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Diagnosis and Treatment of Abdominal and Thoracic Aortic Aneurysms Including the Ascending Aorta and the Aortic Arch

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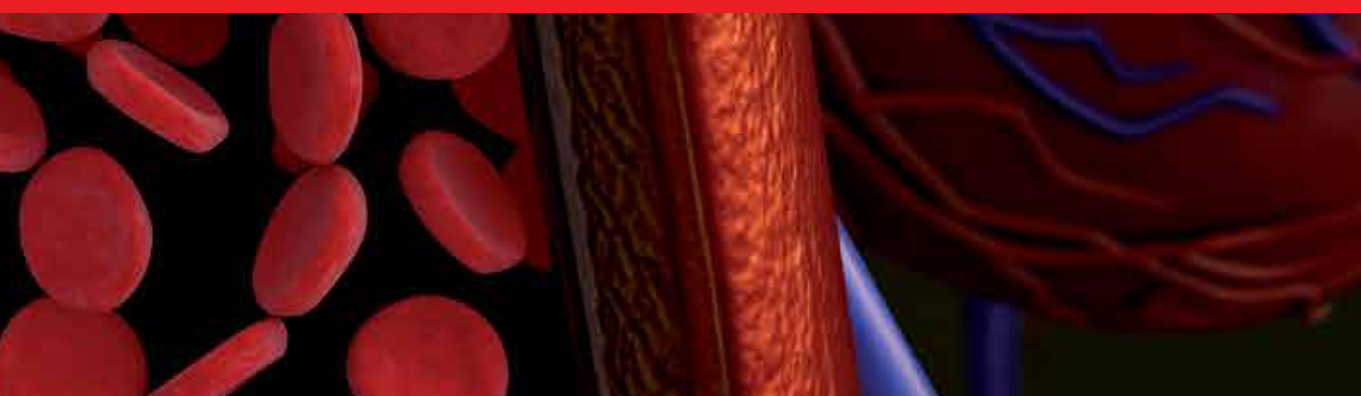

DIAGNOSIS AND TREATMENT OF ABDOMINAL AND THORACIC AORTIC ANEURYSMS INCLUDING THE ASCENDING AORTA AND THE AORTIC ARCH

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Meet the editor

Dr. Reinhart T. Grundmann works currently as an independent medical expert. He is a professor of surgery at the University of Cologne and he has the qualification of general and vascular surgery. He is the former medical director of the B.Braun company, one of the leading providers of healthcare solutions. In the last eight years he has been working as the medical director of the Clinics Altotting-Burghausen, Germany. Dr. Grundmann was from 1992 until 2008 the managing director of the Zentralblatt fur Chirurgie and he is currently a member of the Editorial Board of World Journal of Gastrointestinal Surgery. He edited from 2001 to 2005 the Jahrbuch der Chirurgie- the book which provides an information on the latest developments in surgery. Dr. Grundmann already published more than 260 scientific publications, including books and the book chapters. His recent research interests lie in the field of efficiency and efectiveness in surgery. In this frame, he published a workflows on liver surgery, gastric cancer, obesity surgery and surgery for abdominal and carotide artery stenosis treatment.

Contents

Preface

This book considers diagnosis and treatment of abdominal and thoracic aortic aneurysms. It addresses vascular and cardiothoracic surgeons and interventional radiologists, but also anyone engaged in vascular medicine. The book focuses amongst other things on operations in the ascending aorta and the aortic arch. Surgical procedures in this area have received increasing attention in the last few years and have been subjected to several modifications. Especially the development of interventional radiological endovascular techniques that reduce the invasive nature of surgery as well as complication rates led to rapid advancements. Thoracoabdominal aortic aneurysm (TAAA) repair still remains a challenging operation since it necessitates extended exposure of the aorta and reimplantation of the vital aortic branches. Among possible postoperative complications, spinal cord injury (SCI) seems one of the most formidable morbidities. Strategies for TAAA repair and the best and most reasonable approach to prevent SCI after TAAA repair are presented.

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1

Definitions, History and General Considerations Related to the Aortic Aneurysms

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1. Introduction

The objective of this chapter is to present the definitions, history and general considerations related to the aortic aneurysm as an introduction to the other chapters of this book.
The aorta can be affected by a variety of pathological conditions as the aneurysms. Aneurysms are areas of dilation local or diffuse from the aorta. This aneurysms are developed in places of congenital or acquired weakness of the middle wall. Some of them have a clear genetic component and affect young patients. Most pathology is however encountered in the grown-up population and is caused by degenerative diseases (Risberg & Lönn, 2007)

2. History

2.1 Classic descriptions

Even when the aortic disease was described in the Egyptian papyri, the term aneurysm probably comes from the Greek *aneurysma*, which means enlarged or dilated (Cooley, 1999).
The first description of an arterial aneurysm is attributed to Galen in the 2nd century. He wrote,"when arteries are enlarged, the disease is called an aneurysm". If the aneurysm is damaged, the blood drips into quarters, and is difficult to contain. In addition he described the difference between aneurysm caused by trauma and those caused by degenerative disease.
In the same 2nd century, Antyllus, developed and described a technique to treat these injuries. He believed that the clot seals the defect when there were dissection of the wall as well as try to ligation of artery above and below in thoracic aortic aneurysm and evacuated the clot.
In 1542, Fernelius told that the aneurysm originates as a result of thinning of the arterial wall, but is recognized that Vesalius made the first clinical diagnosis of an aneurysm in 1557 (Cooley, 1999; Kouchoukos NT, 1996).
In 1728, Lancisi published *De Motu Cordis et Aneurysmatibus*. In this paper it was proposed the etiology of abdominal aortic aneurysms. Later John Hunter showed that peripheral arteries can surely be ligated and Astley Cooper, one of his pupils, ligated an aneurysm of the aorta. These researchers believed that the ligature could decrease or stop the movement

of blood within the aneurysmal sac, which could cause thrombosis and eventually obliteration. Surgeons applied the ligature to the artery on the proximal side, the distal side, or both sides of the aneurysm. Ligation of aneurysms, however, returned to the extremities vulnerable to ischemic damage. Thus, the treatment of aortic aneurysms remained frustrating even for the best doctors. (Cooley, 1999)

In 1864, Moore inserted a wire of silver in a thoracic aneurysm to induce clot formation, and in 1879, Corradi applied a galvanic current through the wire. For 40 years, the method of combined electrolysis Moore-Corradi was adopted by other researchers. Blakemore and King, created a thermal coagulation device of aneurysms. The next step in the treatment of aneurysms was the stimulation of periarterial fibrosis. With this procedure, the cellophane or other types of plastic film were used as an irritant to cause occlusion of the vessel by tissue production. Harrison and Chandy applied this method to treat of the subclavian artery aneurysm, Poppe and De Oliveira used cellophane or plastic polyethylene films for wrapping aneurysms of the thoracic aorta produced by syphilis. In 1888, Dr. Rudolph Matas, developed a method for internal repair of aneurysms in which continuity of blood flow was restored by a simple intravascular suture of the artery opening directly the aneurysm sac. He described two procedures of aneurismorraphy. One called it the restorative, used for sacular aneurysms. In another technique -the reconstructive-, he excised the sick or injury portion of the vessel and created a tunnel through the remaining normal portion.

2.2 The twentieth century

In 1900, sir William Osler said, "There is no greater illness that leads to the clinical humility than aneurysms of the aorta" by the complexity and the limited treatment options and the outcome of the same.

In 1944, Alexander and Byron successfully resected an aneurysm of the descending aorta associated with aortic coarctation, but did not try to restore the aortic continuity.

In the same year, Ochsner treated a small sacular aneurysm of the descending aorta with good results.

On 28 April 1950, Denton A. Cooley conducted its first surgical treatment of aortic aneurysm, and in 1951, reported a work entitled "Surgical considerations of intrathoracic aneurysms of the aorta and large vessels". Gross and his colleagues, began the modern era of vascular grafts and employed preserved homografts to treat aortic coarctation (Cooley, 1999).

Those aneurysms that appears large in radiological studies, thin-walled and adhesions to the posterior side of the sternum recommended that before doing the surgical approach via median sternotomy, a left lateral thoracotomy was conducted to put a cannula to decompress the left ventricle. This maneuver to empty the heart, decreases the tension within the aorta, and in case of rupture when the sternum was opened, represents support in aspiration and control of bleeding.

In 1956, Cooley and DeBakey described a technique for the replacement of the ascending aorta with a synthetic graft distal to the coronary arteries ostia. In 1960, Mueller et al. combined the replacement with a supracoronary graft and the bicuspidization of an incompetent aortic valve. In 1963, Starr and collaborators described a replacement with a supracoronary graft and replacement of the valve.

In 1964, Wheat and colleagues described a radical technique of resection of the aortic wall, carrying the small buttons of adjacent tissue to the coronary ostium, replacement of the

aorta with a graft, and prosthetic aortic valve replacement. In 1968, Bentall and Bono described a technique for replacement of the ascending aorta and aortic valve with a tubular graft containing a valve prosthesis with latero-terminal reimplantation of the ostium of the coronary artery graft. This technique reduces the risk of recurrent proximal aortic aneurysm. (Kouchoukos, 1996; Gelsomino et al., 2003).

In the following decades (1970s, and early 1980s), the results of thoracoabdominal aortic aneurysm and descending thoracic aortic aneurysm repair were extremely different from center to center. (Safi, 2007).

Until the development of vascular grafts, prosthetic valves and the improvement of extracorporeal circulation techniques, surgical treatment of aneurysms of the ascending aorta was limited to the plication of the aorta or aneurismorraphy (Gelsomino et al., 2003)

Graft prosthetic, valved conduits or procedures with placement of an endovascular graft within the site of the aneurysm are currently used. (Cooley 1999; Gelsomino et al, 2003; Saiki et al., 2003; Girardi et al., 2002)

Traditionally the gold standard treatment has been surgery with a short-term treatment mortality incidence of 10-20% for elective procedures. In recent years, endovascular aortic repair of descending aneurysms has shown great promise. In 1991 Volodos and his group published the first report on endovascular stent grafting for a thoracic aortic lesion (Volodos et al, 1991), while the clinical first series was published by the Stanford group in 1994 (Dake et al, 1994)

The first endovascular thoracoabdominal aneurysm operation using branched grafts was reported by Chuter in 2001 (Chuter et al, 2001)

3. Classification

In the last decade, the descending thoracic aneurysms were classified only based in the aortic extension they affect: The upper half, lower half, or entire thoracic aorta, named as types A, B, and C, respectively. During the clamp-and-sew technique, it was showed that the maximum incidence of neurological deficit involved types B and C. Safi and coworkers consider these using the modified "Crawford classification," (table 1) (Safi, 2007).

Type	Description
Extent I	from the left subclavian artery to above the renal arteries
Extent II	from the left subclavian artery to below the renal arteries
Extent III	from the 6th intercostal space to below the renal arteries
Extent IV	involves the total abdominal aorta from T12 to below the renal arteries
Extent V	from the upper extent of the 6th intercostal space to the lower extent above the renal arteries

Table 1. Modified crawford classification

It was found that the extent of the aneurysm correlated with a high incidence of neurological deficit (31%), the highest being in extent II. In the clamp-and-sew technique, the clamp time and the extent of the aneurysm correlated to neurologic deficit (Svensson et al. 1993).

In regards to the aortic dissections present the classification of DeBakey (table 2), and in table 3 the Stanford proposed by Daly et al in 1970 (Kouchoukos, 1996; David TE, 1997; Kato et al., 2002).

Type	Description
(I)	The tear of the intimate usually originates in the proximal ascending aorta and extends to the ascending aorta, aortic arch, and variable-length to the thoracic aorta descending and abdominal.
(II)	The dissection is limited to the ascending aorta.
(III)	Dissection can be limited to the descending thoracic aorta (type IIIa) or extended proximally and affect the ascending aorta and aortic arch.

Table 2. DeBakey's classification for aortic dissection.

Type	Description
A.	It includes all the dissections involving the ascending aorta, regardless of their place of origin and its extension, corresponds to the types I and II of De Bakey.
(B)	It includes the dissections in the ascending aorta is not affected, this corresponds to the type De Bakey III

Table 3. Stanford classification for the aortic dissections.

4. General concepts

Aneurysms are characterized by degeneration of the media resulting in a weakness of all the layers of the aortic wall. Its recognized that 50% of the thoracic aneurysms are originated in an aortic dissection. These are truly pseudoanurysms since not all layers of the aortic wall are engaged. (Bickerstaff et al. 1982).

Once expressed, the formation of the aneurysm is progressive because some level of intraluminal pressure and tangential wall tension, increases with the square of the radius and are described as the aneurysms sac.

The risk of rupture is related to the largest diameter of aorta with a fatal outcome in 33-50% of the patients, while comorbidities are responsible for the remaining deaths (Bickerstaff et al. 1982; McNamara et to 1978).

In many cases, based in clinical findings and comorbidities, regular observation and medical management are indicated, but surgical treatment has been recommended if the sac diameter of the aneurysm reaches 5.5 cm even for asymptomatic cases (Lederle et al., 2007), but the criteria has been modified due to the higher risk of rupture with a great diameter; and in symptomatic aneurysms, immediate treatment is required, regardless of diameter.

If we find an aneurysm with a diameter of over 3 cm it must be monitored with ultrasonography every 12 months. When the diameter of the aneurysm has reached 5 cm in a man or 4.5 cm in a woman the ultrasonographic checks are carried out every 6 months (Powell & Greenhalgh, 2003).

Hypertension and other cardiovascular risk factors should be treated effectively. The systolic blood pressure should be lowered quickly to around 100- 120 mmHg. First aid treatment includes chewed antihypertensive drugs (i.e nifedipine), nitrate (or nitroprusside) infusion to beta-blocker, and effective analgesia.

The mortality from a ruptured aneurysm is 90%. Also, the surgery is a priority in patients with symptoms that suggest expansion or compression of an adjacent structure.
Short-term mortality for stent grafting of the aorta for aneurysms and type B dissections are less than for open surgery (Lepore et al., 2002; Lönn et al. 2003).
The aim of endovascular aortic repair is to prevent rupture of the aneurysm sac by its exclusion and decrease of the pressure on the wall of the aneurysmal sac stress, or to reduce the pressure in the false lumen with subsequent obliteration. Now with the new improved stent grafts for thoracic use. The endovascular procedure may increase its application as less invasive than standard operative repair and patients who were previously not eligible for surgery may now be considered for treatment, with lower risk than open surgery.

4.1 Thoracic aorta aneurysms

About 20% of the aortic aneurysms are located in the thoracic aorta (Bickerstaff et al. 1982).
The etiology for the thoracic aneurysms do not differ in any segments of the aorta. They can be due to degeneration, medial noninflammatory atherosclerotic degeneration, chronic dissections, trauma or infectous diseases (mycotic or syphilitic). The most common connective tissue disorder associated with aneurysm is the hereditary disorder Marfan's Syndrome. More rarely, Klipper-Feil syndrome or Turner's syndrome among other syndromes may involve the aorta (Kouchoukos, 1996; David, 1997; Greenberg & Rischer, 1998)
Aneurysms of the thoracic aorta are typically those that affect the aortic ring and ascending aorta (Figure 1), aortic arch or descending aorta. (Von Fricken, 2002).

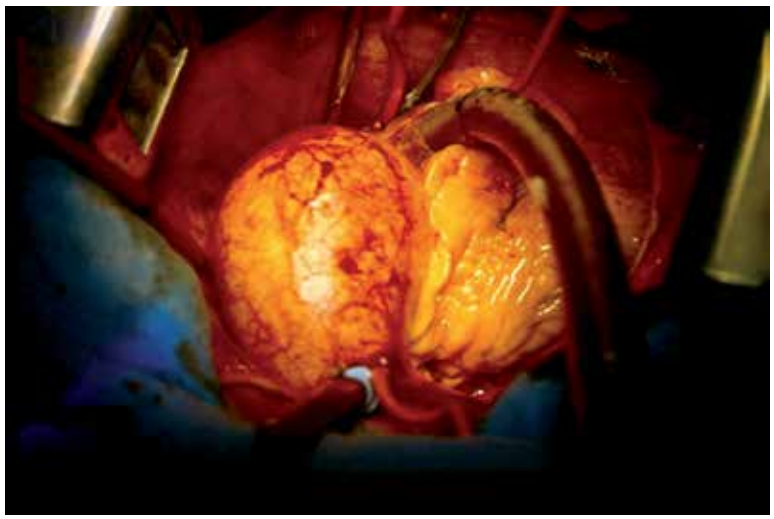

Fig. 1. Aneurysm of ascending aorta without extension to supraaortic branches.

There is a pathological disorder which precedes the formation of an aneurysm in the thoracic aorta in 60% of the cases is the dissection. (Kouchoukos, 1996; Von Fricken, 2002; Kato et al., 2002)
In regards to our experience, the frequency by gender was higher in the male than the female, similar to that reported in the literature. (Ramirez-Vargas et al., 2003; Miyairi et al, 2002; Colombi et al, 1983; Cabrol et al, 1986; David & Feindel, 1992)

Early population-based studies have been demonstrated to 5-year survival rate for untreated thoracic aneurysms of only 13 per cent (Bickerstaff et al. 1982), and for patients with degenerative aneurysm 3-year survival was 35% (McNamara et al. 1978).
Usually thoracic aortic aneurysms are asymptomatic. So if pain appears, suggests expansion, equal as tracheal or bronchial compression. Sometimes the neck veins are dilated due to the compression caused by the aneurysm.
The thoracic aortic aneurysms may be visible as an incidental finding on a chest x-ray film, but improved diagnostic accuracy and more frequent use of CT and echocardiography accounts for the relative increase in the frequency of aortic aneurysms. Transoesophageal echocardiography is a good primary investigation. Computed tomography, magnetic resonance imaging (MRI), or angiography is often needed for final diagnosis.
The risk for rupture during a 5-year period for thoracic aneurysms was near 20%; and in women was greater than men with a 7:1 ratio (Johansson et al, 1995; Meszaros et al, 2000). However this pattern may differ as Johansson et al. demonstrated when in Scandinavia found an equal sex distribution in ruptured thoracic aneurysms (Johansson et al. 1995).
Aortic valve insufficiency is of particular concern in the ascending aorta aneurysms. This risk is proportional to the increase in size of the aneurysm and on this basis, are new recommendations for an earlier surgical treatment with lower diameters than previously accepted.
The preoperative assessment of coronary mouths or the aortic valve disease is very important to choose the appropriate surgical procedure. The decision to treat an aneurysm should be based on the risk of rupture and the life expectancy of the patient (Greenberg & Rischer, 1998)
On the other side the aneurysms of the descending aorta have an incidence of approximately 30-50/million inhabitants/year (Joyce et al. 1964).
Repair for the ascending aorta aneurysms is an open standard replacement of the diseased segment of the aorta and if needed combined with a new valve insertion and reattachment of the coronary arteries with a synthetic valved aortic graft as shown in figure 2 (Gelsomino et al., 2003; Cabrol et al, 1986; Carias de Oliveira et al., 2003).

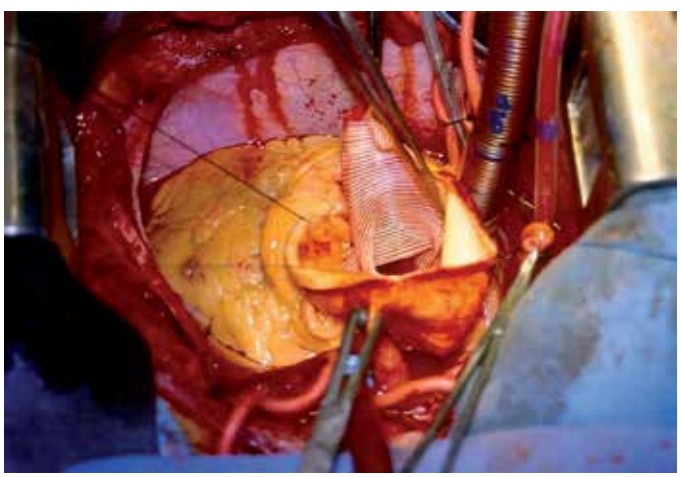

Fig. 2. Surgical treatment of an aneurysm of the ascending aorta with a mechanical valved graft.

