Recent Advances in the Management of Acute Aortic Syndrome

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1. Introduction

Type A acute aortic dissection is one of the most serious cardiovascular conditions and is associated with significant morbidity and mortality. A half century ago, Hirst et al published a milestone article describing the linearized mortality rate of one percent per hour after the onset of an ascending aortic dissection [1]. Hence, the importance of accurate, quick and reliable diagnosis, as the timing of procedure is vital for optimal management of this highly lethal condition. Despite improvements in the diagnostic modalities, surgical techniques and perioperative care, the overall mortality remains high, between 10% and 30% [2].

Due to its major role in systemic perfusion, the aorta and its main branches after dissection are often challenging when trying to prevent surgical morbidity and mortality. The complexity of aortic dissection presents not only a pure cardiovascular surgical task, but also consideration must be given to protection of the myocardium, cerebrum, peripheral tissues and organs. An early fatal result of aortic dissection is due to ischaemic injury to the brain or heart, although longer peripheral ischaemia can cause multiorgan failure resulting in extended hospital stay, increased morbidity and mortality. Alexis Carrel highlighted the risks of surgery in 1910 with the following short summary on aortic interventions: “The main danger of the aortic operation does not come from the heart or from the aorta itself, but from the central nervous system.” Even a century later, we are still trying to optimize cerebral protection, despite having significantly wider range of diagnostic and therapeutic modalities.

Advances in our understanding of varying pathologies of aortic dissections have improved as have the technological developments in the modes of detection. These advances together with improved therapeutic options have raised expectations for better outcomes.

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2. Acute aortic syndrome

The term “acute aortic syndrome” (AAS) became widely accepted in the last decade. It involves not only aortic dissections, but intramural haematomas and penetrating atherosclerotic ulcers in the same anatomical location. This constellation of presentations have similar emergency status, diagnostic and therapeutic requirements. As a definition, AAS is an acute pathophysiological process involving the tunica media of aortic wall, which results in rupture or any further life-threatening complications.

2.1 Epidemiology

Population-based epidemiological studies suggest an incidence of AAS of about thirty cases per one million people per year. Eighty percent is represented by acute aortic dissections, 15% by intramural haematomas and 5% as penetrating ulcers. Seventy percent of the affected population is male with an average of 60 years [3]. A Swedish epidemiological study found the same incidence in an observational period between 1987 and 2002 among 4425 cases. In this study, the incidence of AAS has increased by 50% in men and 30% in women over study period. This may be related to enhanced diagnostics, although a further component could also be the increasing age of the population. Overall, 20% of affected patients died before reaching a medical facility, 30% during the hospital stay and further 20% over the following 10 years [4]. Both circadian and seasonal variations have been observed in the occurrence of AAS, with the peak frequency found between 0800hr and 0900hr, with an increased likelihood during the winter period. The most likely explanation is a link to the circadian variation in blood pressure [5, 6].

2.2 Pathophysiology

The mechanisms leading to AAS arise from many sources, although preexisting medial degeneration is proven to be an important risk factor for acute aortic dissection. Cystic medial necrosis is a hallmark of the histology, especially in aortic aneurysm patients. Microscopic features include decreased amount of vascular smooth-muscle cells, mucoid deposits and elastin deficiency [7]. However, over 80% of acute dissections occur in absence of a pre-existing aneurysm. The International Registry of Acute Aortic Dissection (IRAD) has collected an impressive amount of data for the demography of patients who present with AAS. The most commonly associated factors are:

- Hypertension
- Atherosclerosis
- Elderly
- Previous cardiovascular surgery, especially previous aortic aneurysm or dissection repair
- Connective tissue disorders (Marfan’s syndrome, Ehlers-Danlos’ syndrome, Erdheim-Gsell’s syndrome)
- Infective involvement of the aortic tissue (Lues, Takayashu aortitis)
- Congenital causes (PDA ampulla, Sinus of Valsava aneurysm, bicuspid aortic valve)
- External factors (Trauma, cocaine abuse)

Improvements in the resolution of aortic imaging has led to the identification of pathological submodalities, i.e. intramural haematoma or penetrating atherosclerotic ulcer. Histological
findings of these lesions generally demonstrate significant intimal atherosclerosis, which is not a constant finding in aortic dissection biopsies. Studies suggest that aortic dissection is an end process with a wide pathological spectrum, many of which facilitate weakening and/or increased stress of the aortic wall. The chain of pathological events might begin with a small superficial intimal rupture; atherosclerotic ulcers may provide a good milieu for development of such a tear. Alternatively, disruption of vasa vasorum might result in an intramural haematoma, which later ruptures into the aortic lumen or leads to dissection. However, it is likely that many aortic dissections develop without having a pre-stage of intramural haematoma or penetrating ulcer [8].

