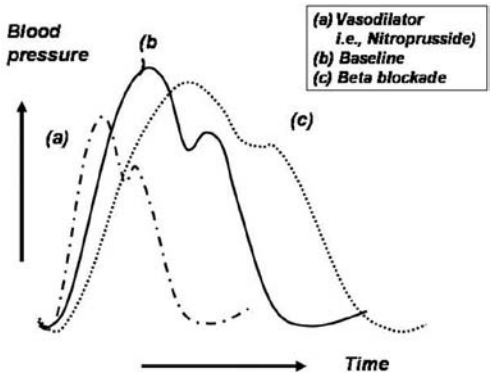

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Fig. 7. Aortic pressure curves under various conditions.
Curve (a), the administration of a vasodilator agent such as nitroprusside; curve (b), the baseline state; curve (c), β-blockade administration.
(a,b) Note the significant decrease in blood pressure and acceleration in heart rate at the expense of a steeper slope of the ascending portion of the curve (representing increased dp/dt).
(c) Although the degree of pressure lowering is usually smaller, the characteristic negative chronotropy and inotropy result in a blunted upstroke of the blood pressure curve, representing decreased impulse and dp/dt.[32]

lysyl oxidase (found in concentrated form in certain types of peas) was used to effect medial degeneration by interfering with the formation of elastin and collagen cross-links.[33] These studies examined the effects of chronic administration of various drugs on the risk of aortic rupture.

It is important to note that BP management alone does not suffice to control aortic dissection (Fig. 7). Nitroprusside was successful in controlling the arterial hypertension, but it could not halt the progress of the dissection. Propranolol alone was also insufficient in limiting propagation of dissection. The best results were obtained with a combination of nitroprusside and propranolol or with trimethaphan (an autonomic ganglion blocker with effects on both contractility and vascular resistance).[34] Vasodilators as sole therapy drop the peak systolic pressure, but may actually increase dp/dt, reflecting reflex sympathetic discharge in response to the drop in BP, with attendant chronotropic and inotropic stimulation. This phenomenon is demonstrated in the leftmost curve in Fig. 7. The increase in dp/dt from sole vasodilator therapy has been associated with an increase in ruptures of the dissected aorta.[32] On the other hand, β-blocker therapy, though producing a smaller drop in BP, decreases both chronotropy and inotropy with attendant fall in dp/dt. This decrease in dp/dt from β-blocker therapy is depicted in the rightmost curve in Fig. 7. It is the combination of vasodilator therapy with the sympathetic control of β-blockade that constitutes effective "anti-impulse therapy" for acute aortic dissection. Some human studies have also been performed. One study in Marfan patients showed propranolol to be less effective in the presence of a dilated aortic root than had been hoped, because its intravenous (IV) use acutely failed to reduce dp/dt.[35]

Based on these historical studies, aggressive reductions in dp/dt, as well as BP, have come to constitute the basis for medical therapy of acute aortic syndromes. These treatments, though developed many decades ago, have continued to represent the standard of care even in modern times.

Medical Management First and Always

Medical management of acute aortic dissections starts at first suspicion, often prior to diagnosis and differentiation between the ascending and descending types of dissection. This phase of intensive medical management is essential to prevent exacerbation or rupture of the dissection before the patient is placed on cardiopulmonary bypass for aortic replacement.

ICU support and monitoring

Strong suspicion of aortic dissection should result in an immediate shift of the patient to an ICU, where hemodynamic stabilization is achieved and BP, cardiac rhythm, urine output, and neurological status are closely monitored for any change resulting from aortic complications.[30,36] If there is a suspicion of dissection in the brachiocephalic