Although important progress in surgical methods, brain preservation and myocardial protection and the postoperative care, often the surgical treatment of thoracic aortic aneurysms remains a challenge for the cardiothoracic surgeon (Greenberg & Rischer, 1998).
The surgical treatment of aortic aneurysm may be associated to another procedures: myocardial revascularization, implant for mitral valve prosthesis, correction of coarctation of the aorta or closure of an atrial septal defect, as we reported (Ramirez-Vargas et al., 2003). Other publications have also referred surgical procedures combined with the treatment of aneurysms of the thoracic aorta as tricuspid valve surgery and closure of the interventricular septal defect (Schulte et al, 1983; Massih et al, 2002; Levine et al. 1968).
In our experience, the time of aortic cross clamping and cardiopulmonary bypass give a similar average result compared to other series (Ramirez-Vargas et al., 2003; Kouchoukos, 1996; Gelsomino et al., 2003; David & Feindel, 1992; Tominaga et al., 2003).
The main type of cardioplegic solution was St. Thomas in 88.5% and only 11.5% was used HTK solution. Oster and cols, employed HTK for myocardial protection in a study with good results (Oster et al, 1983).
Several options have been used to reduce the incidence of neurological and renal complication which include: circulatory arrest with deep hypothermia, selective anterograde cerebral perfusion, retrograde cerebral perfusion, drainage of cerebrospinal fluid, placement of ice on the head in patients undergoing aortic arch surgery mainly (Ramirez-Vargas et al., 2003; Girardi et al, 2002; Oster et al, 1983; Di Eusanio et al., 2003; Griepp, 2003; Bachet et al, 1999; Deeb et al, 1999; Dossche et al., 1999).
The most commonly used approaches include the median sternotomy for treatment of aneurysm in the aortic arch. There are others such an "L" incision, with an incomplete median sternotomy and a previous thoracotomy is performed giving a greater advantage in the visualization of the surgical field and all the advantages that this leads well as its main disadvantage is the pain of the wound. For the approach of the distal aortic arch and descending aorta is preferred a postero-lateral thoracotomy (Gelsomino et al., 2003; Kay et al, 1986; Colombi et al, 1983; Tominaga et al, 2003; Kazui et al, 2002; Levine et al, 1968)
Femoral cannulation for cardiopulmonary bypass, remains the standard option for surgical repair of acute aortic dissection type. However, the retrograde perfusion has the potential risk of embolization of detritus of atheroma, extension of the dissection and poor perfusion (David & Feindel, 1992; Ergin et al., 1999). We use in 20.5% of this pathology femoral artery canulation (Ramirez-Vargas et al., 2003). Other sites for canulation have been described. One of this is the axillary artery which has the advantage for heart operations performed with cardiopulmonary bypass in the presence of occlusive peripheral disease, atherosclerosis of the femoral vessels, or distal extension of dissection (Careaga et al, 2001; Oberwalder et al., 2003; Murray & Young, 1976; Ergin et al, 1999; Galajda et al., 2003; Minatoya et al., 2003; Karmy-Jones et al, 2001)
Hospital-acquired early postoperative mortality has been reported by 4% to 20%. We had an early postoperative mortality of 7.7%. The main causes were perioperative myocardial infarction, left ventricle failure with low cardiac output, acute dissection, shock, hemorrhage (Ramirez-Vargas et al, 2003; Kouchoukos, 1996; Gelsomino et al., 2003; Girardi et al, 2002; Cabrol et al, 1986; Di Eusanio et al., 2003; Bell et al., 2003; Kay et al, 1986).
Other consideration is the association of aortic aneurysm and coarctation is a known entity. Aortic artery may become occlusive in the site adjacent to who has the greater narrowing as a result mainly of haemodynamic effects, dissection or aneurysm inflammatory or infectious. (Kouchoukos et al, 2003)

It is rare in children because the total of aneurysms prevalence increases as the individual grows, so that it approaches 20% when the patient is in the final stages of the third decade of life (Schuster & Gross, 1962)
The formation of aneurysms may be a late complication of a surgical repair or endovascular, but is less frequent in the absence of corrective procedures. Aneurysms are most frequent in intercostal arteries and can be isolated or multiple and followed in order of frequency by the aortic segment located after a coarctation, aortic and finally into the left subclavian artery isthmus (Kouchoukos et al, 2003).
Coarctation of the aorta-surgical treatment has provided successful mostly in the last decade. (Kouchoukos et al, 2003; Schuster & Gross, 1962; Parks et al, 1995; Bell et al., 2003).
The formation of aortic aneurysms associated with coarctation of the aorta is rare (Parks et al, 1995; Bell et al., 2003)
There are currently endovascular techniques for the correction of aortic aneurysms associated or not to aortic coarctation. However, in this association the recommended procedure is open surgery (Bell et al., 2003; Knyshov, 1996)

4.2 Abdominal aneurysms

The incidence of rupture of abdominal aortic aneurysms is estimated to be 9.2 cases per 100,000 person-years (Bengtsson & Bergqvist, 1993). Ruptured aortic aneurysms remain the 13th leading cause of death in the United States with an increasing prevalence (Coady et al., 1999); This may be attributable to improved imaging techniques, increasing mean age of the population, and overall heightened awareness (LaRoy et al, 1989).
Due to the age profile of the patients, atherosclerotically damaged vessels in one or several organs increase the risk of complications for surgical treatment of this patients as pulmonary disease, reduced FEV 1, renal, abdominal and cardiovascular complications, which contribute to a significantly increase of morbidity. However all symptomatic patients need immediate surgery. We must remember that about 30% of the patients have clinically significant cardiovascular, stroke, renal, or peripheral atherosclerotic disease.
The mean age of this population is between 59 and 69 years with a male to female ratio of 3: 1 (Bickerstaff et al. 1982). Branched devices have incorporated side branches and their use is for those aneurysms with no neck/proximal landing zone at all. These advanced devices can be classified according to target region (abdominal or thoracic or thoracoabdominal) and subdivided into fenestrated or branched stent-graft systems (Melissano et al, 2004; Verhoeven et al., 2005).

4.3 Thoracoabdominal aortic aneurysms

On the other side the thoracoabdominal aortic aneurysms (TAA) constitute about 10-15% of all aortic aneurysms. This type of aneurysms are probably the most difficult to treat. Chronic dissection is the cause of these aneurysms in approximately 20% of the cases (Svensson et al. 1993).
Women seem affected as often as men which is at variance with abdominal aneurysms which predominantly are to male disorder. So, the 85% of the patients are men for the abdominal aneurysms and 10 per cent of men are aged 75 years or more.
In the table 1, present the Crawford classification for the thoracoabdominal aneurysms according to their size. Type II aneurysms are the most extensive and difficult to treat. They also have the highest morbidity and mortality.

Modern treatment of TAA was pioneered by Stanley Crawford who introduced the "inlay" - technique (Crawford, 1974).

Type0	Description
(I)	Descending aorta + part of visceral branch
(II)	Descending aorta + abdominal aorta
(III)	Distal part of descending aorta + abdominal aorta
(IV)	Visceral branches

Table 1. Crawford classification of thoracoabdominal aortic aneurysm

By using motor evoked potential to monitor motor function of the spinal cord during surgery the risk for paraplegia can be reduced further to around 2% (Jacobs & Mess, 2003).
Preventive measures must be largely preoperatively, such as coronary artery by-pass grafting or percutaneous coronary interventions, and a proper risk assessment must be performed.
The most frequent risk factors of aortic dissection are degenerative disease of the middle and high blood pressure (Oberwalder et al., 2003).
In the pathology added in our series of patients with aneurysm, the most frequent were: Aortic valvular disease, chronic smoking, systemic arterial hypertension and Marfan syndrome, coarctation of the aorta, coronary artery disease similar to that reported in world literature. (Ramirez-Vargas et al., 2003; Kouchoukos, 1996; Gelsomino et al., 2003; Miyairi et al, 2002; Tominaga et al., 2003; Kazui et al., 2002)
The complications that have been reported early as ventricular failure, ventricular arrhythmias and hemorrhage are similar to that reported in our series. In addition other authors report paraplegia, stroke, renal failure, myocardial infarction, and respiratory failure. (Gelsomino et al, 2003; Girardi et al, 2002; Tominaga et al, 2003).
The ejection fraction of the left ventricle in our series was from 20% to 78%, varying with the reported in another series with a greater average 65%. (Kouchoukos, 1996)
Probably due to the risks involved in elective repair, a large proportion of patients, approximately 25% are treated urgent due to acute symptoms (Coselli et al, 2000).
On this basis its very recommended the diagnose of aortic aneurysm rupture, monitor before a small aneurysm, found incidentally or through screening, until it reaches in size where the benefit of surgical repair outweighs the risks associated with such surgery. Always remember the possibility of aortic dissection in a patient with severe pain suggestive of acute myocardial infarction (AMI) but without clear electrocardiogram (ECG) findings. All patients with aortic dissection must be referred to a hospital immediately.
Finally, in the decision of surgical intervention we must consider the age of the patient, his state of health, their symptoms and the size of aneurysm (McKneally, 2001), or the reason why surgery is required. As an example to the above mentioned, in our experience there was need to operated a septuagenarian patient who had been treated with the placement of a mechanical valved graft by thrombosis of the same. This was an emergency procedure and was only made the thrombectomy with a good result and recovery for the patient (Careaga-Reyna et al., 2006).
Is very important to define the diagnosis of aortic dissection vs acute myocardial infarction in aortic dissection because thrombolysis is contraindicated.

5. Conclusion

With this brief presentation, we can conclude that aortic artery aneurysms are not a recent pathology. The frequency of cases has increased by the greater care of the physician in the clinical evaluation and the availability of technological resources. The aortic aneurysm is a complex pathology, current therapeutic options allow to offer more secure procedures, with less morbidity and even patients than before were not considered candidates for treatment by the presence of other diseases now after a complete evaluation can be included for open or endovascular surgical procedures.

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2

Presentation of Abdominal Aortic Aneurysm in Clinical Practice, a Review

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1. Introduction

Patients with abdominal aortic aneurysms (AAA) may present with musculoskeletal pain patterns (Bassano, 2006). In approximately 7% to 8% of patients with low back pain (LBP), the cause is due to non-mechanical spinal conditions or visceral disease (Jarvik & Deyo, 2002). A contained retroperitoneal rupture of AAA is very rare, but may have a long history of less apparent clinical signs (Al-Koteesh et al., 2005). Approximately half of diagnosed AAAs are detected clinically; these are usually >5 cm in diameter (Beck et al., 2005). Accidental discovery is common when plain film radiographs are taken for evaluation of back pain. Ultrasonography of the abdomen is accurate and reliable in detecting AAAs (Fleming et al., 2005), but there needs to be a clinical reason before deciding to do these evaluations. This stresses the importance of a thorough history and physical examination.

2. Clinical history

It can be quite challenging to recognize the symptoms found in clinical history that support the need for a screening abdominal exam. Patients that do have an abdominal aortic aneurysm can present in three different categories. These categories consist of patients without significant symptoms, patients with symptoms due to a bulging AAA, and patients with symptoms due to a chronic contained ruptured AAA where the containment of the rupture keeps the leak slow enough as to not cause immediate death (Cates, 1997).

2.1 Aortic aneurysms without significant symptoms

The first category is obviously the most difficult to discover in clinical practice. Although most patients with AAA present with symptoms, 66%-75% of the cases of AAA are asymptomatic (Beck et al., 2005; Crawford et al., 2003, de Boer et al., 2010). What is even more disturbing is the fact that there is a considerable amount of patients with a chronic AAA rupture that have less than apparent clinical symptoms signifying the need for a screening for abdominal aortic aneurysms (Al-Koteesh et al, 2005). It is also unfortunate that most patients that have an asymptomatic AAA will remain asymptomatic until it finally ruptures. If they are fortunate, the size of the aneurysm draws the attention of the patient and physician prior to rupture (Crawford et al., 2003). Mass screening will benefit this group since this is the only way to detect these.

2.2 Symptomatic aortic aneurysm

In the second category, it is also difficult to discern between a patient that has an AAA and a patient that has another cause for the same complaint. Compared with non-inflammatory AAA, 65% to 90% of patients with inflammatory AAA are symptomatic (Ahlawat & Cuddihy, 2002). Some of these patients do present as patients having typical musculoskeletal problems and/or abdominal pain (Crawford et al, 2003). A feeling of fullness or heavy pulsations in the abdomen may be an early symptom (Crawford et al, 2003). Often, patients with this condition present with epigastric pain radiating into the flank/back region (Patel & Kettner, 2006). Sometimes patients with this sort of condition find it difficult to achieve a position which eases the pain (Mechelli et al, 2008). Other symptoms that a patient with AAA may have, include costovertebral angle pain, suprapubic pain, groin pain or leg pain (Hadida & Rajwani, 1998). Other patients may present with a dull constant aching pain paired with weight loss and occasional night sweats. These symptoms are generally considered "red flags" (Ahlawat & Cuddihy, 2002).

2.3 Chronic contained ruptured aneurysm

The third category is an emergency situation. Here again the symptoms are still the same, except there are added symptoms from the hypotension due to loss of blood. Depending on the rate of leaked blood from the rupture, the severity of the symptoms can differ. In general, the pain is severe in most patients, but atypical presentations are just as common. The symptoms can also vary depending on where the rupture is and what structures are compromised by the haematoma. For instance, a retroperitoneal haematoma that places stress on a iliopsoas muscle can very well cause irritation of the femoral nerve, making it appear a femoral neuropathy. This may imply that a patient presenting with a sensory deficit of the anterior thigh could be someone who is in need of an immediate medical referral (Ramasamy et al, 2001; Al-Koteesh et al, 2005). Symptoms can result from compression (e.g. ureter), erosion of vertebral bodies, or occlusion of blood supply (Hadida & Rajwani, 1998; Yokomuro et al, 2008).

These three categories demonstrate that in many cases the history alone gives no reliable information about a potential AAA. Many of these patients may very well end up presenting with low back pain and try various therapies to help lessen these conditions. It is also probable that there could be actual musculoskeletal symptoms at the same time as symptoms from an AAA. Other differential diagnoses include any abdominal pathology related to the structures compressed. It is suggested that the atherosclerotic plaques from someone with an AAA can increase risk of ischemia and thus lead also to disc degeneration (Al-Koteesh et al, 2005). This means that anyone presenting with degenerative disc disease symptoms could also have an underlying AAA that was the initial cause. Evaluating the risk factors in history is, therefore, very important.

3. Risk factors

In the clinical history, the presenting complaint gives information on the signs and symptoms. Since patients in primary contact practices do not necessarily present with symptoms that point directly to an abdominal aortic aneurysm (AAA), the review of systems and social history is of value in 'case finding'. This is the consideration of unrelated or intercurrent illness in presenting patients due to the presence of the risk factors associated with, in this case, an abdominal aneurysm (Crawford, 2003).

Age, gender, smoking and family history are the most significant risk factors for developing an AAA (Brown & Powell, 1999; Lederle et al., 2000; Kuivaniemi et al., 2003). These alone are a reason to pay attention to abdominal palpation and auscultation in the physical examination (Mechelli et al., 2008). Apart from these risk factors, there are other characteristics that may be of significance, namely cardiovascular disease and its associated complicating factors like hypertension, hyperlipidemia and atherosclerosis (Patel & Kettner, 2006; Hadida & Rajwani, 1998; Mechelli et al., 2008). COPD, trauma, infectious and inflammatory conditions and autoimmune diseases causing cystic medial necrosis, have also been implicated (Van der Velde, 1998; Weston, 1995). Black race and diabetes have a negative association with AAA. (Lederle et al., 2000).

3.1 Age, gender and race

Most AAA deaths occur in men over 65 years of age (Mechelli et al., 2008; Fleming et al., 2005). AAA is considered uncommon under the age of 50 (Van der Velde, 1998). With aging, the aorta may be less able to withstand the force of the pulsatile blood flow, in which case dilatation can occur (Crawford et al, 2003). The prevalence increases with age. The prevalence rates in men range from 2-9.5% (Cates, 1997; Van der Velde, 1998). Lederle et al. (2000) found that the likelihood of discovering an AAA of 4 cm or larger increases for every 7 year interval of age (OR 1.71; 95% CI: 1.61-1.82).

There is a difference in age-related deaths between men and women. Whereas in men, it occurs mostly over the age of 65, in women this occurs on average around 10 years later (Scott 2002), with a peak approximately at the age of 80 (Mechelli et al., 2008). This may be because of the protective effect of oestrogen, which may delay the process leading to AAA until after the menopause (Van der Velde, 1998). Overall prevalence is 5 to 6 times greater in men than in women (Scott et al., 2002). The inflammatory variant of AAA has male-to-female ratios ranging from 30:1 to 6:1 (Ahlawat & Cuddihy, 2002). Aneurysms occur more often in Caucasian men (Karkos et al., 2000). Even though the prevalence is many times lower in women than in men, it is surprising to note that the risk of rupture is threefold higher in women than in men. This difference is independent of age, initial AAA diameter, and body mass index or height. The mean AAA diameter at rupture was 5 cm in women and 6 cm in men (Brown & Powell, 1999).

3.2 Smoking and lung function

Smoking is a primary risk factor for AAA: it increases AAA growth rates by 15% to 20% (Brady et al., 2004). A history of smoking in this context is defined as lifetime consumption of more than 100 cigarettes in a lifetime. Deaths associated with AAA have increased since the 1950s. Part of this can be explained by improved diagnostic methods, better surgical techniques and general aging of the population, but this does not explain the increase completely. The deaths parallel the increase of tobacco use in those decades (Crawford et al, 2003; Van der Velde, 1998). The excess prevalence associated with smoking accounts for approximately 75% of all AAA of 4.0 cm or greater (Lederle et al., 2000). There is a significant association between the amount of cigarettes currently smoked and the depth of inhalation and the risk of AAA. This risk increases with an increasing amount of cigarettes and deeper inhalation into the lungs (Franks et al., 1996). There is, however, no association for any blood marker of smoking.

Smoking is also the only modifiable factor in AAA. It increases the risk for AAA, but abstaining from smoking can slow the growth of the aneurysm (Brady et al., 2004).

Inflammatory AAA represents 3% to 10% of all AAAs. A significant percentage of patients with inflammatory AAA are active smokers, when compared to non-inflammatory AAA (Ahlawat & Cuddihy, 2002). There is an 8:1 preponderance of smokers compared to non-smokers (Cates, 1997).
Poor lung function and smoking go hand in hand; both influence the rate of rupture of an aneurysm. Smokers are considered to be less healthy in general than non-smokers: they exercise less and exercise reduces the risk for cardiovascular disease (Kawachi et al., 1993). Several studies have shown an association between poor lung function (lower mean FEV_1) and AAA rupture (Brown & Powell, 1999; United Kingdom Small Aneurysm Trial Participants, 2002). Other studies report that after correction for number of years smoked, the connection between AAA rupture and COPD was lost and is not a risk factor (Lederle et al., 2000). Overall, patients that were former smokers after AAA surgery had a lower risk of death than those who reported that they were current smokers.
The mechanism by which smoking influences the development of an AAA is not known. It is thought that smoking influences the aortic elasticity negatively, which promotes AAA formation (Lederle et al., 2000). Increased amounts of the proteolytic enzymes collagenase and elastase have been observed in individuals that smoke as well as people with chronic obstructive pulmonary disease. This causes degradation of the aortic wall and atherosclerosis, thereby slowly weakening the aortic wall (Crawford et al., 2003; Lederle et al., 2000; Van der Velde, 1998; Cates, 1997).

3.3 Family history

Family history is an important issue. When considering patient history, special issues that require attention during a physical examination are easier to identify (Donahue, 1997). The probability of a patient having AAA is nearly twice that of someone without a (male) relative with a history of AAA (Lederle et al., 2000). It is found that a significantly higher percentage of patients with inflammatory AAA have a family history of AAA compared with patients with non-inflammatory AAA (Ahlawat & Cuddihy, 2002). Men who are first-degree relatives of a known aneurysm patient are especially at risk. Studies have reported prevalence rates of 12% to 33% in first-degree relatives (Crawford et al., 2003; Kuivaniemi et al., 2003; Van Vlijmen-van Keulen et al., 2002; Patel & Kettner, 2006).
The exact mode of inheritance is not known, but thought to be multifactorial with more than one environmental and genetic risk factor (Kuivaniemi et al., 2003). Defects are found in collage type I and III or other components of the connective tissue matrix, elastin and fibrillin, the inflammatory cell-derived matrix metalloproteinase, their inhibitors, autoimmune components and components related to atherosclerosis. Some say there may be autosomal dominant inheritance; however, others say that the sex-chromosome linked susceptibility is thought to account for male predisposition (Van Vlijmen-van Keulen et al., 2002; Cates, 1997). Association of certain collagen diseases, such as Marfan's syndrome and Ehler-Danlos type IV syndrome do seem to suggest a gene defect (Van der Velde, 1998).

3.4 Other risk factors

Coexisting conditions like cardiovascular disease can have an influence on the elasticity of the arteries, thereby causing weakening of the aortic wall. In the case of inflammatory AAA, 10-47% of patients have been reported to have arterial occlusive disease (Ahlawat & Cuddihy, 2002). Several authors have reported the presence of cerebral arterial disease,

peripheral aneurysms or claudication as a sign in the clinical history demanding further questioning and examination. At least a third of patients with femoral or popliteal aneurysms will have an AAA (Karkos et al, 2000; Crawford et al., 2003; Patel & Kettner, 2006). Suspicion is raised when a patient comes in with low back pain and mentions a history of myocardial infarction (Crawford et al., 2003). A history of coronary artery disease also carries an increased risk (OR 1.52; 95% CI: 1.37 to 1.68)(Lederle et al., 2000). Hypertension and older age are more strongly associated with AAA than with coronary artery disease even though risk factors of coronary artery disease show overlap with those of AAA (Kishi et al., 1997). Hypertension is associated both with increased risk of rupture as well as increased prevalence of AAA. It is a continuing haemodynamic burden on the aortic wall, which may further weaken the aortic wall (Crawford et al., 2003; Brown & Powell, 1999). Higher systolic as well as diastolic blood pressure has been found in aneurysm patients. When combined with a history of smoking and a positive family history, the association becomes even stronger (Franks et al., 1996; Kishi et al., 1997). With uncomplicated hypertension, screening is generally not indicated, but in the case of low back pain, especially when no apparent cause is found, careful physical examination is indicated (Crawford et al., 2003). Since hypertension can be influenced, it is especially important to regulate blood pressure in patients with smaller AAAs. Hyperlipidemia and atherosclerosis generally increase the risk of complications within the cardiovascular system, and with this increases the risk of AAA (United Kingdom Small Aneurysm Trial Participants, 2002; Mechelli et al., 2008; Patel & Kettner, 2006). Medication is said to be necessary to reduce the rate of expansion of aneurysms, even though no medical treatment has shown to influence this rate over time (Thompson et al., 2009).

Diabetes actually decreases the risk for AAA, even though it increases the risk for atherosclerosis (Lederle et al., 2000; Brady et al., 2004). Its effect is not yet fully understood, but the release of proteolytic enzymes and cytokines is implicated and the inhibitory effect of diabetes on this process may be a factor in the pathogenesis of AAA (Golledge et al., 2008). Certain infectious and inflammatory conditions are known to weaken the aortic wall. Diseases like Takayasu's disease and Marfan's syndrome can cause cystic medial necrosis, also causing weakening of the aortic wall, which predisposes to aneurysms (Hadida & Rajwani, 1998).

4. Signs in clinical examination

The usefulness of the clinical examination to detect AAA is limited. However, abdominal palpation and auscultation are important, especially when there is a suspicion of a non-mechanical or abdominal pathology for low back pain or when patients do not respond to the treatment. Most non-ruptured AAAs are asymptomatic, apart from a pulsating mass in the abdomen (Engel, 1996). There is a difference in chronic and acute rupture. Chronic is often misdiagnosed as back pain, spinal cord compression or more unusual presentations (Al-Koteesh et al, 2005). Acute rupture more often gives pain as described in the history findings.