2.3 Presentation and diagnosis

Although the typical symptom is described as sharp, tearing, ripping chest pain, the presentation is diverse and about 10% do not complain of pain; sometimes the aortic pathology is an accidental clinical finding. In some patients shoulder or back pain occurs or just a husky voice, with or without shortness of breath and/or haemophthysis. Hypotension or shock is seen in 25% of patients, whereas hypertension can also be a presenting symptom, although more often found in type B dissections. Further findings, such as migrating pain, neurological deficits, acute abdomen, cardiac failure, myocardial ischaemia, aortic valve regurgitation are less common. Connective tissue diseases are characterized by additional specific symptoms, i.e. skeletal, pharyngeal or lens abnormalities and extreme laxity [3].

Early acute diagnosis can be vital, as an emergency surgery may be indicated. Blood pressure control is essential, and a goal of systolic ≤110 mmHg is recommended. The administration of β-blockers, sodium-nitroprusside, calcium-channel-blockers with analgesia is helpful, if indicated. In some advanced dissections resustitative measurements such as intubation and pericardiocentesis may be required.

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Table 1. Efficacy of different imaging modalities in AAS.
In patients with suspected acute aortic dissection various investigations are performed on admission including blood tests, electrocardiography, chest radiography, echocardiography, computed tomography and magnetic resonance imaging. Some investigations, such as ECG, chest radiography and routine blood tests do not carry sufficient sensitivity and specificity to exclude or confirm the diagnosis of an acute aortic dissection. Biomarker assays are increasingly utilized in the diagnosis of AAS, i.e. elastin fragments, smooth-muscle myosin heavy-chain protein, D-dimers, but are not widely available and provide only supporting evidence. The definite diagnosis can only be established using an imaging modality [9]. Table 1. summarizes efficacy of different imaging modalities in AAS. Table 2. shows the diagnostic features of the imaging modalities currently available in a hospital setting.

Table 2. Diagnostic features of imaging modalities in AAS.

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2.4 Management of AAS

Currently, there are no randomized trials available to guide the management of AAS. The European Society of Cardiology has developed guidelines for diagnosis and management of aortic dissection based on a task force of international societies [10], although in most of decision making clinical pathways are usually based on case series or registries, systematic reviews, local experience, consensus based guidelines. Following initial stabilization of the patient, after diagnostic measurements and imaging, a treatment should be tailored to the pathological entity:

- **Type A dissection**
  
  Over 50% mortality in the first 48 hours without surgical intervention, only 1-10% survives the first 5 weeks on conservative treatment. The perioperative mortality is 10-30%. Contraindications are quite limited as type A dissection is a highly lethal condition without surgical treatment, although age >80 years, ongoing coma with definitive extensive cerebral lesions (but not localized ischaemia or paraplegia!) or extensive abdominal necrosis may be contraindications for surgery. A subacute type A dissection, is a rare finding that requires an elective/semi-urgent operation as the patient has already successfully survived the high mortality period may now benefit from a well planned elective procedure [10].

- **Intramural haematoma**
  
  Classical therapeutic indication as for type A dissection, although in an uncomplicated and non-progressing situation, without ongoing pain and periaortic bleeding, patients can undergo surgery on an urgent basis (within 24 hours) rather than as an emergency. Over the age of 80 years, accompanied by significant comorbidities, conservative therapy in an intensive care
facility with the support of repeat imaging should be considered. If sudden progression occurs, a surgical intervention may be life saving. In this patient group 40% of intramural haematomas resolve after 4 years of follow up without mortality according to a small patient cohort study [11]. Another study demonstrated 34% regression of the disease, while 36% progressed into a dissection (12% acute type A dissection, 24% localized dissection) and 30% resulted in aneurysm formation over long term. They have also demonstrated, that a rupture or dissection is a very rare phenomenon with an aortic diameter of <60 mm at any location with an intramural haematoma [9]. These observations guide the clinical management of intramural haematomas, despite the lack of large multicentric studies, each patient requires a tailored individual management plan. As penetrating atherosclerotic ulcers are usually incidental operative or postmortem findings and are seldom discovered at imaging, there are no widely discussed clinical therapeutic strategies available.