Table 1. Intravenous agents for treatment of ascending dissection

Name	Category	Loading dose	Maintenance dose	Adverse effects	Caution
Sodium nitroprusside	Vasodilator	0.3 mcg/kg/min to 3 mcg/kg/min; max. limit for an adult is 10 mcg/kg/min for 10 min	1–3 mcg/kg/min	Nausea, vomiting, agitation, muscle twitching, sweating, cutis anserina & cyanide toxicity, tachycardia	In patients with hepatic or renal dysfunction
Propranolol	β-blocker	1–3 mg (given at 1 mg intervals over 1 min). Can be repeated in not less than every 4 hours	1–3 mg every 4 hours	Hypotension, nausea, dizziness, cold extremities, reversible hair loss, bradycardia	In patients with bradycardia or history of CHF and bronchospasm. Max. initial dose should not exceed 0.15 mg/hr
Esmolol	β-blocker	500 mcg/kg bolus	Continuous 50 mcg/kg/min up to 200 mcg/kg/min	Hypotension, nausea, dizziness, bronchospasm, dyspepsia, constipation, increases digoxin level	In patients with CHF or asthma or on concomitant CCB therapy
Labetalol	α- & β-blockers	20 mg over 2 min, then 40–80 mg every 10–15 min (max. 300)	Continuous IV at 2 mg/min & titrate up to 5–10 mg/min	Vomiting, nausea, scalp tingling, burning in throat, dizziness, heart block, orthostatic hypotension	In patients with lung disease, concomitant CCB therapy
Diltiazem	CCB	0.25 mg/kg IV bolus (up to 25 mg)	5–10 mg/hour by continuous infusion	Heart block, constipation, liver dysfunction	In patients with heart failure, concomitant β–blocker therapy
Enalapril	Vasodilator ACE inhibitor	0.625–1.25 mg bolus	0.625–5 mg every 6 hours	Precipitates fall in BP in high renin states, variable response, renal failure	In patients with high possibility of MI, renal dysfunction
Fenoldopam	Dopamine D1 receptor agonist	0.03–0.1 mcg/kg/min initially	0.1–0.3 mcg/kg/min, max. 1.6 mcg/kg/min	Tachycardia, hypotension, headache, nausea, flushing, hypokalemia, elevation of IOP	In patients with glaucoma

CCB, calcium channel blocker; ACE, angiotensin-converting enzyme; IV, intravenous; BP, blood pressure; IOP, intraocular pressure; CHF, congestive heart failure; MI, myocardial ischemia.

trunk, or if BP is significantly higher on the left than on the right, the arterial line should be placed on the left.[37]

Pain control

Pain should be treated promptly with intravenous morphine because the pain itself can contribute to a hyperadrenergic state, exacerbating acute hypertension and tachycardia as well as dp/dt.

Volume management

Rapid volume expansion should be considered in the setting of hypotension in a patient with suspected aortic dissection, given the possible presence of cardiac tamponade or aortic rupture. The possibility of pseudohypotension, which occurs when arterial pressure is being measured in an extremity with dissection-compromised circulation, should be ruled out before the administration of intensive medical therapy. BP should be measured in multiple extremities. Hypotension or shock constitutes a sign of ominous prognosis[38] and should be treated with volume resuscitation; inotropic support is reserved as a secondary treatment.

Management of tamponade

In the case of tamponade, pericardiocentesis appears to be contraindicated, based on a small study of 4 patients (along with the unpublished experience of experienced aortic physicians and surgeons). Three of 4 patients subsequently developed electromechanical dissociation and death within 40 minutes of successful pericardiocentesis.[39] Adverse outcome after pericardiocentesis may be due to a rebound increase in intra-aortic pressure, thereby leading to recurrent hemorrhage and lethal cardiac tamponade. The main treatment of cardiac tamponade is volume administration, despite high CVP, to improve cardiac filling against external pressure in the pericardial space. The only effective treatment for tamponade from rupture of ascending aortic dissection is surgical therapy.

Anti-impulse therapy

Cornerstones in the medical management of hypertensive and most normotensive patients with suspected acute aortic dissection are anti-impulse therapy and BP control. The initial therapeutic goal is an elimination of pain and a reduction of systolic BP to 100 to 120 mm Hg (mean arterial pressure of 60 to 75 mm Hg) or the lowest level compatible with adequate vital organ perfusion.[37,40]

Conclusion

As we have seen, much of the original work that underlies current treatment protocols for acute type A dissection was conducted on Tygon tubing mock aortas or on the aortas of aneurysm-prone turkeys. Yet the principles of anti-impulse therapy for acute dissection have stood the test of time. As dissection surgery has become better and better, we have recognized that there may be a role for interval or permanent medical therapy for specific groups of acute type A dissection patients discussed in this article. The very consideration of medical management for acute type A dissection represents a "back to the future" paradigm shift reminiscent of the earliest recommendations for dissection treatment many decades ago before surgical therapy was feasible or safe.

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