Blood pressure in most cases will be either normal or high (Crawford et al., 2003; Hadida & Rajwani, 1998; Ahlawat & Cuddihy, 2002; Yokomuro et al, 2008; Cates, 1997). Pulse rate and rhythm are generally normal. In case of a ruptured aneurysm, there is often hypotension with a high pulse rate (Van der Velde, 1998).

On visual inspection, a pulsatile mass may be visible at or slightly above the umbilicus in the epigastrium (Patel & Kettner, 2006; Hadida & Rajwani, 1998). Ecchymosis may be present as an atypical finding. This may be somewhere over the abdomen, but can appear as low as the scrotum or popliteal fossa (Dargin & Lowenstein, 2008).

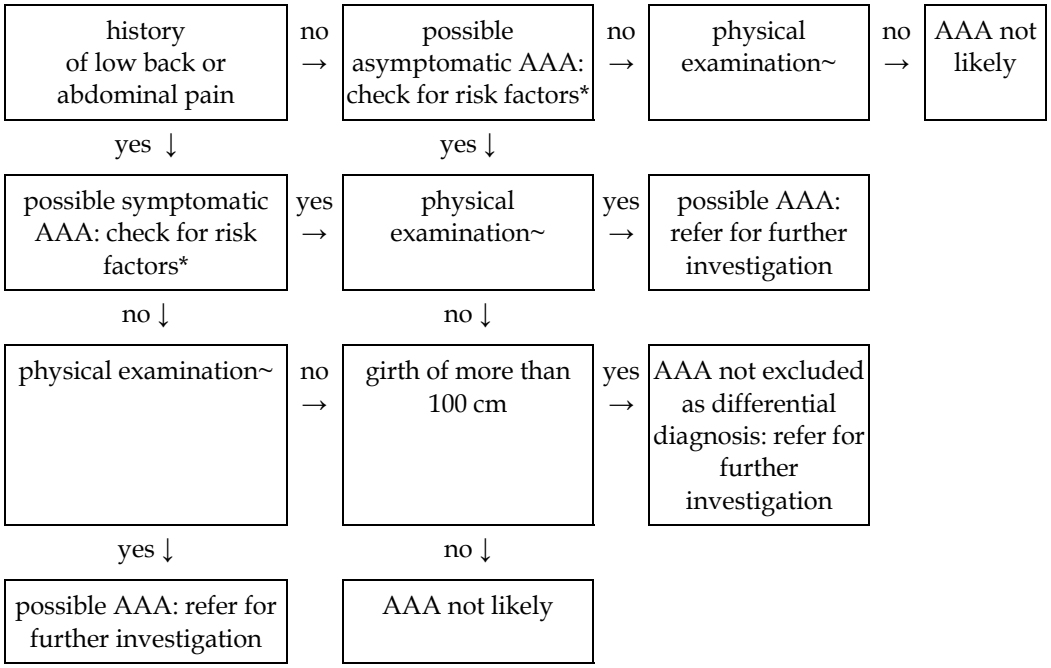
Palpation of the lower extremity pulses is also important, even though it is often unremarkable (Thorkeldsen, 1993; Yochum, 1994; Yokomuro et al, 2008; Donahue, 1997; Engel, 1996). Peripheral aneurysms increases suspicion of AAA; absent pulses may indicate atherosclerosis: another risk factor for AAA (Patel & Kettner, 2006; Pierce, 1998). The abdominal aorta can be palpated at or slightly above the umbilicus in the epigastrium in the supine position with the knees bent. In the case of AAA, a prominent and often nontender, mass with pulsations or thrills is felt in the coronal as well as the sagittal plane (Ahlawat & Cuddihy, 2002; Patel & Kettner, 2006; Hadida & Rajwani, 1998; Pierce, 1998). Pulsations of an AAA tend to push more laterally than anteriorly (Cates, 1997).

In thin people, an abdominal pulse can easily be felt. But the accuracy of detecting AAA is dependent upon the patient's girth as well as the size of the aneurysm. When the patient's girth is 100 cm or greater, very few AAAs are palpable. However, as aneurysm size increases, the chance of clinical detection increases. The sensitivity of detecting an AAA with a diameter greater than 5cm in a patient with an abdominal girth of less than 100cm is 100%, but this percentage decreases quickly with a smaller aneurysm (Fink et al., 2000). Karkos et al. (2000) found that physical examination missed more than a third of those detected radiologically, but they also say that clinical examination still plays a paramount role in the detection of AAAs. Physical examination cannot be relied upon to exclude AAA. If the history has enough signs and risk factors present, a referral for an ultrasound evaluation may be warranted (Lynch, 2004).

Another screening tool for AAA that is always mentioned is auscultation for an abdominal or femoral bruit. Lederle et al. found that it does not contribute to the diagnosis of AAA. It is, however, part of the routine in many case reports. A negative physical exam in a patient with a girth of more than 100 cm with risk factors of AAA present still warrants referral for ultrasound evaluation (Ahlawat & Cuddihy, 2002; Mechelli et al., 2008; Hadida & Rajwani, 1998; Pierce, 1998).

5. Implications for treatment of the accompanying musculoskeletal complaints

The significance of AAA to the therapist treating the patient is the potential for rupture during treatment (Beck et al., 2005). In the case of a large AAA, lumbar spinal manipulative therapy is an absolute contra-indication. It is, however, likely that patients with smaller AAAs and mechanical low back pain are receiving spinal manipulative therapy. Knowing the prevalence of AAA, it seems reasonable to assume that many patients have been treated without detrimental effect. It is, however, important to modify the techniques for patients who are considered at high risk after history taking. It is advised to minimize torsional stress to the lumbar spine and use more graded mobilisation or manipulation during exhalation, to decrease the intra-abdominal pressure (Weston, 1995). In the clinical setting, management of patients with AAA is limited (Pierce, 1998). A delay in referral in order to offer a trial of spinal manipulative care is unacceptable (Crawford et al., 2003). Table 1 gives an outline of the steps to be taken in clinical practice.



~ physical examination includes: blood pressure, pulsating mass in abdomen, peripheral aneurysm
* risk factors include: age over 50, male gender, Caucasian, smoking, positive family history, co-existing cardiovascular disease

Table 1. Flow sheet Aortic Abdominal Aneurysm in clinical practice

6. Conclusion

Abdominal aortic aneurysms can be very difficult to identify. Careful history taking and case finding is important to decrease the chance of missing the diagnosis. Presentation can vary from totally asymptomatic to excruciating pain. Combining these with the risk factors gender, age, history of smoking and family history of AAA will furnish a good indication for the physical examination and possible referral for further screening.

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3

Screening for Abdominal Aortic Aneurysm

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1. Introduction

A fast-growing body of literature is providing evidence in favor of screening men for abdominal aortic aneurysm (AAA). Several large, randomized trials published in the past few years have consistently shown that screening reduces AAA-related mortality.[18]

2. Cost-effectiveness of screening

Longer-term mortality benefit and cost-effectiveness for abdominal aortic aneurysm (AAA) screening are uncertain.[18]
In addition to the mortality benefit, evidence indicating that screening is highly cost-effective is increasing.[2, 34] In light of this evidence, national screening programs are now being considered in many countries.[47, 46]
However, there is little evidence regarding long-term outcomes after AAA screening; almost all of the evidence from randomized trials is limited to the first 4 years after screening.[18]
It is therefore expected that cost-effectiveness of screening will improve over time.[18]
It is expected that the lifetime cost-effectiveness of screening will be highly favorable. Furthermore, these results show that the mortality benefit of an approximate 50% reduction in AAA-related death in patients invited to be screened is maintained at 7-year follow-up. The risk for AAA rupture remains low in patients with normal results on initial screening.[18]
Patients with AAA detected in selective screening at the vascular laboratory had a high level of morbidity and inferior long-term survival when compared with the general population. Elective AAA repair rate was lower in this group than in patients with AAA detected in general screening programmes, with an acceptable perioperative mortality rate. Despite these factors, selective screening for AAA among patients referred to the vascular laboratory for suspected arterial disease was cost-effective under most assumptions with an estimated ICER at base-case of 11 084 Euro/LYG compared with non-screening.[28]
Screening appears to reduce hospital AAA mortality and to be cost-effective.[25]
The benefit of inviting men aged 65-74 to screening for abdominal aortic aneurysm continues at about the same rate 7-10 years after screening, as observed in previous years. The reduction in number of deaths related to abdominal aortic aneurysm in MASS is estimated as 42% at four years[34], 47% at seven years[18], and now 48% at 10 years. This is surprising as it might be expected that ruptures of the aneurysm in those originally screened as normal and incidental detection of abdominal aortic aneurysm in the control group would erode the benefit over time.[45]

A crucial problem is the extent to which those screened as normal will go on to develop an aneurysm that ruptures and whether rescreening of participants after a normal scan is justified at any stage.[45]

Women are generally not considered a suitable target population for abdominal aortic aneurysm (AAA) screening. The main reason is not only the low prevalence of AAA but also a development of the disease later in life and an inferior relative long-term survival in women with AAA. However, other aspects of the disease, such as the higher rupture rate, indicate that AAA in women may be more severe than in men. Screening reduced the AAA rupture incidence by 33% and the AAA-related death rate by 35%. The cost per life year gained was estimated at $5911. The incremental cost-effectiveness ratio was similar to that found for screening men, which reflects the fact that the lower AAA prevalence in women is balanced by a higher rupture rate. Screening women for AAA may be cost-effective, and future evaluations on screening for AAA should include women.[50]

Cost-effectiveness was rather insensitive to variations in prevalence >1%. Below this level, however, the cost per life year gained increased rapidly.[50]

The rupture rate has a large impact on the cost-effectiveness of a screening program,10 and the higher rupture rate among women compensates for the lower prevalence and reduces the cost per life year saved by 64%.[49]

The sensitivity analysis showed, however, that the incremental cost per life year gained was lower than what is generally considered cost-effective, even if the rupture rate among women with AAA was assumed to be the same as for men.[50]

The life expectancy of the screened individuals is a key variable for the cost-effectiveness ratio.[49]

The incremental cost per life year gained for screening all 65-year-old women for AAA was lower than what is generally considered cost-effectiveand was similar to that for screening men at the same age.This reflects the fact that in women, a low prevalence is balanced by a high rupture rate.[50]

3. Treatment decisions

The major problem with AAAs is the risk of rupture. AAA is often asymptomatic and if left undetected they will continue to expand and may eventually rupture.[11]

Decisions about the treatment of AAAs are traditionally based upon the maximum cross-sectional diameter. If the AAA diameter is 5.5 cm or larger then intervention is generally deemed appropriate.[11] The diameter of an AAA is a well established objective criterion for selecting patients for treatment and when assessing the results following endovascular repair.[11]

New treatments for abdominal aortic aneurysm may impact on a national screening programme and increase its effectiveness. Endovascular repair of aneurysms rather than conventional open repair is now used more widely for elective surgery but was used for only 9% of the elective procedures in MASS. In patients who are fit for open repair, and anatomically suitable for endovascular repair, endovascular repair has lower operative mortality than open repair and fewer deaths related to abdominal aortic aneurysm in the longer term[10, 12, 13, 21]; it may therefore be preferred by both patients and surgeons. Reliable evidence comparing endovascular repair of abdominal aortic aneurysms with open repair is currently available only up to four years of follow-up; it shows no difference in all cause

mortality[21] but a substantial incidence of graft problems (for example, leaks around the graft or movement of the graft) and need for reinterventions after endovascular repair.[13, 10]
The quality of life data collected in the trial around the time of screening showed no clear adverse or beneficial effects of screening or any long term effects after surgery.[34, 29]
Patients with a detected AAA have yearly revisits to follow the expansion of the aneurysm. They are offered elective open surgery, if they are healthy enough, when the AAA has grown to >55 mm, has expanded rapidly, or has caused symptoms. Some patients with detected AAA fulfill the criteria for elective surgery at the time of screening and will be offered surgery as soon as possible.[50]

4. Age and screening

The prevalence also depends on the age of the screened population. However, the present lack of age-specific prevalence data in women makes a more precise analysis of the optimal screening age difficult.[50]
The results suggest that aortic screening may be worthwhile extending to a wider age band. By focusing follow-up, this should give greater value for younger men in terms of community productivity and allows for selective intervention in the elderly.[32]
The United States Preventative Services Task Force (USPSTF) recommends one-time screening for AAAs in men 65 to 75 years of age who have ever smoked and recommends against routine screening in women, and the Screening Abdominal Aortic Aneurysms Very Efficiently Act supports only a screening program for AAA in male ever- smokers when they turn 65 years old.[5]
The mortality benefit of screening men aged 65-74 for abdominal aortic aneurysm is maintained up to 10 years and cost effectiveness becomes more favourable over time. To maximise the benefit from a screening programme, emphasis should be placed on achieving a high initial rate of attendance and good adherence to clinical follow-up, preventing delays in undertaking surgery, and maintaining a low operative mortality after elective surgery. On the basis of current evidence, rescreening of those originally screened as normal is not justified.[45]
The reduced benefit of screening elderly males is due to the reduced life expectancy and to the demonstrated increased mortality after AAA repair.[30]

5. Sex and screening

Among men, the rupture risk of an AAA was estimated at 0.8% per year among those with an AAA attending a screening and 1.9% among those with an AAA not attending a screening or not invited to a screening.[49] Women were estimated to have a threefold higher rupture risk than men.[37] Thus, the corresponding annual rupture risks were 2.4% and 5.7%, respectively, for women with AAA. Sixty-five percent of men with ruptured AAA die before surgery, and an additional 14% die during surgery, corresponding to an operative mortality of 40%.[49]The rate of surgery for ruptured AAA was lower for women[50] and the operative mortality was higher. Thus, the total mortality for AAA rupture was estimated at 86.3% for women compared with 79% for men.[50]
The Chichester screening trial is the only published evaluation of screening for AAA in women. Some 9342 women aged 65 to 80 years (mean age, 72 years) were randomized, with no difference in rupture rate between the screened and the control groups after 10 years

follow-up. The authors concluded that it was neither clinically indicated nor economically rational to screen women.[40] However, a possible limitation that is likely to counteract the possible benefits of screening women is the biased mortality data based on official statistics. With a low autopsy rate, the reliability is limited in determining mortality rate from ruptured AAA. The autopsy rate has decreased to an overall 11% in Sweden, and is almost nonexistent among women >80 years old.[1]

Among 2257 AAA patients enrolled in the UK Small Aneurysm Trial (UKSAT) or Small Aneurysm Study, the risk of rupture was, independently of age and initial AAA diameter, associated with female sex. The rupture rate was three times higher in women compared with men. [37]

Only one RCT, the Chichester trial, included women (n = 9342) aged 65‑80 years old. In this trial, the prevalence of AAA >3 cm among women (1.3%) was substantially lower than in men (7.6%). The subgroup analysis addressing the effect of screening in women concluded that screening followed by surgery did not reduce mortality.[41]

In women, the incidence of ruptured AAA was similar in the control and screening groups, and in general the incidence of death from ruptured aneurysm increased with age, since more than 70% of ruptures occurred among women > 80 years.[41]

On the basis of the low prevalence of AAA in women and the unfavorable RR, screening of women may not be beneficial or cost effective.[41]

The evidence available from the Chichester trial regarding the effect of population screening in women should be considered with caution because of the possibility of confounding factors or biases. The gender analysis was a subgroup analysis and, as expected, the number of participating women was considerably lower than men. Since the risk factors associated with increased risk for surgery are the same as those associated with increased incidence of AAAs, it is possible that many women were excluded, giving a falsely lower incidence of AAAs (ascertainment bias).[5]

Before making a final decision on the effectiveness of AAA screening in women, a number of features unique to women should be considered. The lower prevalence of AAA in women is most likely due to their lower burden of risk factors compared with men. The evidence supports that like in men, for women the probability of AAAs is increased among smokers (odds ratio (OR) 3.8), those aged >70 years (OR 1.8), family history (OR 2.6), and pre-existing cerebrovascular disease (OR 3.20).[20]

Like coronary heart disease, the increase in prevalence of AAA among women appears to occur approximately one decade after men. Because of this 10-year delay in onset, and lower burden of AAAs likely due to the currently more favorable cardiovascular risk factor profile of women, the cost effectiveness of screening and repair of AAA to prevent death does not favor screening at present.[5]

However, we must also consider the observation that although women have a lower incidence of AAA, when they are found to have an AAA > 3 cm the risk of rupture is greater than that of men, [33, 6] and mortality associated with surgery for ruptured aortic aneurysms is higher compared with that in men.[41]

This higher risk of rupture in women may be because the prevalence of the disease was defined as an aorta with a diameter >3 cm, which is the usual threshold used for men, and it does not take into account the smaller size of a normal aorta in women. Thus, an aneurysm of 5 cm in a woman may have a higher rupture rate because it is equivalent to an aneurysm of 6 cm in a man. Given the state of the evidence, a number of outstanding issues should be

considered for the screening of AAA in women. First, the evidence does not support population-based screening over 65 years of age, due to the low incidence of AAA. However, it would be reasonable to recommend targeted screening of 'higher risk women', including those of an older age, who are current or had a long history of smoking, as well as those with co-existing vascular disease.[5]

In men, an AAA diameter of 55 mm generally justifies elective repair, whereas it has been suggested that women may benefit from a lower threshold for surgery. A lower threshold diameter for surgical repair in women (≤50 mm) may reduce the difference in surgery rate and the likelihood of an AAA to rupture. In the UKSAT, the mean AAA diameter at rupture was 50 mm for women and 60 mm for men. They concluded that different thresholds should apply to women than men when AAA repair is being considered.[37] In the Chichester trial, however, a threshold diameter of 60 mm did not result in higher rupture rate.[40]

The relative long-term survival after surgery for AAA was found to be better in men than in women, although the crude long-term survival was similar between men and women, because women in general have a longer life expectancy. The assumed additional relative mortality in women with AAA compared with men increased the cost per life years saved by 30%.[50]

the decrease in AAA-specific mortality among women invited to screening was only 32% compared with 50% among men. The explanation lies in the complex relations between mortality, risk of rupture, and risk of elective surgery. If women had an identical compliance and rupture rate as men, the model would generate a decrease in AAA-specific mortality of 43%.[50]

6. Size of aneurysm

Within group of detected aneurysms, surveillance involved rescanning: annually for those with diameters of 3.0-4.4 cm and every three months for those of 4.5-5.4 cm. Patients were referred to a hospital outpatient clinic for possible elective surgery when the aneurysm reached 5.5 cm, the aneurysm had expanded by 1.0 cm or more in one year, or symptoms attributable to the aneurysm were reported.[45]

The prevalence of the disease is, however, highly dependent on the definition used.[26] In most population-based screening studies including women, an AAA was defined as the maximum infrarenal aortic diameter being ≥30 mm, as proposed by McGregor.[31] Because the normal aortic diameter differs by gender,[44] a fixed diameter may not be an optimal definition of AAA and may partly explain the differences seen in prevalence between men and women.

In the Chichester trial, four of the 10 women from the screened group who had AAA rupture or emergency repair initially had a normal scan.[40] This may be the result of how an AAA was defined, where a fixed diameter may result in false-negative findings, or a consequence of the natural history of AAA development among women.

7. Rescreening

Two of the RCTs looked at the need for rescreening in individuals with <3 cm AAA: the Viborg trial repeated an ultrasound examination (USE) 3 to 5 years after the first one and found that new AAA > 3 cm occurred in 28% (95% CI 21-35), but none were clinically

significant (the largest <48 mm); and the Chichester trial rescreened patients with aortic diameter <3 cm every 2 years and identified 4.1% AAA, which were all <3.8 cm in diameter.[30]
Recommending rescreening those with an initial normal scan would only become justified in subsequent years if future analyses show that there is a further noticeable increase in ruptures in this group that is not sufficiently offset by the reduction in number of deaths related to abdominal aortic aneurysm for those with an aneurysm detected (or rendered unimportant by the overall toll of mortality from all causes).[45]

8. Psychological effects of screening

The offer of screening causes transient psychological stress in subjects found not to have AAA. However, diagnosis of an AAA seems to impair QL permanently and progressively in conservatively treated cases. This impairment seems reversible by operation. Nevertheless, the impairment seems considerable, and must be considered in the management of AAA and in the final evaluation of screening for AAA. [26]
Several concerns have been raised about the utility of population-based screening for AAA. It has been proposed that patients who are found to have "small" aneurysms will experience a diminished quality of life related to concern about rupture.[17]
For strategies toward other target groups, and management of small AAAs, prediction models and cost-effectiveness analyses are needed to provide guidance.[14]

9. Family history and screening

The ADAM study found that a family history positive for presence of AAA is associated with a two-fold increase in the risk of having an AAA with no difference between men and women.[30]
Familial AAA do not expand faster nor are they associated with unusual locations, but they may occur earlier in life. Screening causes psychological side effects, and it could therefore be offered to male first-degree relatives from the age of 60, and be confined to ultrasonographic scanning of the infrarenal abdominal aorta at five-year intervals. [23]
Aging brothers of patients with known abdominal aortic aneurysm have the highest risk for developing the disease; the prevalence of the disease in siblings older than 60 years of age is 18%.[39]
Ultrasonographic screening is recommended in brothers (50 years) of patients with aneurysms of the abdominal aorta.[4]

10. Screening methods

10.1 Physical examination

A focused physical examination has been investigated as a screening tool to identify AAA. Sensitivity has been reported in the range of 76% to 85% and specificity 85% for AAA >5 cm with moderate interobserver agreement (kappa = 0.5).31 The diagnostic properties of physical examination require further investigation.[30]

10.2 Ultrasonography

Ultrasonography is the detection method of choice for AAA screening: it is cheap and noninvasive and can be used easily in a community setting.[36]

Results from a large, pragmatic randomized trial show that the early mortality benefit of screening ultrasonography for AAA is maintained in the longer term and that the cost-effectiveness of screening improves over time.[18]
Ultrasound screening to identify abdominal aortic aneurysms (AAA) >5cm followed by surgery reduces cause-specific mortality among individuals older than 65 years. This benefit is not apparent among men older than 75 years, 5 and there is some controversy regarding the benefit of screening for AAA among women.[5]
The United Kingdom Multicentre Aneurysm Screening Study (MASS)[18,46] has provided most of the worldwide randomised evidence for the mortality benefit after ultrasound screening for abdominal aortic aneurysm.[8, 16] The UK screening programme for men aged 65 is based closely on the protocol and procedures in MASS. Some uncertainties relating to screening remain, however, including its long term benefit in terms of mortality and cost effectiveness, whether rescreening those with a previously normal scan is warranted, and the extent to which incidental detection of abdominal aortic aneurysm erodes the benefit of a systematic screening policy over time. It might be expected that the mortality benefit seen in the early years after one-off screening would decrease over time. MASS, started in 1997, runs more than 10 years ahead of the UK national screening programme and is uniquely positioned to tackle these uncertainties and to inform the development of the national programme.[45]
The neck of the aneurysm and suprarenal aorta might be more difficult to visualize with ultrasonography, and most ultrasound screening studies report only the maximum anterior-posterior diameter. However, ultrasonography also can provide information about the size and shape of the luminal thrombus in an AAA and the presence of iliac aneurysms.[36]
It is able to define the diameter of the infrarenal aorta in 98% (95% CI 92-94) of individuals, with a sensitivity and specificity of 100% and 98%, respectively. The correlation between observers for ultrasound measurements of the abdominal aorta is high (Spearman coefficient = 0.99), but abdominal girth reduces the precision of the measurement.[30]
Abdominal palpation has only moderate overall sensitivity for detecting AAA, but appears to be highly sensitive for diagnosis of AAAs large enough to warrant elective intervention in patients who do not have a large girth. Abdominal palpation has good sensitivity even in patients with a large girth if the aorta is palpable.[15]
Many large AAAs currently remain undetected until rupture, and many small AAAs that will never rupture are detected incidentally and repaired, with some resulting morbidity and mortality. Both scenarios contribute to aortic aneurysms remaining a leading cause of death. Recent randomized trials have demonstrated a substantial reduction in AAA-related mortality from ultrasonographic screening and resulting elective repair. If the U.S. Preventive Services Task Force recommends AAA screening, health plans, including Medicare, will probably follow with coverage and the era of AAA screening will begin. Meanwhile, it is reasonable to offer 1-time ultrasonographic screening to men 65 to 79 years of age who have ever smoked, especially if elective repair can be reserved for AAAs 5.5 cm or larger. If screening is accompanied by prudent use of elective repair, the mortality associated with AAA may at last be reduced. [19]

10.3 Computed tomography (CT) scan

The accuracy of radiographers in performing AAA CT measurements is encouraging. Variability exists for both professions, and in some instances may be clinically significant.