- **Typ B dissection**
  As this diagnosis generally requires conservative medical treatment in an intensive care setting, we only briefly discuss the indications for surgery. Medical treatment is associated with a mortality of 20%, compared to surgery, which has much higher mortality of 30%; medical therapy is therefore considered first. Classical operative indications are progressive organ malperfusion, ongoing pain with uncontrollable hypertension. In the last decade stent grafting of the affected region has become an alternative option as it can treat these problems at a low risk profile in most of the cases and without need for further cardiovascular surgery [12].

### 3. Surgical considerations and recent techniques for repair of type A dissections

#### 3.1 Perfusion approaches in type A dissections

Cannulation of an extended type A dissection often represents a challenge for surgeons when either the subclavian or lower limb arteries are involved in the process. There are some alternative cannulation sites published in current literature i.e. brachiocephalic trunk, right common carotid artery, transapical cannulation, although we prefer an innovative method through non dissected aortic wall on lesser curvature at level of Botallo`s ligament using a Seldinger technique.

Our first experience was a 50 year-old man with sudden onset of ripping chest pain, admitted unconscious accompanied by anisochoria. Computed tomography scan revealed an extensive type A aortic dissection. The dissection began exactly over the aortic valve; maximal diameter of ascending aorta measured 60 x 55 mm. On the lesser curvature of arch, particularly at Botallo`s ligament, preservation of the true lumen with an intact wall was observed, although the dissection involved all supraaortic vessels. Visceral arteries originated from the true lumen except the left renal artery. Dissection in both iliac arteries was also present. Rapid deterioration of the patient with cardiovascular instability led us to cannulate at Botallo`s ligament applying a minimal invasive cannulation method with a Seldinger technique [Figure 1, 2]. At Botallo`s ligament the aorta is firmly bound to pulmonary trunk with a mass of connective tissue, which usually protects it from a complete dissection in this area. Position of cannula has to be guided by either transoesophageal or epiaortic ultrasonography. With this rapid and safe cannulation method extracorporeal circulation can be easily established, thus reducing the risk of perioperative shock and increased mortality [13].
Fig. 1. Seldinger cannulation of a type A aortic dissection (first dialation step)

Fig. 2. Arterial cannula in situ at Botallo’s ligament
Cardiopulmonary bypass via axillary/subclavian artery has become an alternative perfusion site in the past decade, predominantly in acute aortic dissections but also for patients with severe aortic atherosclerosis [14-20]. Despite several advantages of axillary/subclavian artery cannulation such as dominantly antegrade perfusion of the aorta, this technique is not without its complications. Establishment of axillary/subclavian artery inflow may not be ideal for providing rapid antegrade perfusion in cases with hemodynamic instability, as dissection and cannulation can take too long. In small patients, a limitation of CPB pump flow due to a narrow axillary artery may be a concern [21, 22]. Applying the standard technique, however, only the right hemisphere is continuously perfused, which can result in malperfusion of the contralateral hemisphere, as Merkkola et al demonstrated, up to 17% of the patients having incomplete circle of Willis [23]. Even with a complete circle of Willis, concern has been raised, if this type of perfusion alone can sufficiently supply the left hemisphere.

Transapical cannulation is another technique for establishing reliable antegrade arterial access, as described by Wada et al [24]. In large cohort of 138 patients, cannula was placed through a 1 cm apical incision into true lumen via aortic valve under transoesophageal echocardiography guidance. Impact of causing an acute aortic insufficiency in this context is not discussed in detail. This technique carries disadvantage of resulting in prolonged cardiopulmonary bypass times, since no additional manipulations can be performed during cooling phase, i.e. inspection and preparation of aortic root.

Right carotid artery cannulation, performed by Urbanski in 100 patients, including 27 with type A dissections, provides another possible alternative, but also carries the risk of left hemisphere malperfusion and potential complications when the vessel is de-cannulated [25]. Experience with innominate artery cannulation by Di Eusanio et al includes 55 patients with only two in acute aortic dissections [26], so it is difficult to evaluate the efficacy of this method due to the small experience.