Observers should be aware of measurement variability issues and have an understanding of the factors responsible. Careful and repeat measurements of AAAs around 5.5 cm are recommended in order to define treatment.[11]
A good level of agreement exists between radiologists and radiographers in performing CT measurements of maximum AAA diameter. Variability for both professions does exist and can be significant in certain situations, observers should be aware of the existence of variability especially when making treatment decisions. It is technically feasible for radiographers to perform such measurements, whether this area of role extension should be explored needs further investigation. Understanding the factors which play a role in observer variability is paramount; variability may be decreased if using standardised measurement protocols, 3D techniques and computer-assisted measurements. If the latter is to be accepted then these measurements will require validation and clinical checking before prescribing treatment.[11]

10.4 Magnetic Resonance Images (MRI)

It seems that MRI screening of older men with LBP for AAA, especially in smokers or patients with a recent history of smoking, is advantageous. Further studies are needed to determine the best modality and the most feasible method of screening.[42]

10.5 Plasma levels of plasmin-antiplasmin-complexes

Three proteolytic systems seem involved in the aneurysmal degradation of the aortic wall. Plasmin is a common activator of the systems and could thus be predictive for the progression of abdominal aortic aneurysms (AAAs).[24]
The levels of elastase have been found elevated in the circulation and aneurysmal walls compared with those with aortic occlusive atherosclerosis.[3, 7, 9]Furthermore, circulating levels of Cystatin C B, the major inhibitor of cysteine proteases, have been reported decreased in aneurysmal cases compared with a sex-matched and age-matched control group.[43] Finally, the levels of various metallodependent proteases (MMPs), especially MMP2 and MMP9, have been found elevated in aneurysmal aortic walls compared with aortic walls of occlusive atherosclerosis[35, 38], and we have earlier reported a positive significant correlation between the plasma level of MMP9 and the expansion of small AAAs.[27]The progression of AAA is correlated with the PAP level, which seems to have a predictive value similar to the best serologic predictor known, serum-elastin-peptides.[24]

10.6 Genetic screening

Nine functional positional candidate genes on AAA1 locus on chromosome 19 were investigated. Two of the genes, *CD22* and *PEPD* showed modest level of evidence of being involved in AAA pathogenesis. This evidence came from a nominal association of SNPs residing in these genes to AAA, identification of novel sequence changes and expression of these proteins in aneurysmal tissue. If replicated in independent studies, the findings provide important information about AAA pathogenesis. Association testing of the functional positional candidate genes on the AAA1 locus on chromosome 19q13 demonstrated nominal association in three genes. *PEPD* and *CD22* were considered the most promising candidate genes for altering AAA risk, based on gene function, association evidence, gene expression, and protein expression. [22]

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4

Color-Doppler Ultrasonography in the Monitoring of Endovascular Abdominal Aortic Aneurysm Repair

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1. Introduction

The introduction of endovascular stent-graft repair for aortic aneurysm has engendered considerable enthusiasm and interest from vascular specialist. With progressive improvement in imaging, clinical experience, and stent-graft design, and the use of adjuvant procedures, a substantial number of patients are now candidates for endovascular repair of an aortic aneurysm. Endoluminal aneurysm repair, however, currently is at a critical point. Unquestionably, endoluminal aneurysm repair can reduce substantially the need for intensive care and length of hospital stay, and survival is reportedly improved when compared with open repair. Although the use of stent-grafts for the treatment of thoracic and abdominal aneurysms has increased dramatically there is little midterm or long-term proof of its efficacy. Endovascular aortic aneurysm repair (EVAR trial participants, 2005) has an initial postoperative benefit versus open AAA repair as a result of decreased early morbidity and mortality (EVAR trial participants. 2005; Lederle et al., 2007). However, as shown in EVAR trial 1 (EVAR trial participants, 2005), stent-graft-related complications are observed in approximately 40% of patients within 4 years after EVAR, resulting in a 20% reintervention rate to reduce the ongoing rupture risk. Persistent blood flow into the aneurysm sac and outside the graft lumen (endoleak) represents the most frequent complication after EVAR and is considered a procedural failure, since it is associated with aneurysm enlargement and possible rupture. The reported incidence of endoleaks ranges from 10% to 45%, and lifelong surveillance is required for early detection and treatment.

As with the entire field of endovascular surgery, imaging techniques and recommendations regarding their use are changing rapidly. Only long-term follow-up data determine which methods will become standard. Currently, the imaging modalities best suited to achieve the above goals are plain film radiographs of the abdomen (chest) and CT angiography with specialized 3D reconstruction protocols (Fig. 1). In centers of excellence, color or power-Doppler ultrasound is a useful adjunctive modality and ultimately may decrease the required frequency of more expensive studies such as CT. The modalities for postoperative imaging of endoleak may be surrogate or direct (May et al., 2005). The surrogate modalities include plain abdominal x-ray and measurement of AAA diameter by B-mode ultrasound or CT. Because the majority of endografts have a radio-opaque metallic frame, a plain abdominal x-ray is a useful investigation (Fig. 2). It may demonstrate faulty fixation more

clearly and earlier than contrast CT, and it may lead to the detection of endoleaks. The accuracy of detecting migration can be improved by following a protocol of performing A-P, lateral, and oblique views at the level of the umbilicus. Studies have confirmed that the presence of an endoleak is usually associated with an increase in the size of the aneurysm sac. Measurement of AAA diameter by B-mode ultrasound can therefore be used as a surrogate method of detecting endoleaks. CT may also be used for a similar purpose, with the option of monitoring an increase in volume of the sac in addition to the diameter of the sac. The direct methods of imaging for endoleaks include CDU, contrast-enhanced CT, and angiography. Contrast-enhanced CT has been accepted as the gold standard for detecting the presence of an endoleak. Once an endoleak has been detected, however, carefully planned arteriography is more useful in characterizing the origin and nature of the endoleak. CDU has the advantage of imaging type II endoleaks in real time, as distinct from contrast CT and arteriography, both of which have to ray on accurate timing to image the contrast arriving in the sac via collateral circulation (Prinssen, 2004).

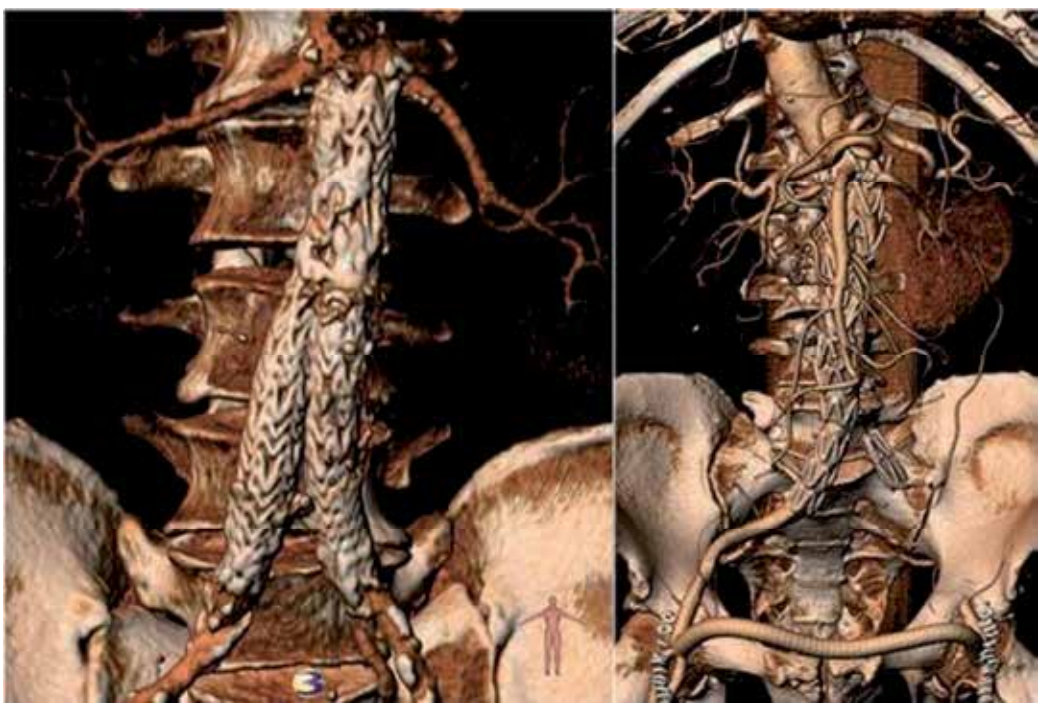

Fig. 1. CT angiography with 3D reconstruction. *Left*: Excluder bifurcated endoprosthesis (W.L. Gore and Associates Inc, Flagstaff, Ariz). *Right*: Talent aortouniiliac endoprosthesis (Medtronic Ave, St. Rosa, Cal), left common iliac occluder and femoro-femoral crossover bypass.

The goals of postprocedural imaging are to confirm and redocument the appropriate placement of the stent-graft, to assess better the effectiveness of the stent-graft in initially excluding the AAA (detecting flow in the sac), to follow the long-term fate and size of the AAA sac and ensure its stability, to detect remote stent-graft failure (structural or functional) and to better characterize and possibly treat any endoleaks. Increase in aneurysm size after EVAR is associated with an increased risk of AAA rupture and may

require reintervention or conversion to open repair to prevent AAA rupture. Imaging evaluation should be able to show aneurismal size, changes in aneurysm size, position of stent-graft, evidence of change in position of the endoprosthesis, structural integrity of the device, endoleaks and change in the characteristics of the endoleak.

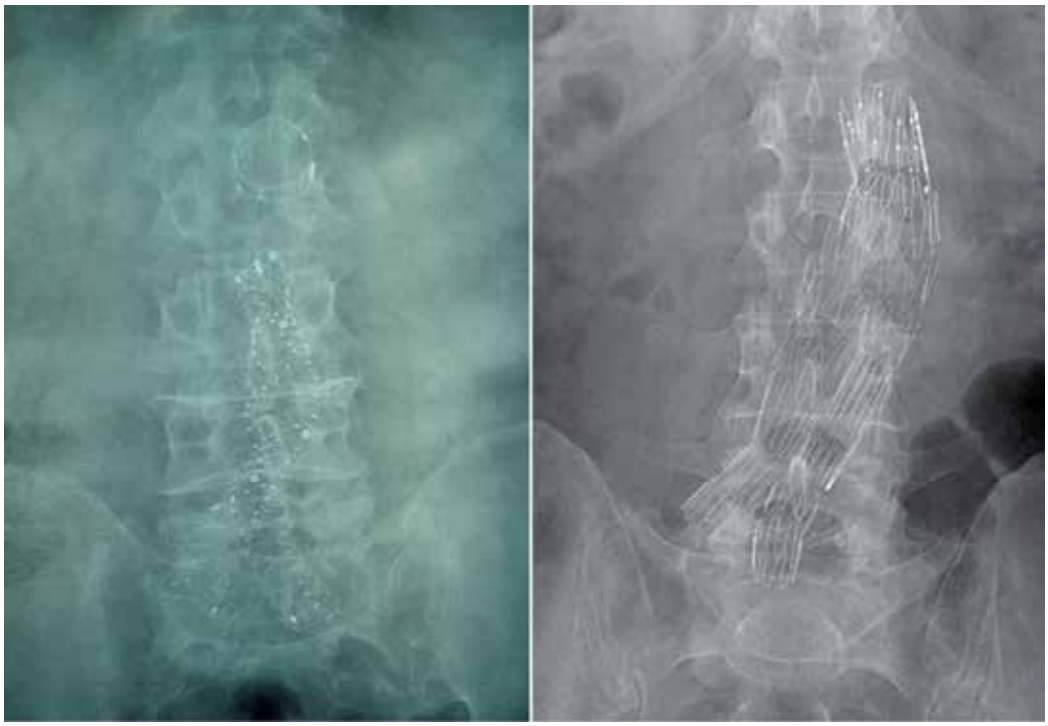

Fig. 2. Plain abdominal x-ray. Left: Anaconda bifurcated endoprosthesis (Vascutek Inc., a Terumo Company, Renfrewshire, Scotland, UK). Right: Zenith bifurcated endoprosthesis (Cook Medical Inc., Bloomington, Ind).

2. Endoleak after EVAR

In addition to preoperative imaging, adequate surveillance imaging modalities capable of detecting complications and treatment effects, are necessary. Follow-up imaging is directed toward repeated assessment of the aneurysm size, detection of endoleaks, and monitoring of the structural and positional integrity of the stent-graft.

An endoleak is a condition associated with endovascular stent-grafts, defined by persistent blood flow outside the lumen of the stent-graft but within the aneurysm sac or adjacent vascular segment being treated by the stent-graft. Endoleaks are usually associated with nonregresion or even expansion of the AAA. An endoleak is evidence of incomplete exclusion of the aneurysm from the circulation. There is evidence that an endoleak may resolve spontaneously, but a proportion of those that do persist are associated with late aneurysm rupture. Although intrasac pressure may approach systemical arterial pressure in the presence of an endoleak, some type II endoleaks have been associated with a decrease in aneurysm volume and intrasac pressures that are substantially less than systemic pressures (Van Sambeek, 2004). With or without an endoleak, an aneurysm that does not decrease size

during follow-up cannot be considered to be adequately treated. Under these conditions, regular monitoring is required until definitive exclusion of the AAA is achieved. An endoleak can be classified according to the time of occurrence. An endoleak first observed during the perioperative (<30 days) period is defined as a "primary endoleak", and detection thereafter is termed a "secondary endoleak". Further categorization requires precise information regarding the course of the blood flow into the aneurysm sac (Table 1). CDU could enable a better understanding of the mechanisms underlying some endoleaks and may provide more precise analysis in cases involving endoleaks due to collateral recirculation.

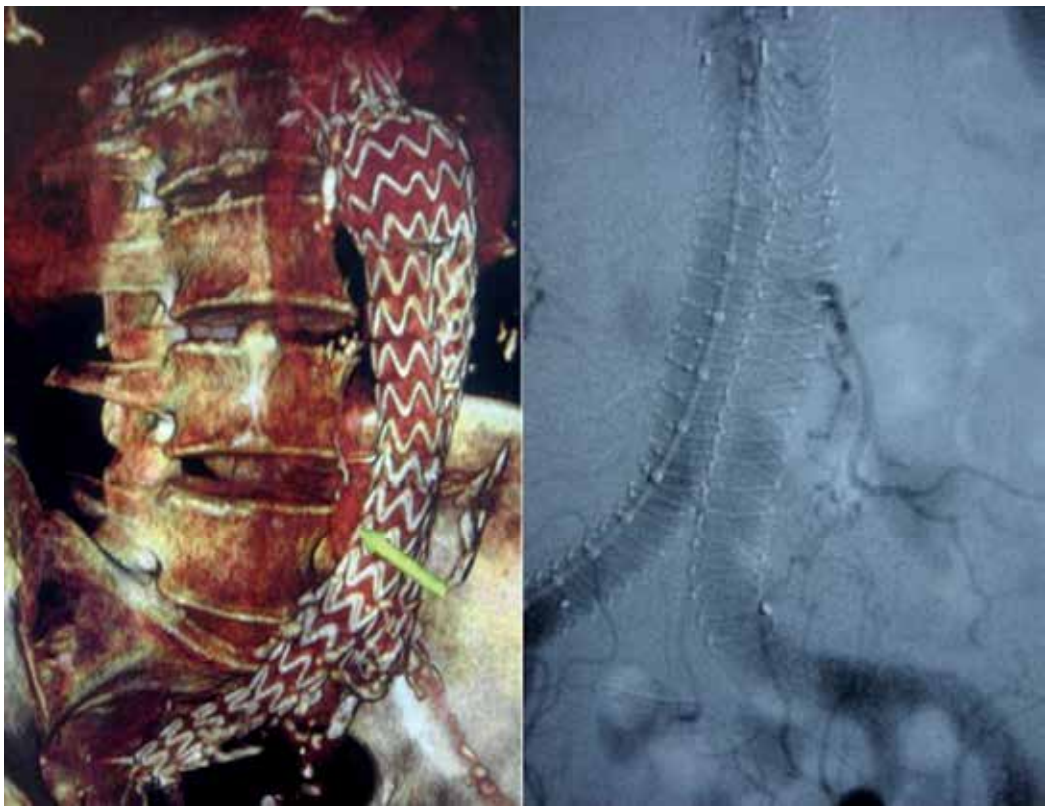

Fig. 3. *Left*: CT angiography with 3D reconstruction. Endurant bifurcated endoprosthesis (Medtronic Ave, St. Rosa, Cal) with a type II endoleak originated from the inferior mesenteric artery, yellow arrow. *Right*: Arteriography. Anaconda bifurcated endoprosthesis (Vascutek Inc., a Terumo Company, Renfrewshire, Scotland, UK) with a type II endoleak originated from a left lumbar artery.

A type I endoleak is indicative of a persistent perigraft channel of blood flow caused by inadequate seal at either the proximal (Ia) or distal (Ib) stent-graft end or attachment zones. In the case of an aorto-mono-iliac prosthesis, a type I endoleak may also refer to blood flow around an iliac occlude plug (Ic). A type II endoleak is attributed to retrograde flow from the inferior mesenteric artery (IIa), lumbar arteries (IIb), or other collateral vessels (Fig. 3). Origin and outflow sources of a type II endoleak could be specified, such as lumbar-lumbar, lumbar-inferior mesenteric artery (IMA), accessory renal-lumbar/IMA, hypogastric-

lumbar/IMA, or undefined. It should be emphasized that any connection with a proximal or distal attachment zone will classify the endoleak as a type I endoleak. Flow hemodynamics of type II endoleaks affect the endoleak´s persistence and treatment outcome. Therefore, a new, more detailed classification of leaks, particularly type II endoleak, is required that is based on Doppler waveforms and flow velocities (Fig. 4).
A type III endoleak is caused by a component disconnection (IIIa) or fabric tear, fabric disruption, or graft disintegration (IIIb). Type IIIb endoleak can be further stratified as minor (<2mm) or major (>2mm). A type IV endoleak is caused by blood flow through an intact but otherwise porous fabric, observed during the first 30 days after stent-graft implantation. This definition is not applicable to fabric-related endoleaks observed after the first 30-day period. Type V endoleaks are those in which bloodflow can be visualized within the aneurysm sac but the source cannot be identified. If an endoleak is visualized in imaging studies but the precise source cannot be determined, the endoleak is categorized as an endoleak of undefined origin. It is recognized that an AAA can continue to enlarge after endovascular repair, even in the absence of a detectable endoleak, and that this enlargement may lead to aneurysm rupture. This phenomenon is currently defined as "endotension". Explanations for persistent or recurrent pressurization of an aneurysm sac include blood flow that is below the sensitivity limits of detection with current imaging modalities or pressure transmission through thrombus or stent-graft material.

Type	Cause of perigraft flow
I	Inadequate seal at proximal end of endograft
	Inadequate seal at distal end of endograft
	Inadequate seal at iliac occluder plug
II	Flow from a collateral vessel (lumbar, IMA, accessory renal, hypogastric) without attachment site connection.
III	Flow from a modular disconnection
	Flow from an inadequate seal at modular junction
	Flow from a fabric disruption
IV	Flow from porous fabric (less than 30 days after graft placement)
V	Flow visualized but source unidentified

Table 1. Classification of endoleak. Modified from Chaikof et al., 2002.

The origins of the endoleaks were also correctly identified with duplex. Sac refilling by a lumbar artery or the IMA is readily visualized by color coding, which also determines flow direction. It is then relatively easy to differentiate a type I proximal endoleak from a type II endoleak. One difficulty, however, remains with distal attachment sites where reverse flow can also be demonstrated without aneurysm sac reperfusion and be labeled as a distal type I endoleak. CDU appears to be an excellent tool for the evaluation of high-flow endoleaks within the aneurysm sac; however, it appears limited in making the distinction between type I and type III endoleaks.

3. Ultrasound surveillance after endovascular aneurysm repair

The most reliable diagnostic alternative to CTA in post-EVAR life-long surveillance is still heavily debated. CDU imaging is routinely used in vascular screenings because it is easy to perform, inexpensive, portable, safe, and widely available. This technique performs poorly

in endoleak detection, with high false-negative and false-positive results, principally due to echo reflection by the metallic portion of stent-graft, presence of calcifications, meteorism, obesity, and slow endoleak flow, which does not allow distinction of color signals coming from vessel walls and surrounding tissue from those derived from corpuscular hematic components.

The use of CDU as the preferred imaging modality in the follow-up of patients can reduce the biologic hazards associated with CT angiography (Carrafiello et al., 2008). The EVAR procedure and lifelong annual CT follow-up carry a substantial ionizing radiation burden. Patients receive a total effective dose of approximately 60mSv within the first year after EVAR, taking into account procedure-related fluoroscopy and follow-up CT angiography. The mean effective dose of CT angiography for EVAR follow-up is approximately 15 mSv. The stochastic risk of a fatal radiation-induced tumor is estimated to be 5%/Sv radiation. Therefore, the risk of cancer induction of one CT angiography procedure is approximately 1 in 1,500 (International Commission on Radiological Protection, 2007), indicating the relevance of reliable alternatives to annual CT angiography for post-EVAR follow-up, particularly in younger patients. Second, CT angiography requires the administration of iodinated contrast agents, which are associated with nephrotoxic effects. Renal dysfunction is a comorbidity found in 80% of patients with aneurysms, and is the most important risk factor for contrast agent-induced nephrotoxicity. No major side effects, including nephrotoxic effects, have been reported for ultrasound contrast agents, which favors the use of contrast enhanced untrasound (CEUS) for post-EVAR follow-up.

The advantages of duplex ultrasound in the follow-up of patients with aortic endografts include the ability to collect accurate residual aortic sac diameter measurements serially over time. It is a very sensitive method for endoleak detection with adequate time and when a protocol is used. Ultrasound can often identify the source for endoleak classification and can readily evaluate for limb dysfunction or any other hemodynamic impairment. It is inexpensive and reproducible and requires no contrast and there may be an additive effect of CT with ultrasound in the follow-up of patients with these devices placed. The disadvantages of using duplex ultrasound may be the time commitment involved in a busy vascular laboratory. Additionally, there is a need for high-resolution equipment for the adequate performance of this examination. It is a technically challenging, subjective study that is highly dependent on the examiner and interpreter but it can be a valuable tool in the assessment of patients with aortic endografts. Ultrasound data are often influenced by the ability of the technologist as well as the quality of the equipment available. Therefore the results obtained with ultrasounds are much harder to reproduce from center to center, while CT can be easily standardized using a reproductible protocol for obtaining the scan. Unfortunately, interrogation of aortic endografts by either methodology can be challenging, with many subtleties to the images obtained. As a result, the best methodology for surveillance may not be one or the other, but a combination of the two. The unique ability of ultrasound to look at flow allows interrogation of the residual aneurysm sac around the endograft in ways that are likely not possible using conventional CT scans. The important aspects of endograft surveillance are the detection of endoleaks, changes in the endograft limbs, routine measurement of maximum aneurysm size and device migration.

The benefits of CT scan as an imaging modality compared with CDU imaging include that it is highly reproducible, less influenced by body habitus and offers faster image

acquisition. However, among the limitations of CT scans is repeated radiation exposure, potential contrast-related complications, including allergy and renal insufficiency, and high cost. CDU imaging is more accurate than CT in detecting problems that threaten graft patency, such as migration, kinking, and stenosis. Color-flow images give physiologic as well as anatomic information that CT does not. CDU imaging accurately predicted all seven cases where graft patency appeared threatened. The ability to quantify and compare serial examination in a cost-effective, contrast-free, and radiation-safe manner suggests that CDU imaging should be the gold standard for EVAR limb patency follow-up. CDU imaging can almost always accurately determine if structural defects are causing a flow-related problem and graft migration. The safety of routine triphasic CT scanning for all patients undergoing follow-up post EVAR must be questioned. Although late type II endoleaks are more likely to be picked up in the delayed post-contrast phase, there is little evidence to suggest that this translates to a clinically significant advantage, in a group of patients in whom most aneurysms remain stable or shrink following treatment. Beeman et al. (2009), showed that cost savings is substantial when CDU imaging alone is used for midterm follow-up *vs* the accepted approach that required multiple CT scans. Bendick et al. (2003a), reported that eliminating CT as a surveillance tool after EVAR would represent a 3-year cost savings of >$16,000 per patient. In fact, new surveillance paradigms have already been suggested to reduce the charges associated with EVAR. Kim et al. (2008), estimated that current reimbursement for long-term EVAR surveillance and secondary procedures using traditional protocols average a net loss of $2,235 per patient.

A systematic review by Sun in 2006 was undertaken to investigate the diagnostic value of CDU compared with CT angiography for the detection of endoleaks and measurement of the aneurysm sac (the most commonly used criteria to assess the success of endovascular AAA repair). Twenty-one studies met the criteria and were included for analysis. The results are showed in table 2. The sensitivity in the detection of endoleaks was significantly improved with contrast material-enhanced CDU compared with unenhanced CDU; however, no significant difference was found regarding the specificity, PPV, NPV, and accuracy between unenhanced and enhanced CDU. CDU was insensitive in measurement of aneurysm diameter compared with CT angiography in most situations. These results showed that CDU has not reached the diagnostic accuracy necessary to be a reliable alternative to CT angiography in the follow-up of endovascular AAA repair.

Iezzi et al. (2009), in the only prospective study to address this issue, shows CEUS imaging significantly improves the diagnostic performance of CDU imaging in endoleak detection in patients with endovascular aortic stent-grafts. Reported no significant difference in sensitivity for endoleak detection between analysis of arterial phase image alone, unenhanced and arterial phase images, and arterial and delayed phase images, after the initial follow-up at 1 month. Its sensitivity and negative predictive value are similar to multislice CTA (97.5% and 97.3%, respectively), and its specificity and accuracy are satisfactory (81.8% and 89.3%) but not ideal because the false-positive rate is nearly 10%. These findings support previous studies evaluating aortic stent-grafts by CEUS imaging vs CTA, where sensitivity for endoleak detection was 50% to 100%, with many false-positive results. Furthermore, CEUS imaging seems to be more sensitive than CTA in diagnosing low-flow endoleaks, CTA failure may have resulted from shorter imaging duration than with CEUS imaging.

	Sensitivity	Specificity	PPV	NPV	Accuracy
Unenhanced CDU	66% (52%-81%)	93% (89%-97%)	76% (65%-87%)	90% (86%-95%)	91% (86%-97%)
Enhanced CDU	81% (52%-100%)	82% (68%-97%)	58% (26%-90%)	95% (87%100%)	98% (91%-100%)
CT angiography	97.5% (61-100%)	81.8% (73-100%)	96.5% (56-98%)	97.3% (71-100%)	89.3% (92-100%)

Table 2. CDU compared with CT angiography (Sun, 2006; Iezzi 2009). PPV: positive predictive value; NPV: negative predictive value.

Type 2 endoleaks are the most common endoleak following EVAR. Arko et al. reported that type 2 endoleaks intrasac flow velocities (IFV) <80 cm/second were likely to resolve without treatment and that those with velocities >100 cm/second were related to large branch vessel diameter and multiple endoleaks. They also suggested that higher velocity endoleaks were more resistant to transarterial embolization. Beeman et al. in 2010, found that IFV did not correlate with likelihood of closure of type 2 endoleaks, nor did high IFV predict sac enlargement. In addition, the velocity and multiplicity of type 2 endoleaks was not additive for AAA sac expansion. In other words, those with multiple branch endoleaks did not have higher velocities and, therefore, a greater chance at sac expansion post-EVAR.

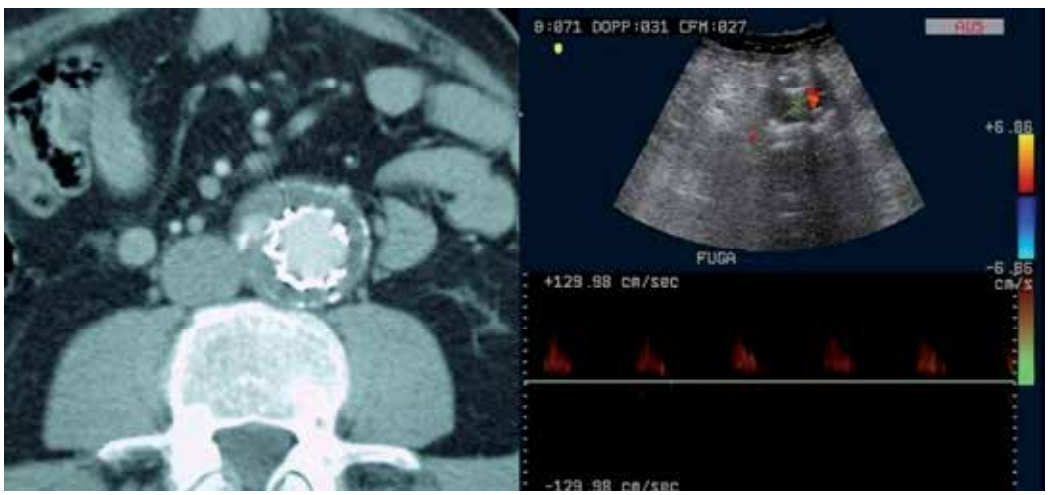

Fig. 4. An example of a type II endoleak as demonstrated on CTA. Intravenous contrast is seen outside stent-graft and within aneurysm sac. This was shown to originate from the inferior mesenteric artery, and was not associated with an increase in aneurysm sac size, and so was managed conservatively. CDU scan demonstrates the same endoleak.

Meier et al. (2001), suggested that spectral Doppler waveform (SDW) patterns can differentiate endoleaks that spontaneously seal from those that persist. They suggested that bidirectional to-from waveforms in endoleaks type 2 may precede occlusion, while

waveforms that remain biphasic with characteristics similar to normal peripheral arterial flow appear to predict persistent endoleaks. The findings of Beeman et al. (2010) contradict their results. Bidirectional to-from waveforms could be predictive of AAA sac enlargement due to the following mechanism: if an endoleak can connect a higher pressure inflow source (lumbar or IMA) with an outflow vessel such as another nearby lower pressure lumbar vessel we would see biphasic SDWs much as normal peripheral arteries. However, if the lumbar or IMA has only an inflow source into the AAA sac and no nearby lumbar or other feeding vessel, the SDW would reveal the to-and-from SDW. The to-and-from SDW reflects the lack of an outflow source vessel and thus increases the diastolic pressure in the AAA sac; the net effect is to increase the mean pressure in the AAA sac. The presence of multiple type 2 endoleaks and bidirectional SDW may be the strongest predictive factors of increased sac diameter (Beeman et al., 2010). A to-from signal was associated with spontaneous sealing and a mono-biphasic waveform was associated with endoleak persistence (Parent et al., 2002).

4. Imaging protocol

The CDU is performed according to a protocol, which included the evaluation of the flow through the endograft, the perigraft flow, the renal and the iliac arterial flow, the maximum diameter of the aneurysm, and the presence of branch vessel flow. Because of the anatomy of the aneurysm stent-graft repair and the location of the endoleaks, we feel that several important aspects are essential to a complete examination of the aneurysm sac with duplex scan imaging. On the basis of the study of Sato et al., the following 4 criteria were developed to determine whether an adequate study had been performed to evaluate endoleaks:

1. A satisfactory B-mode image of the AAA sac and the stent-graft.
2. The satisfactory use of color Doppler (CD) scan imaging without an excessive overgain or undergain.
3. A CD scan assessment of the entire AAA sac outside the graft in both the transverse and the longitudinal views to screen for endoleaks.

The use of spectral Doppler scan waveform analysis outside the graft and within the AAA sac to confirm or reject potential endoleaks suggested with CD scan assessment.

All studies should be performed on a high resolution duplex ultrasound scan system with color-flow capability with technologists who are cognizant of the stent-graft structure, implantation site (aortobiiliac grafts, aortouniiliac graft with femorofemoral bypass grafting), and potential sites for endoleaks (Fig. 5). Low frequency (range, 2.25 to 5 MHz), curved array, phased array or mechanical sector, and pulsed Doppler scan transducers are used. Patients are studied after an overnight fast in the supine position. The graft, proximal and distal stents, and the abdominal aortic aneurysm (AAA) sac are imaged in B-mode, and size measurements of the AA sac are performed. The CD scan is added, and the settings are optimized to avoid excessive overgain (ie, color artifact that completely fills the entire color box) or undergain (ie, absence of color flow within the aortic graft). The color box size is adjusted to completely encompass the AAA sac but not made so large as to encourage artifact. The entire AAA sac outside the graft is assessed systematically by CD scan imaging in both sagittal and transverse views. Perigraft leaks are suspected with reproducible, pulsatile, CD scan flow images outside the graft and within the AAA sac. The focus is

directed at the following potential leak sites: the superior and inferior stent attachments; the anterior mid-AAA sac (inferior mesenteric artery); and the posterior mid-AAA sac (lumbar arteries). A power Doppler scan may be added to assist in the detection of perigraft flow. Because spectral Doppler scan waveform will differentiate true endoleaks from color artifacts, all suspected endoleaks are evaluated by spectral Doppler scan waveform analysis. The presence of an arterial signal confirms the presence of an endoleak. Color artifacts may result from low color sensitivity settings so that pulsatility of the adjacent tissue is imaged as color signals. For all endoleaks, location, flow direction, and extent of AAA sac involvement are determined. An attempt is made to identify the origin and direction of the flow in the inferior mesenteric artery. In cases without evidence of endoleak or inadequate CD scan visualization, a systematic sampling of the AAA sac should be performed with spectral Doppler scan waveform signals to evaluate for possible endoleaks (Sato).

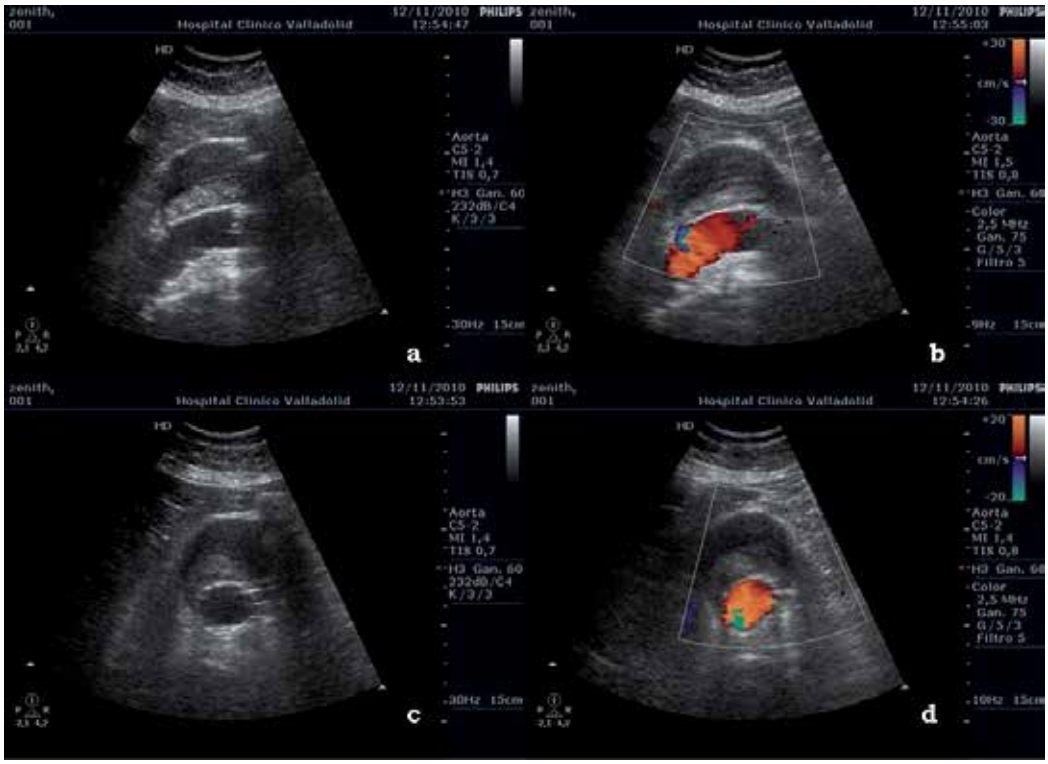

Fig. 5. Ultrasound scan imaging, main body endograft. Longitudinal view (a,b) and cross-sectional view (c,d) with no evidence of endoleak.

Endoleak surveillance is best performed with sensitive color-flow Doppler scale settings to show low-flow channels. These lower scale settings may produce color reverberation artifacts that obscure low-flow endoleak signals posterior to the stent-graft. Coronal views with the patient in a decubitus position may improve image quality in this posterior region. Endoleaks can be distinguished from artifacts by their reproducibility, uniform nature, and persistence during diastole when artifacts usually recede. Pulsed Doppler spectral waveform sampling of extrastent flow is used to document flow direction. Gray-

scale images of some endoleaks are characterized by pulsatile lucencies adjacent to the stent-graft. Some, low-flow leaks may be seen as a small color spot at the stent wall during diastole. Reproducibility and persistence help differentiate these leaks from scale-related artifacts.

A Power Doppler (PD) instrument can be helpful when the proper angle of insonation is difficult to achieve with certainty, because it is insensitive to angle considerations (Fig. 6). PD also can be helpful in low-flow situations, but care must be taken not to overinterpret artifacts caused by motion of the graft wall, which is more common in endografts that are not fully supported throughout their length. Lastly, duplex or PD can aid in the acquisition of a Doppler waveform for the flow within a suspected endoleak to analyze the direction of flow, to provide an estimate of the "resistance" of the endoleak from a nearby collateral vessel. In most cases, however, the latter information will not be of critical importance. All endoleaks related to endograft attachment sites or endograft perforations will flow from the attachment site toward a branch vessel and will have relatively low resistance and high flow. Most branch-to-branch endoleaks (ie, lumbar artery to lumbar artery), will have "to and from" waveforms. Nevertheless, any endoleak should be taken seriously no matter what the Doppler information suggests regarding its flow characteristics.

The keys to optimizing the yield of duplex ultrasonography are: have the patient prepared properly for an abdominal study; employ an experienced technologist educated about endovascular grafts, endoleaks, etc; have a physician who knows the specific endograft configuration in the room at the time of the study or available nearby; and, if possible, use contrast enhancement.

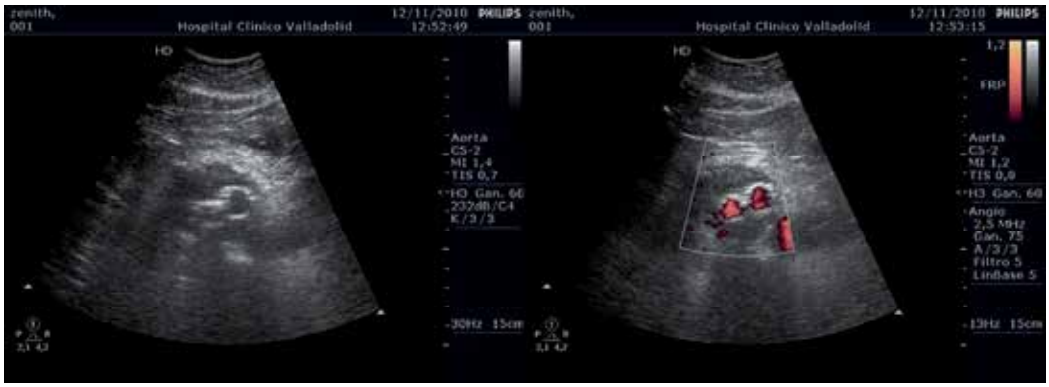

Fig. 6. Cross-sectional duplex ultrasound scan image of aortic bifurcated stent-graft with no evidence of endoleak with power-doppler imaging.

5. Contrast-enhanced ultrasound

A number of studies have indicated that CDU may be used for EVAR (Wolf et al., 2000; Manning et al., 2009). Non-contrast enhanced ultrasound correlates with CT angiography in determining change in AAA size over time, but has low sensitivity and positive predictive value in endoleak detection compared with conventional CT angiography (Manning et al., 2009; Elkouri et al., 2004; Raman et al., 2003). CEUS may be an alternative to CT angiography in the follow-up of patients after EVAR. As ultrasound reduces exposure to the

biologic hazards associated with lifelong annual CT angiography, including cumulative radiation dose and nephrotoxic contrast agent load, CEUS might be considered as a substitute for CT angiography in the surveillance of patients after EVAR (Ten Bosch et al., 2010). CEUS utilizes a non-nephrotoxic contrast agent offering safer post-EVAR surveillance. However, to replace the current gold-standard for endoleak detection, any alternative imaging modality must accurately identify endoleaks with high sensitivity and specificity. In this technique, harmonic imaging is used rather than conventional grayscale. Since the ultrasound beam entrains the microbubbles to resonate at a certain frequency, imaging at that harmonic frequency results in dramatic improvements in blood flow imaging. What is sacrificed is grayscale quality; harmonic imaging loses grayscale quality as blood pool imaging is improved. Therefore the ability to evaluate blood flow is improved while the imaging of the endograft and aneurysm sac is degraded. For endoleaks, the advantage is a shortened examination with more certainty as to the presence or absence of perigraft blood flow. The combination of conventional CDU with contras-enhanced imaging when appropriate may ultimately prove to be the new standard in aortic endograft surveillance.