Fusco et al presented their results in femoral artery cannulation in 2004 [27]. With a conversion rate of 2.5% to ascending aortic cannulation, they conclude that femoral cannulation is appropriate and yields excellent clinical results. They are not aware of having encountered retrograde embolism from the descending aorta, probably since atherosclerosis is less common in dissection patients.

### 3.2 Cerebral protection in dissection surgery

Avoiding neurological damage is one of the main aims of dissection surgery, as Carrel emphasised a century ago. Deep hypothermia with circulatory arrest (HCA) is the most common technique for cerebral protection in aortic surgery with a well defined safe period for circulatory arrest, of 45-50 minutes at a core temperature of 20°C. Systemic hypothermia to extend the period of safe cerebral ischaemia has been the mainstay of neuroprotection for many decades [28, 29]. Safety of this approach relies on adequate systemic cooling and if this is incomplete, it risks the patient for neurological injury. Introduction of selective antegrade carotid perfusion (ACP) has prolonged this safe period. A combination of cold selective antegrade cerebral perfusion and deep/moderate hypothermic circulatory arrest allows adequate protection for the body and is not associated with higher risk of cerebral microemboli [30, 31]. The efficacy of selective antegrade cerebral perfusion as an adjunctive to hypothermic arrest has been proven by numerous publications [32, 33].
Unilateral brain perfusion, i.e. right subclavian/axillary artery, right carotid artery, brachiocephalic trunk is safe under monitoring with near infrared spectroscopy (NIRS), as nearly 1/5 of the population has an incomplete circle of Willis. Therefore a significant number of patients require bilateral ACP, on the other hand, in the rest population it is still debatable, if in left haemisphere the same temperature can be achieved as the contralateral hemisphere, with unilateral perfusion, after blood has perfused the right side. Further concern is raised with unilateral perfusion, that by aiming for bilateral equal brain saturations, the right haemisphere is may be slightly overperfused, leading to right hemispheric oedema. Near infrared spectroscopy does not provide this type of information, so unilateral perfusion enhances but cannot guarantee cerebral protection. These latter considerations require further research, although applying bilateral ACP may resolve these issues.

In our practice, during HCA, selective antegrade cerebral perfusion is applied through both carotid arteries (DLP Retrograde Coronary Sinus Perfusion Cannula with manual Inflating Cuff®, Medtronic Inc., Minneapolis, USA) at a flow rate adapted to keep a constant cerebral $O_2$ saturation each side with a perfusion pressure of 35-40 mmHg [Figure 3]. Cerebral monitoring is performed using NIRS, with the aim of maintaining brain tissue oxygen saturation measures at 65-70% continuously during perfusion, which should correspond to the induction values.

Fig. 3. Selective antegrade carotid perfusion
Retrograde cerebral perfusion via superior vena cava may also be undertaken, although in arch surgery carotids are available for ACP. If the carotids are severely destroyed by dissection, retrograde cerebral perfusion may be considered as an option, so long carotids are replaced by tube grafts. However, retrograde cerebral perfusion is associated with a significantly higher incidence of temporary neurological complications, later extubation, longer ICU-stay, hospitalization, than ACP [34].

In a study of 4670 patients who underwent extensive aortic surgery between 1985 and 2002 at the Heart Centre Leipzig, Germany, superiority of ACP over retrograde cerebral perfusion or stand-alone deep hypothermia was confirmed. ACP was associated with 5-14% mortality and 4-10% permanent neurological deficit, retrograde cerebral perfusion showed 12-22%; 10-20%, stand-alone deep hypothermia 15-30%; 8-24%, respectively.

Rigorous patient temperature monitoring is crucial to a balanced cerebral protection during CPB. As a standard body temperature measurement, rectal monitoring has been widely used for decades in many departments. In the past decade tympanic and urinary bladder temperature monitoring has been studied and suggested as an alternative to gold standard. Tympanic measurements provide a very good estimation of the brain temperature with minimal delay in the changes due to its close proximity to the central nervous system [35, 36]. Tympanic measurements are well established even in everyday body temperature measurement with portable thermometers in general health care. However, to obtain reliable values from the tympanic membrane, debris free status of the ear channel has to be proven by otoscopy prior to placement of probe, followed by a good heat insulation of ears by i.e. using swabs to prevent accidental heat loss due to theatre ventilation system.