In this year, Mirza et al. (2010), have published a systematic review and bivariate meta-analysis about duplex ultrasound and CEUS versus computed tomography for the detection of endoleaks after EVAR. Twenty-one studies provided sufficient data for inclusion in the meta-analysis about unenhanced ultrasound. Overall, unenhanced duplex ultrasound was compared to the gold-standard of contrast-enhanced CT in 2601 patients. From the bivariate analysis, the pooled sensitivity was 0.77 and pooled specificity was 0.94. The summary ROC curve plotted using fixed-effects meta-analysis had an area under the curve of 0.91. Whatever, seven studies about enhanced ultrasound (285 patients), provided sufficient data for inclusion in this analysis. From the bivariate meta-analysis, the pooled sensitivity was 0.98. The pooled specificity was 0.88. The summary ROC curve plotted using fixed-effects meta-analysis had an area under the curve of 0.96.

There might be a relationship between blood flow characteristics and CT angiography and duplex ultrasound leakage detectability. In fact, in all patients with a nonvisualized leakage with CT angiography and CDU, the perigraft flow visualized at CEUS was characterized by very slow flow dynamics, with diffuse and delayed aneurysm enhancement. The contrast medium did not concentrate in a confined part of the sac, but it spread into the thrombus. The delayed appearance of the leak, its spreading throughout the sac, and its very slow flow could be the key factors in the explanation for the undetectability of endoleaks with CT angiography. It would be interesting to investigate whether performance of CT scanning with longer delay (>3-4 minutes after contrast agent administration) increases CT sensitivity in the detection of endoleaks in patients with enlarging aneurysms and no evidence of other complications (Napoli et al., 2004).

CEUS imaging is more specific than CTA in endoleak classification thanks to longer duration of enhancement, lack of metallic artifacts, and angio-dynamic evaluation of the leak during the dynamic phase (Fig. 7). CEUS advantages include minimal invasiveness, rapidity, good tolerability and no adverse events have been registered. On the other hand, CEUS imaging also has some limitations. Patient habitus (obesity) and bowel gas can interfere with imaging, and the patient must cooperate. The results of the ultrasound are operator-dependent, and obtaining quality images requires training and specific skills.

Furthermore, CTA provides superior information related to graft anchoring and integrity, aneurysm morphologic changes, or visceral vessel patency (renal arteries).

5.1 Sonographic constrast agents

Sonographic contrast agents enhance the capability of color duplex imaging to detect endoleaks (McWilliams et al., 2002; Napoli et al., 2004). Are typically microbubbles of a perfluorocarbon gas encapsulated within a thin lipid or human albumin shell for stability while circulating in the blood pool. The microbubbles have a range of diameters from 2 to 5 microns, with a suspension of approximately 5 x 10^8 microbubbles per mL of fluid. The microbubbles slowly dissolve as the shell is metabolized, and the perfluorocarbon gas is eliminated through the lungs with normal respiration; a 1 mL bolus injection of the contrast agent will allow approximately 3 to 4 minutes of enhanced visualization and scanning time. At diagnostic ultrasound scan frequencies of 3 to 5 Mhz, the reflectivity of the microspheres is much greater than that of whole blood, increasing signal strength for imaging 100 to 1000 times.

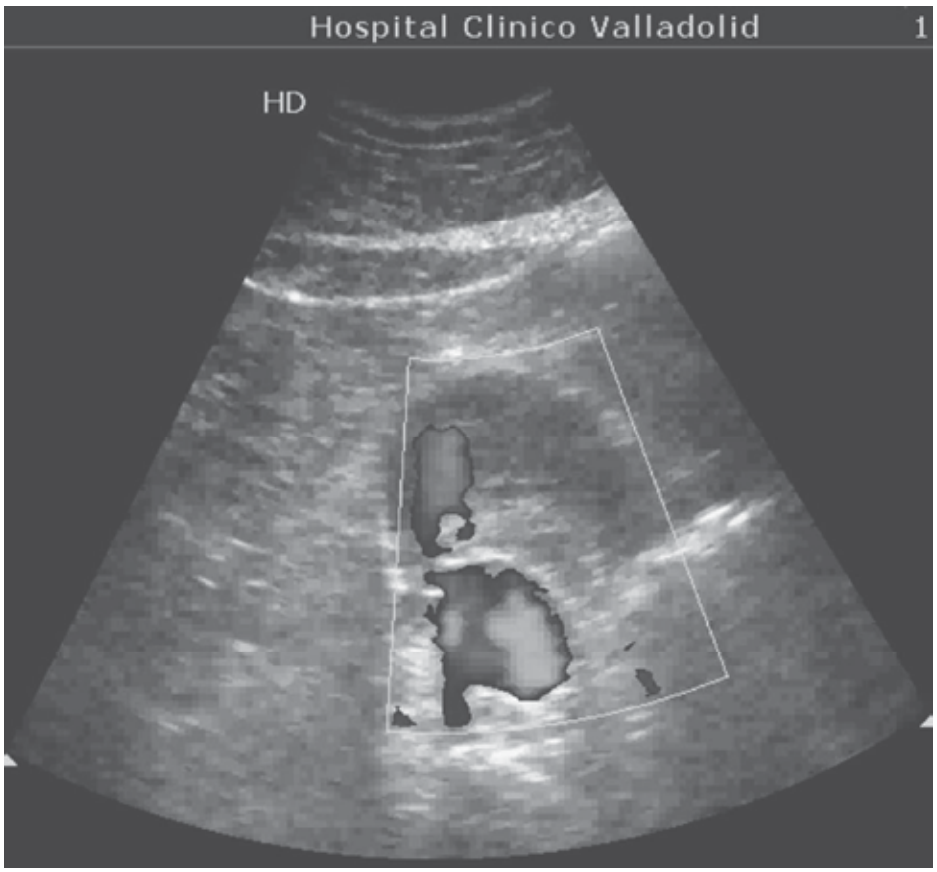

Fig. 7. CEUS demonstrating a type II endoleak.

An additional advantage of the contrast agent is the nonlinear behavior when insonated with the ultrasound scan beam; the returning signal has strong components of both the fundamental transmitted frequency and the second harmonic, at twice the transmitted frequency. This allows imaging with the technique of tissue harmonics, which further suppresses returning echoes from stationary structures and effectively enhances the blood flow signal in the image. As applied to the surveillance of stent-grafts, it is hypothesized that increased ultrasound scan signal will arise from wherever blood is flowing, including the aneurysm sac in the case of an endoleak, with suppression of the stationary echo from the thrombus within the sac with tissue harmonic imaging to improve the contrast between these two in the resulting image (Bendick et al., 2003b). Ultrasound scan contrast agents and tissue harmonic imaging appeared less susceptible to the presence of patient obesity or bowel gas. System default settings for harmonic imaging of the contrast agent may also help eliminate some of the operator dependence in acquiring technically adequate ultrasound scans. In addition, imaging with contrast may make it easier to evaluate the position of the proximal attachment site of the stent-graft relative to an anatomic reference point, such as the origin of the real arteries, because imaging of these vessels is also enhanced with the contras agent.

Second generation sonographic contrast agents consist of stabilized microbubbles of sulphur hexafluoride gas, which is eliminated through the respiratory system, surrounded by a phospholipid shell. These microbubbles improve blood flow echogenicity by resonating with low-intensity ultrasound, which enhances backscatter and thereby increases the detected signal (Carrafiello et al., 2008). Bubble destruction during imaging is minimized, allowing real-time scanning for several minutes. No adverse events, such nephropathy, have been reported for ultrasound contrast agents. The clinical applicability of ultrasound investigation may be operator-dependent variability as well as by patient-related limitations such as obesity. There is the potential for hypersensitivity or an allergic reaction to the albumin shell of the contrast agent, which can be treated with antihistamines.

5.2 Technique

a. **SonoVue** (Bracco, Milan, Italy): A diluted sonographic contrast solution is administered by continuous intravenous infusion (240 mL/h) for a period of 15 minutes. Sonographic contras solution is obtained by mixing 5 mL SonoVue containing 8 μl sulfur hexafluoride microbubbles per millimeter with 55 mL saline solution. Continuous real time tissue harmonic imaging for endoleak detection was performed for 15 minutes during sonographic contrast agent infusion at a mechanical index for 0.4-0.5 at low acoustic power (Ten Bosch et al., 2010). According to the package insert recommendation of the manufacturer, in which the optimal dose for vascular examination was fixed at 2.4 mL, in which a lower dose (1.5 mL) appeared to be sufficient for endoleak detection in the majority of patients. The agent is administered into an antecubital vein at a dose of 1.5-2.4 mL, followed by a flush of 5mL saline solution.
b. **Levovist** (Schering Company, Berlin, Germany): which contains 99.9% D-galactose and 0.1% palmitin acid, is a crystalline powder that is mixed with injectable water. In this suspension, the microparticles bind tiny air bubbles, enhancing the Doppler signal quality when injected intravenously by up to 25 dB without increasing

background noise. This is a clear improvement in the signal-to-noise ratio (Heilberger et al., 1997).

c. **Optison** (Mallinckrodt, Saint Louis, Missouri): a 1 mL bolus of ultrasound scan contrast agent is given via injection into an antecubital vein, followed by a flush of 5 mL of normal saline solution. The contrast agent is allowed to circulate in the blood pool for approximately 1 minute, and then the aortic stent-graft and aneurysm sac were again scanned from the level of the diaphragm to below iliac limb attachment points in longitudinal and cross-sectional scanning modes (Bendick et al., 2003b).

6. Color duplex ultrasound limitations

The major disadvantages of the CDU are related to the proper instrumentation and to technologist dependency. In addition, satisfactory images cannot be obtained in some patients because of technical inability (ie, obesity or excessive intestinal gas). A review of the CDU studies from multiple centers for the EnACT stent-graft trial (Sato et al., 1998), revealed that most of the studies were suboptimal in the evaluation for endoleaks. Although approximately 90% of the studies were technically possible, as indicated with satisfactory B-mode images, complete evaluation for endoleaks as outlined in the methods described was obtained in only 19% of the studies. The most glaring deficiencies were the failure to assess the entire AAA sac with CD scan imaging and the failure to use spectral Doppler scan waveform analysis outside the graft but within the AAA sac to confirm suspected endoleaks. Errors in technical settings could be identified in some cases (ie, poor gain or focal zone settings). Most of the incomplete CDU studies for endoleaks appeared to be the result of a lack of a standardized protocol for the technologist to improve the accuracy for endoleak diagnosis with CDU technology. Others have shown improved sensitivity of CDU in identifying endoleaks when intravenous ultrasound scan contras agents are added to the study.

Ultrasound examinations may carry a number of well known limitations. First, operator dependency might limit reproducibility of the results. It is clearly true that assessment of a CT scan is less operator-dependent. Unfortunately, interobserver variability for endoleak detection by CEUS could not be assessed because this would require repetitive sonographic contrast agent infusions. Second, patient habitus may interfere with ultrasound imaging, as patient obesity or bowel gas. CDU imaging with contrast may prove to be especially useful for obese patients but is not necessarily any better in most patients, especially considering the extra cost and more difficult technique required to use this method.

A potential drawback of CEUS is the inability to detect kinking and migration of the stent-graft. Plain abdominal radiography may be used for the detection of graft migration and structural failure. In addition, sonographic contrast agents are not available worldwide yet, which may limit the applicability of CEUS techniques. Interobserver variability in technical factors can be another important limitation in the diagnostic value of CDU imaging. Furthermore, ultrasound scanning measurements have been noted to underestimate the true size of the AAA when compared with CT. Nevertheless, there is a good correlation between CDU and CT in determining aneurysm size changes over time.

Even if the technologists are very experienced, the use of relatively older equipment and short scan times may be the main culprit in an inadequate correlation between CDU and CT

in the detection of endoleaks. Most large hospital laboratories have not uniformly upgraded to newer equipment. Therefore, it is essential that clinical decisions based on CDU be undertaken only after a review of local results indicates equivalent or superior results with this modality when compared to CT scanning. Congested waiting lists for vascular studies and an inability to attract enough trained technologists have limited the ability of hospital laboratories to devote longer time periods to each study. The lack of additional diagnostic utilities of CDU over CT scanning under these conditions has led to abandon CDU as a routine test for EVAR surveillance. Based on literature, conditions in which ultrasound imaging alone can be proposed for EVAR follow-up can be listed as follows (Long et al., 2005).:

- High quality of technical conditions of ultrasound imaging: such examination requires at least from medium- to high-end ultrasound scanner.
- High quality of medical conditions of ultrasound imaging: it must be performed by a trained senior operator really involved in AAA follow up and having an accurate knowledge of AAA endovascular treatment. Precise data concerning preoperative AAA diameter, nature of stent-graft, operative report, and events before discharge and during follow-up, such as complementary procedures, must be clearly communicated.
- Previous ultrasound imaging evaluation: evaluation of ultrasound performance for AAA diameter measurement and endoleak detection (especially type I) compared with CT remains essential in each ultrasound laboratory. A common protocol for measurements of AAA diameter with ultrasound and CT is highly recommended.
- Selection of patients: patients must be good candidates for ultrasounds. Poor echogenicity may represent a transient or definitive contraindication for ultrasound follow-up; it should be determined by the operator himself; a score of ultrasound image quality as proposed by Sato could be established.
- Absence of type I endoleak: a type I endoleak at discharge or during follow-up is a definitive contraindication for ultrasound follow-up, until the real utility is proven for ultrasound performance;
- Retraction of AAA: a clear decrease in AAA diameter diagnosed with ultrasound or unenhanced CT studies allows for ultrasound alone follow-up until suspicion of regrowth.

7. Conclusions

The use of endovascular techniques to repair AAAs has gained wide acceptance in the surgical community. Disadvantages of endovascular repair include late complications and the need for long-term surveillance to monitor possible sequelae, such as endoleaks, migration, aneurismal dilatation, or possible graft thrombosis. The optimal follow-up of patients after EVAR is still unknown and the repeated exposure to radiation, inconvenience for patients, and cost involved are important. The modality for long-term follow-up has been debated and there is a need for accurate, cost-effective means of postoperative surveillance.

Ultrasound offers the advantages of low cost and lack of radiation exposure. High-quality ultrasound reliably excludes endoleaks in patients after stent-grafting of AAA. Although

duplex ultrasound is often used to augment CT scanning in post-EVAR follow-up, evidence suggest it is unsuitable for sole use in endoleak detection after EVAR. As ultrasound precludes the risks of contrast-induced nephropathy and ionizing radiation load, CEUS might be considered as a substitute to CT angiography as the primary imaging modality in the surveillance of patients after EVAR, provided those patients are suitable for abdominal/pelvic ultrasound and highly trained ultrasound operators are available. CEUS offers promise as a safe and sensitive modality for endoleak detection, potentially obviating the need for patient exposure to high radiation doses and nephrotoxic agents in recurrent CT imaging. Combining CDU scan with a noncontrast CT and abdominal x-ray is a useful strategy in patients who cannot have radio-contrast. Using both test permits assessment about endoleaks along with aneurysm size, seal zone, and possible graft migration. CEUS imaging is a fast, noninvasive, reliable, and valid alternative to multislice CTA for endoleak detection in endovascular aortic stent-graft patients, and is superior to unenhanced ultrasound imaging.

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5

Abdominal Aortic Aneurysm (AAA): The Decision Pathway in Ruptured and Non-Ruptured AAA

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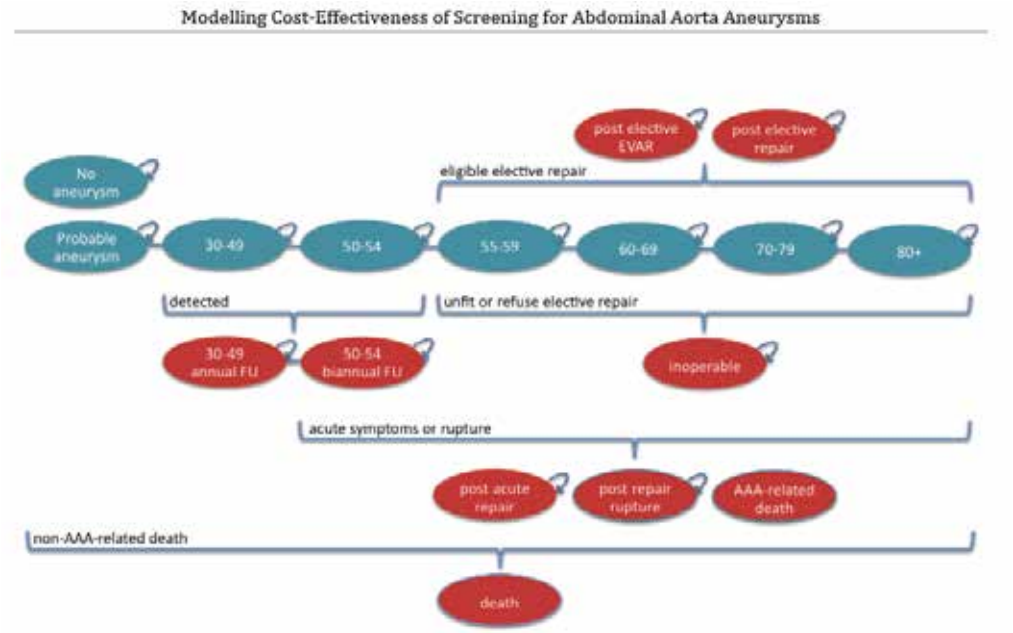
1. Introduction

Abdominal aortic aneurysm (AAA) derives from Greek ανευρυσμα (aneurusma), meaning widening, and can defined as a permanent and irreversible dilatation of a vessel. In 1991 the Society for vascular Surgery proposed as a criterion that the infra renal aorta diameter should be 1.5 times the expected normal diameter. In Europe it is defined as an abdominal aorta greater than 30mm. AAA is assumed to be prevalent in about 4% of males over the age of 65 although variation exists across countries and cause 1.3% of all deaths among men aged 65-85 years in developed countries (Best VA et al.2000). Whether detected incidentally or by screening patients with an AAA ≥ 50 mm will be referred for surgical evaluation in Denmark. Patients detected with aneurysms below the threshold value for referral to surgery will be followed regularly and referred for surgery if their aneurysm grows or if they develop symptoms. Patients with symptomatic or ruptured AAA will be referred for acute surgery where, in some cases of rupture, the patient will die before reaching the hospital (vascular department). A proportion of patients will be unfit for surgery for anatomical or physiological reasons while another proportion will decline to have surgical / endovascular treatment. Until recent years, open surgery was primarily performed but the technique of endovascular aortic repair (EVAR) has now become a part of standard practice in many countries. The availability of EVAR is an important alternative for two reasons: it is less invasive and it is provides a treatment opportunity for a proportion of these patients who are ineligible for open surgery. The natural disease history is progressive and may result in rupture with an associated mortality risk of up to 80%.If an AAA on the other hand is detected at an earlier, asymptomatic state there will be treatment modalities reducing the mortality risk dramatically. An increased awareness of the characteristics of AAA by first contact practitioners might reduce the risk of a fatal outcome with this disorder. In this chapter, we aim to provide and update review of the decision making in regard to elective and rupture treatment of AAA.

2. Indication for elective treatment

Although surgical treatment of non-rupture AAA relies on specific rare indications, such as distal embolisation, urethral compression, contain rupture, mycotic aneurysm, treatment of

intact AAA is essentially prophylactic and aimed at prevention of fatal rupture. The expected functional form of the relationship between risk of rupture and size, it would be appropriate to model relatively small size-intervals for larger aneurysms. Data availability on growth and rupture rates remain limited due to patients being repaired once their aneurysm reaches 55 mm, unless they are unfit or unwilling to receive surgical treatment. It was decided by Morkov model, that the disease process using starting states: definitely no AAA (0-25mm), probably no AAA (25-29mm), small or medium –sized AAA with essentially no risk of rupture (30-49mm), medium–sized AAA close to the iatrogenic threshold (50-54 mm) and four states of large AAAs above the iatrogenic threshold (55-59 mm., 60-69 mm., 70-79 mm. and 80+ mm.). Figure 1 shows the proposed model structure for which the underlying decision pathways and structural assumptions are detailed in the following. The choice of Markov model implies two overall assumptions. First, the so-calls Markova property states that individuals starting in a given state can be modelled in the same way. This means that the route to arriving in a state or time spend in a state has no influence on subsequent parameters. For example, when individuals arrive at acute open surgery their probability for a successful outcome is independent on whether symptoms arose from 30 mm or a 70 mm AAA. Second, the so-called stationary assumption states that parameters are time–homogeneous, and do not vary from one cycle to another. There are limited opportunities for relating assumption, which in the present context were taken advantage of to allow increasing mortality rates as population age.



Note: Blue ovals represent starting states. All numbers refer to abdominal diameter in millimetres. The model structure was applied equally for a scenario with and a scenarario without screening EVAR= elective endovascular vascular aortic repair. FU= folllow up. AAA= Aortic abdominal aneurysm.

Fig. 1. Markov model for the course of abdominal aortic aneurysms

The starting states of AAAs above the threshold for eligibility for elective surgery share the same decision pathway, except that ≥ 80 mm cannot grow to the next state. If the aneurysm

is symptomatic they will be referred to acute surgery following a similar protocol as described for the 55-59 mm AAA whereas if non-symptomatic, they will either be detected and referred for elective surgery or remain undetected in the state (if no growth) or in the next disease state (If growth). The size of the abdominal aneurysm is a universally recognised factor to forecast rupture, and the general consensus is that patients with a large aneurysm >5.5 cm should undergo surgical treatment. The real controversy surrounds the management of small aneurysm and large aneurysm in unfit patients. Indication for surgical treatment is deduced from the estimated risk of rupture, the estimated risk of the surgical procedure, and the estimated life expectancy of the patient. Fig 2: shows proposed management plan for asymptomatic abdominal aortic aneurysms. To be most effective, it should be performed when the rupture risk is high compared with operative risk, in patients who will live long enough to enjoy the long term benefit. It is assumed the elective treatment should be offered without waiting time (since there is no option for rupture while waiting for surgery). In practice, elective surgical treatment might not offered on the same days as indicated but give a 30 –day treatment guarantee in the Danish health care system and discretion of surgeons to prioritize the most sever candidates first this seemed a justified assumption in order to moderate the complexity of model structure.

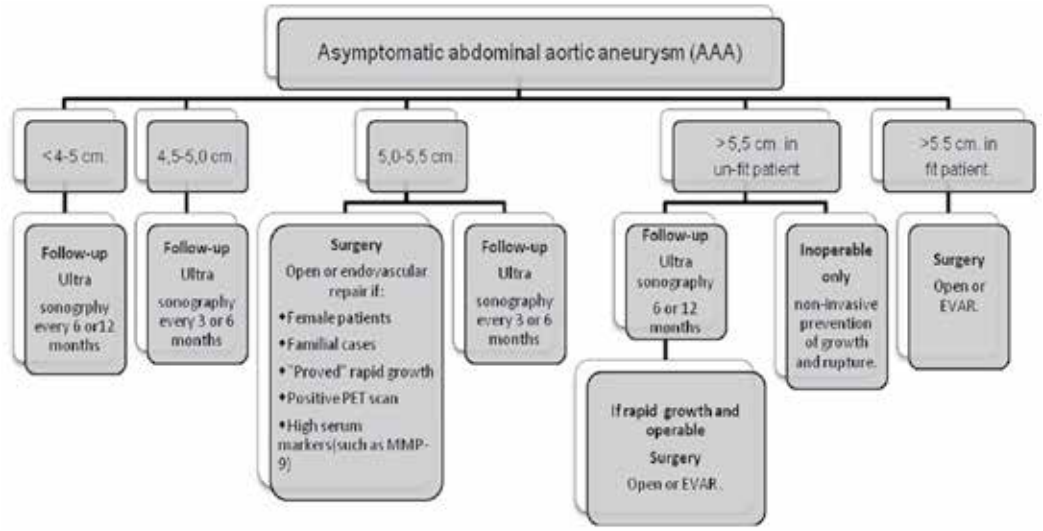


Fig. 2. proposed management of an asymptomatic abdominal aortic aneurysm. EVAR = endovascular repair of AAA.

2.1 Risk of elective aneurysm repair

Reported mortality rate related to elective AAA repair varies among hospitals and surgeons. Mean 30-days mortality rate has been reported between 1.1% and 7.0% (S. Shahidi et al. 2008). Randomized EVAR 1 showed the overall 30days mortality, regardless of the risk factors after open surgery and endovascular repair (EVAR) was 4.6% and 1.5%, respectively.In 2009 the overall 30-days mortality rate in Denmark was 2.7% out of 310 open surgeries and 2.1% out of 196 EVAR. (www.karbase.dk). Most deaths resulting from the repair occurred in the so called high-risk patient. Factors of increased operative risk are

renal failure, chronic obstructive pulmonary disease, and most importantly myocardial ischemia. In this matter, analysis of the EVAR 2 trial data performed by the EVAR investigators did not show a significant difference in either all-cause or aneurysm-related mortality. Thus, outcomes of the EVAR 2 trial have not settled the choice between EVAR and no treatment in this scenario to everyone's satisfaction. In patients with large AAAs who are fit for open surgery, EVAR offers an initial mortality advantage over open, with a persistent reduction in AAA-related death at 4 years. However, EVAR offers no overall survival benefit, is more costly, and requires more interventions and indefinite surveillance with only a brief QOL benefit. It may or may not offer a mortality benefit over non-operative management in patients with large AAAs who are unfit for open repair, but the statistical significance of this comparison is inconclusive. In relation to growth rate /year, there will always be a relative concentration of patients unfit for open surgery in the follow-up program. It is thus assume that the risk of rupture is not affected from that and the high risk patients individually should spotted in the matter of rupture risk/ year and the risk of open/ EVAR treatment, if this is technically possible and acceptable. Patients, who have a very low restricted life expectancy estimated (0-4) year, suggest treating by non-operative management.

3. Rupture abdominal aorta aneurysm, transition to AAA-related death

Related death is defined as consequence of rupture or as consequence of undergoing surgery if death occurs within 30 days postoperatively. A certain proportion of patients with rupture will not reach the hospital alive for emergency surgery. Most patients (92%) with a rupture who reach the vascular clinic alive have a rupture of the posterolateral wall into the retroperitoneal space. Banke A et al, 2008.

3.1 Risk of rupture

The UK small aneurysm Trial 1998 and the US Veterans Administration study led to similar findings despite a lower operative mortality 2.7% vs.5.8%). The conclusion was, infra abdominal aorta aneurysms smaller than 5.5 cm in diameter is safe, where as early surgery is not associated with improved long-term survival. Today it is accepted that AAA diameter is the best predictor of rupture risk. The variability of estimates of rupture risk for particular AAA diameters cited in the literature reflects differences in other factors besides maximal diameter which may vary considerably from series to series, and illustrates that other factors in addition to absolute size must be taken into account in each individual case. It is clear that there is a substantial increase in rupture risk as AAA diameter increase from 5 cm to 6 cm. (Nevit et al., 1989) reported no rupture during 5-years follow-up for AAA < 5 cm, but a 5% annual rupture risk for AAA> 5 cm at initial presentation. Similar estimates were obtained from the larger UK Small aneurysm Trial, where the annual rupture to be 0% (0-5%) for AAA< 4 cm. The long-term report from the UK small aneurysm has shown that the risk of rupture in women was nearly four times higher than in men. The studies of rapid expansion of AAA suggest the size of AAA is probably not the sole useful determinant for risk of rupture (Limet et al., 1991 & Gilmaker et al., 1991). Active investigations have been and still are being done to identify markers other than size that would predict a risk of rupture. The level of serum MMP-9 has been reported to be significantly higher in patients with AAA and also associated with the size expansion rate of these AAA (Sakalihasan et al., 1996).

Preliminary data obtained by PET Imaging of AAA have shown focal uptake of (^{18}F-FDG) is regarded as a functional image of inflammatory response and thus as a potential non-invasive technique to identify unstable AAA that are prone to rupture Sakalihasan et al, 2002. Probabilities of rupture were estimated from the literature. Estimates generated before year 2000 were considered to be outdated due to the introduction of medical treatment (Statin) in the beginning of 1990. After close examination of studies, the EVAR II was excluded since only patients fit for EVAR were included. Table 1 shows the estimated risk of rupture in AAA, as the function of AAA diameter size in centimetre.

AAA diameter size, (cm)	Rupture risk /year
4,0-4,9	0,5-5,0%
5,0-5,9	*3-15 %*
6,0-6,9	10-20 %
7,0-7,9	20-40 %
Over 8	30-50 %

Table 1. Estimated annual rupture risk in AAA.

The simple observation that not all AAAs rupture at a specific diameter indicates that other patient- or aneurysm-variable also effect rupture risk. The risk of rupture is also correlated with co-morbidities as age, lung disease COPD,blood pressure, cardial disease, diabetes. The probability for rupture among high risk patients who are inoperable is likely to be higher than the equivalent in aneurysm-size matched patients. No estimates of ruptures in the group of high risk patients were found to be available in literature. Important information concerning AAA rupture from the UK Small Aneurysm Trial was that patients with 4.0-5.5 cm AAAs , the relative risk of rupture was independently increased by female gender (3.0x), larger initial diameter (2.9x per cm.), current smoking (1,5x), age (1,3x per 4 years), worse COPD (0.6x per L ,FEVI), and higher mean arterial pressure (1.02x per mmHg). In addition to AAA size, many surgeons consider the ratio of diameter to the proximal normal aorta, a 5 cm. AAA in a patient with a 1.5 cm native aortic diameter may or may not to be at greater risk of rupture compared with the same size AAA in a patient with a native aortic of 2.5 cm. The validity of this concept, however has not been proven. The relative comparison between aortic diameter and the diameter of the third lumbar vertebra reported to increase the accuracy for predicting rupture risk, by adjusting for differences in body size (Ouriel et al., 1992). The improvement in prediction accuracy appears minimal, however, when compared with absolute AAA diameter. Although rapid AAA expansion is presumed to increase rupture risk, it is difficult to separate this effect from influence of expansion rate on absolute diameter, which alone could increase rupture risk.

3.2 Open emergency repair of AAA

The selection of patients with ruptured abdominal aortic aneurysms (RAAAs) for emergency repair can be a complex and emotionally charged process. Two possible broad approaches to patients with RAAA exist: an ''all-comers'' approach and a more ''selective'' approach. The all-comers approach offers surgical intervention in every patient, regardless of current status or presence of significant co morbidities. The selective approach would involve an assessment of operative risk predictors and co morbidities in an attempt to identify patients with an unrealistic expectation of a successful outcome. The epidemiology

of AAA is changing. (Best et al., 2000) reported a persistent increase in the incidence of emergency AAA with an associated increase in age-adjusted AAA mortality. The recorded incidence of RAAA varies from region to region in Denmark. The national incidence of operated AAA and RAAA per year has increased in the last 10 years in Denmark: That for operated elective AAA is 6 to 7/100,000 and that for RAAA is 3.5 to 6/100,000 populations (S. Shahidi et al., 2009).

Despite recent advances in anaesthetic, operative, and postoperative care, the high mortality figure has prompted many surgeons to question whether repairing RAAA should even be attempted in the subset of patients with poor physiological reserve. Although some decline has been reported over the years, the overall operative mortality is still in the range of 40-50% (Fig.3). Elderly patients have a restricted life expectancy. In Denmark in 2005-2006, life expectancy for males aged 60, 65, 70, 75, 80, and 85 years old was 18,15.5, 11, 5, 6, and 4.8 years, respective (S. Shahidi et al., 2009). For patients who undergo AAA repair, the 5-year survival rate is reduced compared to age and matched individuals (60-65%) (Barlow AP et al, .1989). Excess mortality in this patient group is substantially attributable to associated co morbidities, particularly coronary artery disease. In order to make this difficult decision more objective, a number of scoring systems have been constructed; however, none of them focuses on practical scores, which can be calculated preoperatively in an elderly surgical patient with RAAA. Is it pointless to operate on an elderly patient with RAAA? Can we exclude such patients from RAAA treatment? What should we do with elderly patients with RAAA?

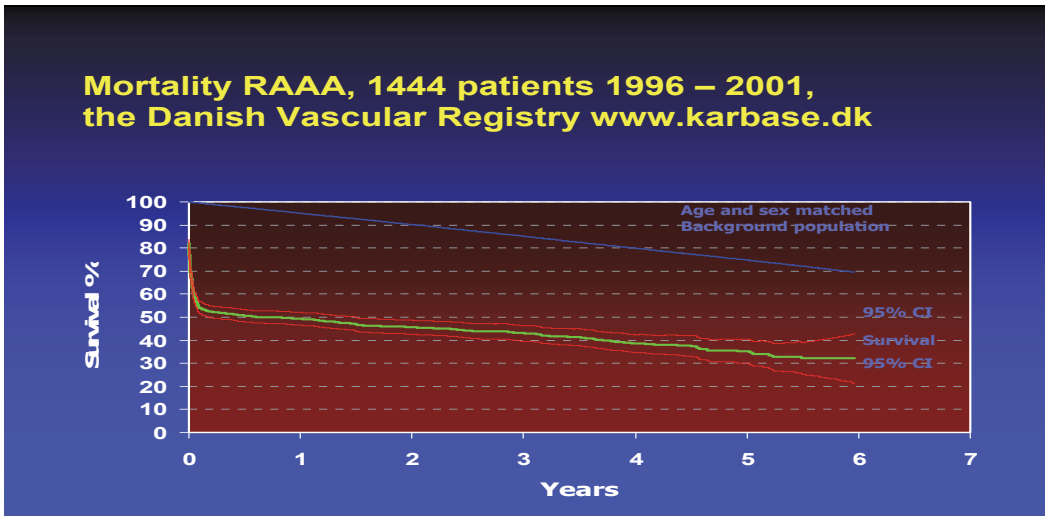
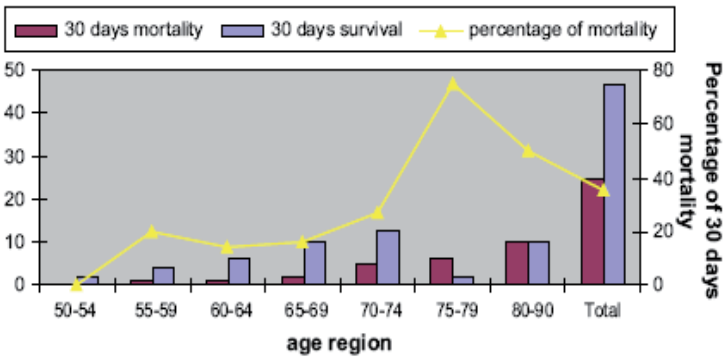


Fig. 3. Overall operative mortality after RAAA compared to background population, shows 40-50% survival reduction in the first 30 days after rupture (www.karbase.dk).

However, repair of RAAA in the elderly generally requires a careful assessment of life expectancy and of the impact of repair-related complications in this specific high-risk subset of patients. It may be still question, if would repair really be the best solution for the elderly patient? Should the patient be palliated? Would the resources we need to use be correctly addressed? These rhetorical questions and issues pose an increasing challenge and discussion for vascular-surgeons. In this respect, ethical problems and cost analysis can be

important components in the decision-making process. Some might claim that the health economy aspects are hardly relevant or that health economy has nothing to do with decision-making concerning the individual patient (at least not yet). Furthermore, some are of the opinion that the cost incurred during prolonged intensive treatment of elderly patients is substantial and that these resources, ideally, should not be wasted on futile endeavours. Currently, as clinicians are increasingly required to accept fiscal autonomy and budgetary responsibility, it is important that the use of health-care resources benefits not only the individual patient but also the wider group of all patients attempting to gain access to health care. This managerial role involves an increasing awareness of cost restraints within the health service, an awareness of the pressure to rationalize limited resources, and the need for awareness both in Denmark and worldwide of the realistic outcomes of a proposed treatment option.



Age groups (years)	30 days mortality	30 days survival	percentage of mortality
50-54	0	2	0
55-59	1	4	20
60-64	1	6	14
65-69	2	10	16
70-74	5	13	27
75-79	6	2	75
80-90	10	10	50
Total	25	47	35

The yellow curve represents the percentage of 30 days mortality in the regions of age groups.
All 3 curves is skewed in the region of (patients 75≤X<80 years age).

Fig. 4. Thirty-day mortality and survival after open repair of RAAA in the regions of age groups[1]: S. Shahidi et al, 2009.

In 2005, the policy of our department was to operate on all patients with an RAAA who reached the hospital alive, who did not refuse surgery, and who did not have a severe terminal malignancy. In some institutions, patients are selected for repair after consideration of age, presentation, and medical co morbidities. A recent survey showed that 97% of U.K. vascular surgeons practice a selective approach (Hewin DF et al., 1998). Many reports have attempted to identify independent predictors for mortality, but there is no ideal scoring system for preoperative assessment of elderly patients needing emergency RAAA surgery (Al Omran et al, 2004, S. Shahidi et al., 2009, 2010). Some preoperative scoring systems

provide approximate estimates of mortality risk, but none has proved sufficiently specific for use on elderly individuals. Among the 72 cases of infra- and juxtarenal open RAAA repair, 30-day mortality was markedly skewed around a median age in the region of 75-79 years. The number of procedures in the different age groups according to 30-day mortality is presented in Figure 3. 2009. Out of 28 elderly patients (39%), eight (11%) were 75-80 years of age and 20 (28%) were aged 80 or more. The 30-day mortality was 75% for patients 75-80 years of age and 50% for patients aged 80 years or more. The 30-day mortality rates for patients in the elderly group was 16 (57%, CI 48-72%), significantly higher than the mortality rate of 9 (20%, CI 12- 33%) in the younger group ($p < 0.001$) (Table 2).

The significant risk factors identified by univariate analysis were then used in a multivariate analysis by means of simple logistic regression with death as the outcome to predict mortality. The logistic regression analysis was repeated to find significant independent risk factors in the elderly compared to the younger groups. As illustrated in Table 2, age ≥75 and creatinine level ≥0.150 mmol/L were the only significant ($p < 0.05$) risk factors in the present study.

Multivariate analysis logistic regression of 30-day mortality among RAAAs ($n = 72$)

Variable	Probability	Odds ratio	95% CI	p
Creatinine ≥0.150 mmol/L	0.0875	7	1.85-28.78	0.0005*
Age ≥75 years	0.0799	3.88	1.62-17.08	0.0014*
Preoperative BP <90 mm Hg	0.0531	1.133	0.127-1.107	0.051

*$p < 0.05$, significant.

Table 2. Multivariate analysis of 30 days mortality from (S. Shahidi et al; 2009).

In this study the age range for 30-day mortality was a markedly skewed distribution around a median age in the region of 75-80 years (Fig. 1). The ROC analysis in our series showed that the age of 75 years gave the greatest area under the curve for predicting 30-day death postoperatively (a cut-off age). Of course, the sample size is small and this would be a bias; but with the above studies and the life expectancy of Danish males in mind, our study suggests that a male patient aged 75 years or more with an RAAA should be considered elderly. There are some other risk score systems.

In another study, we compared of preoperative levels of Base deficit and Lactate in predicting outcome in patients with open repair after RAAA (S. Shahidi et al,. 2010). From January 2006 to December 2008, the medical records of 47 patients with RAAA were reviewed. Of the 47 patients enrolled in the study, 44 were men and 3 were women, with a median age of 71 (CI: 69-73), at admission. Patient's demographics and underlying co-morbidities are listed in Table 3. Twenty-five (53%) patients died within 30 days in the per-operative period. Altogether, there were twelve (26%) on-table deaths; five (11%) patients died within 24 hours after surgery; 8 (17%) patients died of multi-organ failure. Survivors had a median age of 70(range 40-83), which is significantly younger than non-survivors 75(range 59-85) (p=0.009). Pre-operative lactate (p=0.011), pre-operative base deficit (p<0.001), measured blood loss (p=0.002) are significant higher in non-survivors compared with survivors. These data suggest that pre-operative base deficit is a valuable marker better than pre-operative lactate for the identification of the per-operative death of patients with ruptured AAA. A threshold of level of -4.0 mmol/L of pre-operative base deficit had the highest combined sensitivity and specificity for the identification of per-operative death

after repair of ruptured AAA. The sensitivity and specificity of pre-operative base deficit <-4 mmol/L was 80.0% and 86.3%, respectively.

Receiver-operating-characteristic (ROC) curves were constructed to illustrate various cut-off values of pre-operative lactate, and base deficit. The mean ± SE area under the receiver-operating-characteristic curve for pre-operative base deficit was 0.83±0.06 (95% confidence interval 0.71 to 0.95, p<0.001) among non-survivors. Pre-operative lactate level had a mean area under the curve of 0.72±0.08 (95% confidence interval 0.57 to 0.87, p=0.011) among non-survivors. A cut-off value of -4 mmol/L of pre-operative base deficit has 80.0% sensitivity and 86.3% specificity respectively

	Media(range)	Media(range)	P*
	Survivors	*Non-survivors*	
Age	69,5(26-83)	75(56-89)	0.009
Lowest preoperative MAP (mmhg)	104(61-147)	70(0-153)	.029
Pre-operative Hb(g/dL)	9.9(6.6-14.0)	7.3(4.6-12.0)	.001
Pre-operative Cr.mmol/L	150(80-270)	180 (80-390)	.001
Pre-operative Lactat mmol/L	3.7(0.5-15.0)	6.5(1.0-17.0)	.011
Pre-operative base deficit mmol/L	-0.6(-11.9-6.2)	-11(-21.8-3.3)	<.001
Lowest intra-operative MAP (mmhg)	70(0-87)	40(0-82)	<.001
Intra-operative blood loss (L)	3.1(0.6-11)	6.8(1-20)	.002
Intra-operative temperature(Intra blader)	≥ 35 ◦ c	≤34 ◦c	.001
intra-operative blood transfusion (Units)	21(8-66)	28(8-70)	NS

Table 3. Clinical variables in survivors and no survivors after open RAAA repair.

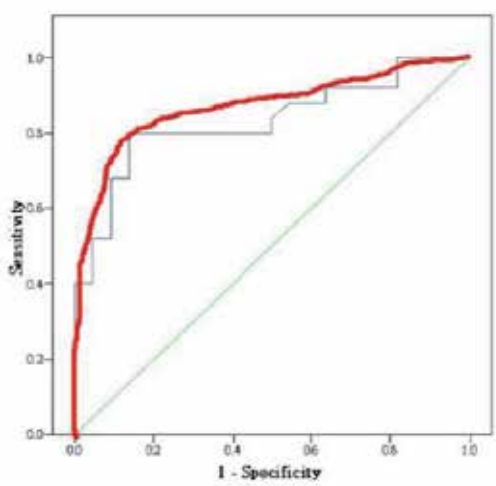


Fig. 4. ROC analysys curve for base difficiet in our study.

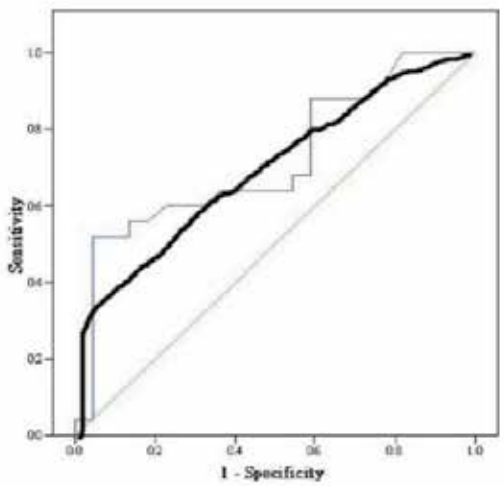


Fig. 5. Roc analysis curve for lactat in our study

Fig. 4 & 5. Receiver operating characteristic curves of preoperative lactate (black), and base deficit (red).

4. Health economic finance

The financing of Danish hospitals is through the national Diagnostic Related Group (DRG system). DRG is classified by diagnosis and surgical procedure according to this system and gives a value estimated by Danish health authorities. Since the majority of the procedures were complicated, the DRG with recorded complications was used. Based on these DRG values, the cost of each of the 30 days gained from surgical repair in these elderly patients could be estimated. The DRG value for the year 2005 was used for all patients. DRG is the average expenses, which depends on two parameters of the ICD-9 diagnosis, e.g., I.713 (RAAA), and the treatment, e.g., KPDG10 (operation for AAA). The average estimated cost of in-hospital treatment of RAAA was €15,350 (DRG) in 2005 in Denmark In 2005, the Danish health authorities estimated the average cost of an operation for RAAA to be €15,350 DRG compared to an elective AAA, which is €8,500 DRG. Concerning the age 75 years, our data show that the respective risk difference (RD) is approximately 0.38 (0.157-0.575), with an estimated NNT of 2.0 (1.74-6.34) (S. Shahidi et al., 2009).