Urinary probes are available built into urinary catheters, so their placement is very convenient, although measurement reliability depends slightly on urine flow [37]. Rectal measurements are less reliable, since faecal matter prevents sudden heat exchange [38]. Nasopharyngeal/oesophageal temperature monitoring in HCA as standard measurement site, has limitations as it may significantly over- and underestimate brain temperatures during the cooling and rewarming phases [39-41]. Akata et al have furthermore demonstrated, that pulmonary artery temperatures closely reflect changes in brain temperatures, but nasopharyngeal/oesophageal measurements could not be considered as a reliable index of brain temperature during the rapid induction of moderate/deep hypothermia [42].

4. Follow-up

As aortic dissections often develop on a background of preexisting aortic aneurysms, this mandates regular follow-up in these patients to facilitate elective intervention when required. These elective operations carry less risks as the patient can be thoroughly prepared using the ideal imaging modalities and optimizing the patient’s medical condition for major surgery. At the Department of Cardiothoracic Surgery, University Hospital Regensburg, Germany there is a regular aortic day-clinic available on weekly basis for pre- and postoperative follow-ups, that has been running for over a decade, which allows this endangered patient population to be monitored on a 6-monthly basis. Regular postoperative monitoring is essential to provide good long term results with the early discovery of endoleaks, progression of aortopathy, control of hypertension, etc. As the AAS population is
young, average age of involved is sixty years [3], regular follow up contributes to the restoration of health in this still relatively active age group. Patients with AAS have a long-term outcome which is less favorable when associated with a past medical history of previous cardiac surgery or generalized atherosclerosis [43]. Surgical repair has been recommended when maximal ascending aortic diameter reaches 50 mm (45 mm at Marfan’s syndrome) or 60 mm when involving the descending aorta, although decision making has to be individualized to patient and other comorbidities [10]. Blood pressure control is essential for these patients, with the aim of maintaining the blood pressure no more than 130/80 mmHg [44]. If there is a well know hereditary component present, the patient’s complete family should be offered the opportunity to be genetically tested and counselled.

Some recent publications have already highlighted the role of angiotensin II in progression of aortic aneurysms, although the relative contribution of its type 1 (AT1) and type 2 (AT2) receptors remain unknown. Habashi et al demonstrated that loss of AT2 expression accelerates the aberrant growth and rupture of aorta in a mouse model of Marfan’s syndrome. Losartan, a selective AT1 blocker reduces aneurysm progression in mice; a full protection required intact AT2 signaling. The angiotensin-converting enzyme inhibitor enalapril, which limits signaling through both receptors, is less effective. Both drugs attenuated transforming growth factor-β (TGF β) signaling in the aorta, but losartan uniquely inhibited TGF β-mediated activation of extracellular signal regulated kinase, by allowing continued signaling through AT2, which shows the protective nature of AT2 signaling and the choice of therapy in aortic aneurysms [45].

International multicentric studies are currently evaluating the possible pharmacological prevention and postoperative medical supportive therapy options in Marfan’s syndrome provided by AT1 blockers, especially losartan in a combination with a β-blocker, such as nebivolol. The key molecule in aortic aneurysms, TGF β, normally attached to extracellular matrix, is free and activated. Under experimental circumstances, TGF β blockade prevents aortic wall damage and dilatation. AT1 blockers exert an anti-TGF β effect; trials are now ongoing for evaluating the effect of losartan compared with atenolol or nebivolol. The third generation β-blocker nebivolol retains the β-adrenergic blocker effects on heart rate and further exerts antistiffness effects, typically increased in aortic aneurysms [46, 47].

After evaluation these ongoing human studies we have more insight to the pharmacological support of AAS and aortic aneurysms, which completes the surgical management possibilities of this severe disease group.

5. References


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Front Lines of Thoracic Surgery collects up-to-date contributions on some of the most debated topics in today's clinical practice of cardiac, aortic, and general thoracic surgery, and anesthesia as viewed by authors personally involved in their evolution. The strong and genuine enthusiasm of the authors was clearly perceptible in all their contributions and I'm sure that will further stimulate the reader to understand their messages. Moreover, the strict adhesion of the authors' original observations and findings to the evidence base proves that facts are the best guarantee of scientific value. This is not a standard textbook where the whole discipline is organically presented, but authors' contributions are simply listed in their pertaining subclasses of Thoracic Surgery. I'm sure that this original and very promising editorial format which has and free availability at its core further increases this book's value and it will be of interest to healthcare professionals and scientists dedicated to this field.

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