5. Discussion

Decision-making in regard to elective repair of AAA requires careful assessment of factors that influence rupture risk, operative mortality and life expectancy. Individualizes consideration of these factors in each patient in each patient is essential, and role of patient preference is of increasing importance. The surgeon should be very aware that the elective treatment of AAA in every case and in any time is only a prophylactic treatment. It is not possible or appropriate to recommend a single threshold diameter for intervention which can be generalized to all patients. Based upon the best available current evidence, 5.5 cm is the best threshold for repair in an "average" patient. However, subsets of younger, good-risk patients or aneurysms at higher rupture risk may be identified in whom repair at smaller sizes id justified. I do believe that delaying in repair until larger diameter may be best for older, higher-risk patients, especially if endovascular repair is not possible. Intervention at diameter < 5.5 cm appears indicated in women with AAA and maybe in patients with rapid AAAs expansion. If a patient has suitable anatomy , endovascular repair should be considered, and it is most advantageous for older, higher-risk patients, who has acceptable life expectancy. The patient with a very low life expectancy should not under-go an invasive prophylactic repair. There is evidence for EVAR clearly reduced perioperative mortality, morbidity and recovery time, however, there is a higher reintervention rate, increased surveillance burden, and a small but ongoing risk of AAA rupture. In my knowledge there is no justification at present for different indications for EVAR , such as earlier treatment of smaller AAA. We are still waiting for long-term outcome of endoluminal repair is better defined and results of randamized trials available, the choice between EVAR and Open repair will continue heavily on patient preference and information.

In the matter of RAAA and emergency repair of RAAA, there are many reports , as the report from the Mayo Clinic showed that advanced age, high Acute Physiology and Chronic Health Evaluation (APACHE II) score, low initial hematocrite, and preoperative cardiac arrest increased mortality rates (Goffi et al,. 1999). The APACHEII is commonly used to assess surgical patients in the ICU, where it was designed to predict outcome, but has seldom been used in preoperative assessment. The APACHE II scores appear to predict

outcome equally well when the age points are omitted. Goffi concluded that fit elderly persons should not be denied an emergency operation because of their age alone. (Hardman et al,. 1996) reviewed 154 patients and identified five independent preoperative risk factors that were associated with mortality: age >76 years, an ischemia electroencephalogram, Hb <9 g/dL, creatinine >0.19 mmol/L, and loss of consciousness. They also reported that all patients who presented three or more variables died. In addition, (Johnston et al., 1994) found that hypotensive patients with raised creatinine had only a 20% chance of survival. The Glasgow Aneurysm Score (GAS), first described in 1994, calculated a risk of mortality with RAAA using age in years: +17 for the presence of shock, +7 for myocardial disease, +10 for cerebrovasculare disease, and +14 for renal disease (Sammy ak et al.). All of these findings strongly suggest that mortality is determined by the severity of physiological insult and the patient's premorbid physiological reserve. Despite the findings of our studies and other studies, there is still no consensus on how to use these preoperative variables. While these clinical variables may prove useful, they must be interpreted with caution and should only act as an adjunct to clinical decision-making. A ruptured aneurysm is lethal in almost every case, unless the patient is operated successfully (Olsen P et al., 1991). That is why the scoring system should be able to differentiate those elderly patients who have no chance of survival from those who are likely to benefit from surgery (S. Shahidi et al., 2009 and 2010). The estimated cost per life after 30 days postoperatively was €40,409 (DRG) for the elderly patient in our cohort in 2005 compared to €18,880 (DRG) in the younger group. This can be compared to the cost per year of life gained by haemodialysis, which is estimated to be at least €50,000 (Winkel M.et al., 1999). Regarding the health economic aspect in RAAA patients, we found only one study. An interesting Norwegian study showed the total survival time of octogenarians treated for RAAA. Over a 20-year period, 53 patients aged 80 years or older were operated for RAAA. The survival time was estimated and related to DRG values in order to estimate the cost of each year of life gained by operating on this type of patient (Aune et al., 2004). The authors concluded that the operative mortality for patients aged >80 years with RAAA is high (47%) but the price of each gained year of life is relatively low. The estimated cost per gained year of life was € 6,817. The accurate cost of each operation obviously varies and is difficult to calculate. That is why we have based our calculation on the DRG cost. There is some evidence of a significant reduction in mortality from AAA in men aged 65-79 years who undergo ultrasound screening. The cost-effectiveness may be acceptable but needs further expert analysis (Mass study 2002). A Cost effectiveness analysis based on a probabilistic, enhanced economic decision analytical model from screening to death (MTV report) from Denmark(showed the estimated costs per quality adjusted life year (QALY) gained discounted at 3% per year over a lifetime for costs and QALYs was £43 485 (£54 852; £71 160). At a willingness to pay threshold of £30 000 the probability of screening for abdominal aortic aneurysm being cost effective was less than 30%. One way sensitivity analyses showed the incremental cost effectiveness ratio varying from £32 640 to £66 001 per QALY. Ehlers concluded screening for abdominal aortic aneurysm does not seem to be cost effective. Further research is needed on long term quality of life outcomes and costs (Ehlers et al., 2008). These findings still need careful consideration in judging whether a co-coordinated population-based screening program should be introduced. The screening program has been implemented in United Kingdom. In Denmark we are waiting for further expert analysis and approval from the Danish health authorities. The screening program would be discussed in other chapters. Open repair is still the predominant procedure for RAAA. Until today, there has been no high-quality evidence to

support the use of (EVAR) in the treatment of RAAA. However, evidence from prospective controlled studies without randomization, prospective studies, and retrospective case series suggests that EVAR is feasible in selected patients, with outcomes comparable to best conventional open surgical repair for the treatment of RAAA (AJAX trial still going on). The numbers of EVAR procedures for this group are small in Europe. The second VASCUNET data-base report from 2008 for 10 year operative outcome of more than 33.000 patients with aortic aneurysms in six countries, Denmark (DK), England (UK), New Zealand (NZ), Australia (AST), Sweden (SW) and Switzerland (SWZ), with participating of 202 hospitals, showed a much less use of EVAR in RAAA in these countries. The percentage of operation type according RAAA and EVAR in these six countries until 2009 was DK=1, UK=4, NZ= 7, SW= 22, AST=8 and SWZ=21 of all ruptures (S. Shahidi et al., 2009). The promising results for EVAR of ruptured abdominal aneurysms may have the potential to significantly lower the mortality in all RAAA patients. That is why the author suggest, all elderly high risk patients, patient with preoperative renal dysfunction and pre-operative base deficit < -4mmol/L should be selected to EVAR, if this is technically possible. Had we chosen not to operate on elderly patients with preoperative serum creatinine 0.150 mmol/L, or elderly patients with a basis deficit -4.0 mol/ l, at least eleven patients would have been denied a life-saving operation. All of these eleven patients were successfully discharged from hospital (S. Shahidi et al., 2009 & 2010; Banke A., 2008).

6. Conclusion and future

The arbitrary setting of a single threshold diameter for elective AAA repair applicable to all patients is not appropriate, as the decision for repair must be individualized in each case.
The most important thing in individual decision-making of this elective prophylactic treatment is the estimated risk of rupture, the estimated risk of the surgical procedure, and the estimated life expectancy of the individual case, and giving the competence to the out-patients for making decision along with the surgeon.
The ideal treatment of RAAA is prevention or to increase the probability of reaching hospital alive in case of rupture. In our experience, after 1-year follow-up, open repair has been life-saving in 77% of patients younger than 75 years, with a low price estimated at € 18,880, and surgical repair has been life-saving in 33%of patients aged 75 years and older at a relatively low price for each life, estimated at € 40,409. The first goal in abdominal aortic aneurysm still is the prevention of rupture; hopefully the next aim in the future will be the prevention of abdominal aortic growth.

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6

Abdominal Aortic Aneurysm in Patients with Coronary Artery Disease: A Review Article

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1. Introduction

Abdominal Aortic Aneurysm (AAA) is defined as a localized and permanent dilatation of the abdominal aorta, beyond 50% of the normal aorta diameter (Schermerhorn, 2009). The prevalence of AAA ranges from 1.3% to 8.9% in men and 1% to 2.2% in women (Sakalihasan et al., 2005; Singh et al., 2001). Incidence of AAA is on the rise in parallel with a globally ageing population, higher clinical suspicion and improved accuracy of imaging methods (Best et al., 2003; Prisant & Mondy, 2004). AAA is an important problem for public health, since AAA rupture is the tenth leading cause of death in American white men 65 to 74 years of age (Upchurch & Schaub, 2006). Most AAA remain asymptomatic until rupture occurs. Half of the patients with a ruptured AAA reach the hospital alive, with an additional operative mortality of 30-60%. On the contrary, an elective AAA repair, recommended in most patients with an abdominal aortic diameter exceeding 50-55 mm or rapid growth (> 1 cm/y), is associated with a mortality risk of 2% to 6% (Kurvers at al., 2003; Sakalihasan et al., 2005). Health organizations recently recommended one-time screening for AAA by ultrasonography for men aged between 65 and 75 years with a smoking history, thereby reducing AAA related mortality rates by 50% (Cosford & Leng, 2007; Ehlers et al., 2008; Ferket et al., 2011; Moxon et al., 2010; Takagi et al., 2010). However, they advised against screening in men below 65 and over 75 years, and in women, since the number of AAA-related deaths that can be prevented by screening these populations is too small. AAA and atherosclerosis share several risk factors, such as male sex, age, smoking and arterial hypertension (Forsdahl et al., 2009). In population – based studies, AAA is independently associated with pre – existing coronary arterial disease (CAD) (Golledge et al., 2006; Kent et al., 2010). The high prevalence of CAD among patients with AAA is well known, with an impact on short term survival after AAA repair (Falk et al., 1997). Indeed, coronary investigation is often required prior to aortic surgery, finding a concomitant CAD prevalence of 31% to 90% (Kioka et al., 2002; Sukhija et al., 2004; Van Kuijk et al., 2009). In contrast, the opposite relationship, namely the prevalence of AAA among patients with CAD, has been explored only in some recent cohorts or in subgroups of patients. The possibility that AAA could be more prevalent in this population, as compared with the general population, has been suggested by these previous studies, with limited, incomplete

and often conflicting results. Accordingly, no specific recommendation is available on AAA screening in patients with advanced atherosclerosis. To our knowledge, we present the first systematic review, based on a thorough literature survey, which delineates the prevalence and predictive risk factors of AAA among CAD patients. We thus aim at identifying CAD patients at high risk for AAA development and discussing the usefulness of AAA screening in such subpopulations.

2. Methods

A systematic English-language literature search has been performed using the MEDLINE/Pubmed, Cochrane and Embase databases to identify all studies on the prevalence and risk factors of AAA among CAD patients, published from January 1985 to January 2011. The key words searched for were AAA and CAD. The title and relevant abstracts have been screened for studies which statistically analyzed prevalence data of AAA in CAD patients. In addition, the references of eligible papers were screened for further relevant studies. Two authors independently reviewed and extracted data from each article using a specific data extraction form: publication year, characteristics of study population including CAD severity, AAA definition, size, prevalence, associated risk factors and circulating biomarkers. Discrepancies were resolved by consensus.

3. Characteristics of abdominal aortic aneurysm in coronary artery disease patients

Seventeen studies (8308 patients) published between 1991 and 2010 were eligible, meeting the predetermined inclusion criteria (table 1). Study population ranged from 72 to 2819 patients. For some studies, only the subgroup of CAD patients received our attention (Abela et al., 2009; Alcorn et al., 1996; Benzaquen et al., 2001; Bonamigo & Siqueira, 2003; Goessens et al., 2006; Jaussi et al., 1999; Nemati et al., 2009).

In these studies, the prevalence or incidence of AAA among CAD patients oscillated between 0.48% and 18.2%, with 8 studies above 9% (upper limit of AAA prevalence in population – based studies). The prevalence of AAA eligible for surgical repair varied from 0% to 5.2 % of the study population, and from 0% to 36.7% of the AAA population (table 2). AAA diameter in these studies ranged between 25 and 87 mm. Five studies included a control population, age and sex matched in most cases, and without angiographic CAD (Bergersen et al., 1998; Bonamigo & Siqueira, 2003; Madaric et al., 2005; Nemati et al., 2009; Wang et al., 2008). AAA prevalence in these control groups were always significantly below the prevalence in the CAD group, ranging from 0 to 3.3%.

4. High heterogeneity of studies

The wide variations in AAA prevalence among the precited 17 studies could be explained by differences in severity of CAD, AAA definition, age and sex distribution, geographical localisation, prevalence of associated risk factors and pre-existing atherosclerosis-related morbidity.

Inclusion criteria clearly stated a wide range of CAD severity: current coronary angiographic data with various thresholds of significant coronary narrowing; data on previous coronary events; data on current or previous coronary revascularisation procedures whether endovascular or surgical. Nine out of the 17 studies included patients

Reference	Study Design, Country	n patients (% male)	AAA (%)
Nevelsteen et al., 1991	Post CABG, Belgium	100 (80)	11*
Alcorn et al., 1996	Aged > 65 years, MI, angina, CABG, significant stenosis on coronary angiography, USA	1244	13.8
Bergersen et al., 1998	Elective CABG patients, USA	192 (65.6)	18.2 (13.0*)
Jaussi et al., 1999	Patients referred for Transthoracic Echocardiography with ischemic heart disease, Switzerland	72	15.3*
Benzaquen et al., 2001	Significant angiographic coronary stenosis, Canada	99 (75)	8.1*
Bonamigo & Siqueira, 2003	Male aged > 54 years, severe ischemic disease (stenosis > 70%) and previous coronary surgery, or important lesions on cardiac catheterism, Brazil	501	6.8*
Monney et al., 2004	Male aged > 60, Post CABG, Switzerland	395	10.1*
Calderwood & Welch, 2004	CABG patients, United Kingdom	118	15.3
Madaric et al., 2005	Age > 60 years, coronary narrowing ≥ 50%, Slovak Republic	109 (90)	14.7 (8.3*)
Goessens et al., 2006	"SMART Study", MI, unstable angina or history of CAD or CABG/PCI, The Netherlands	1034 (83)	3.7 (2.2*)
Wang et al., 2008	Age > 60 years, coronary narrowing ≥ 50%, China	209 (72.7)	0.48*
Abela et al., 2009	Significant coronary stenotic lesions, United Kingdom	87 (77)	13.8
Shirani et al., 2009	Elective candidates for CABG, Iran	2819 (69.6)	2.09
Nemati et al., 2009	CAD (more than 50% constriction), Iran	184	4.3
Dupont et al., 2010	Post CABG, France	217 (87)	6.9
Long et al., 2010	Acute coronary syndrome with coronary stenosis ≥ 50%, France	304 (77)	6.6*
Poon et al., 2010	Elective patients for CABG, China	624 (79.9)	1.8

Table 1. Summary of studies reporting prevalence or incidence (*) rates of abdominal aortic aneurysm (AAA) among coronary artery disease (CAD) patients. CABG: coronary artery bypass graft, MI: myocardial infarction, PCI: percutaneous coronary intervention

Reference	AAA diameter mean (SD), [range] (mm)	AAA > 50 mm % / study population	AAA > 50 mm % / AAA patients
Nevelsteen et al., 1991	[30-65]	4	36.7
Bergersen et al., 1998	43.6 (13.1), [25-70]	5.2	28.6
Benzaquen et al., 2001	38 (14), [27-65]	1	12,5
Monney et al., 2004	38.9 (13)	1.01	10
Calderwood & Welch, 2004		4.2*	27.7*
Madaric et al., 2005		4.6	31.2
Goessens et al., 2006		0.09*	4.34*
Abela et al., 2009	42 (19.6), [30-87]	1.1	11.1
Shirani et al., 2009	30.70 (7.01), [25-61.7]	0.07*	3.4*
Dupont et al., 2010	35.3 (9.1), [26-53]	0.9	13.3
Long et al., 2010	33 (3.7), [30-45]	0	0
Poon et al., 2010	[31.1-59.1]	0.3	18.2

Table 2. Characteristics of abdominal aortic aneurysm (AAA) in coronary artery disease patients (*: >55 mm).

who were candidates for CABG or in the post CABG period (table 1). AAA was diagnosed by abdominal ultrasound, by measurement of either transverse or antero-posterior, or both infrarenal aortic diameters. AAA is conventionally defined when infrarenal aortic diameter is ≥ 30 mm (Moll et al., 2011; Wanhainen et al., 2001; Wanhainen et al., 2008). In the present review, fifteen studies used this definition. However, some studies diagnosed AAA when infrarenal aortic diameter was > 26 mm (Calderwood & Welch, 2004) or ≥ 25 mm (Shirani et al., 2009), while others used additional criteria: infrarenal to suprarenal ratio > 1.2 (Alcorn et al., 1996) or > 1.5 (Dupont et al., 2010), infrarenal exceeding suprarenal aortic diameter by at least 5 mm (Bonamigo & Siqueira, 2003), to compensate for individual variation in the diameter of the adjacent aorta. While two studies exclusively included male patients (Bonamigo & Siqueira, 2004; Monney et al., 2004), the other studies recruited a female patient proportion varying from 10 to 34.4%. Because age is an important risk factor for both CAD and AAA in population – based studies, five studies restricted their study population to patients above 60 years. While most recruited patients had a mean age between 60 and 70 years, some studies exhibited a wide age range (from 34 to 88 years; from 29 to 83 years; respectively) (Long et al., 2010; Poon et al., 2010). In contrast to a majority of CAD patients of Caucasian origin in these studies, we found two studies on prevalence of AAA in CAD patients of Chinese origin (Wang et al., 2008; Poon et al., 2010) and two on Iranian patients (Shirani et al., 2009; Nemati et al., 2009). These 4 studies reported the lowest AAA prevalence. It clearly appears that certain ethnic groups experience a disproportionately smaller burden of AAA (Salem et al., 2009). Emphasis should be done upon the fact that the size of abdominal aorta in these populations was quite smaller than in Caucasian population. Wang et al. and Poon et al. consistently found a mean maximal infrarenal aortic diameter inferior to studies of Caucasian population (Allison et al., 2008; Poon et al., 2010; Wang et al., 2008). Despite such heterogeneity between these observational cross – sectional

studies, one can fairly say that AAA prevalence among CAD patients exceeds that observed in population –based studies. It is also of interest that the prevalence of AAA in CAD patients was comparable to that reported in AAA screening studies of patients with peripheral vascular disease (7% -17%) and cerebrovascular disease (8.4% -20.2%) (Bentgsson et al., 1996; Kurvers et al., 2003; Palazzuoli et al., 2008; Simons et al., 1999).

5. Abdominal aortic aneurysm risk factors in coronary artery disease patients

We shall now stress on the association between AAA prevalence in CAD patients and the various coronary atherosclerosis risk factors or indicators which may be useful to identify patients at increased risk in a screening context. Of importance, some risk factors were examined in some studies but not in others (table 3).

5.1 Gender

Most studies including both male and female patients showed a trend towards a higher male prevalence among AAA cases (table 3) or detected AAA in male patients exclusively, in accordance with results of population – based studies (Dupont et al., 2010; Nemati et al., 2009; Nevelsteen et al., 1991; Wang et al., 2008). Only one study showed a statistically significant association between male sex and AAA prevalence (table 3) (Shirani et al., 2009).

Reference	Male sex	Age	Smoking	Diabetes mellitus	Arterial hypertension
Bergersen et al., 1998	1.78 (0.67-4.7)	5,7 (1,7-18,8)*, §	7 (2,5-19,1)*,§		
Bonamigo & Siqueira, 2003		1,09 (1,034-1,152)*, §	0,96 (0,47-1,95)	1,29 (0,58-2,86)	1,53 (0,79-2,99)
Monney et al., 2004		*, §	2,07 (1,05-4,1)*, §	0,4 (0,14-1,16)	2,67 (1,2-5,96)*, §
Madaric et al., 2005	1,11 (0,28-4,35)	1,05 (0,95-1,17)	4,85 (1,55-15,25)*, §	0,11 (0,01-0,83)*	2,66 (0,33-21,75)
Shirani et al., 2009	3,85 (1,65-8,99)*	age > 65: 1,79*	1,63*	2,32*	1,85*
Nemati at al., 2009		*			
Dupont et al., 2010	NS	1.34 (0.47-3.83)	infinity*	1,7 (0,58-4,99)	0,76 (0,26-2,22)
Long et al., 2010	2,83 (0,64-12,51)	age > 60: 2,74 (1,07-7)*,§	2,01 (0,65-6,18)	0,54 (0,18-1,66)	1,07 (0,42-2,7)
Poon et al., 2010	2.17 (0.49-9.52)	2.68 (0.74-8.96)	NS	NS	NS

Table 3. Odds ratio (95% confidence interval) obtained for association studies between abdominal aortic aneurysm presence and some atherosclerosis risk factors, among coronary artery disease patients. *: $p < 0.05$ by univariate analysis, §: $p < 0.05$ by multivariate analysis, NS: non significant

Poon et al. exclusively detected AAA in male CAD patients when using the common AAA definition "infrarenal aortic diameter ≥ 30 mm" (Poon et al., 2010). However, when using an alternate definition "maximum infrarenal diameter ≥1.5 times the group mean infrarenal aortic diameter categorized by gender", AAA prevalence was greater with 2 out of 19 in female patients (infrarenal aortic diameter of 24.1 mm and 25.1 mm). This goes along with the suggestion by Grootenboer et al. by which the definition of 30 mm in population based studies for the average women is probably inappropriate and leads to an underestimation of AAA prevalence (Grootenboer et al., 2009). In these studies on AAA prevalence in CAD patients, one also notes that infrarenal aortic diameter mean (standard deviation), when available, was significantly lower in female compared to male patients : 15.5 (2.2) mm versus 18.8 (5.6) mm, $p<0.0001$ in Dupont et al. (Dupont et al., 2010), 16.8 (3.2) mm versus 20.2 (3.3) mm, $p=0.004$ in Nevelsteen et al. (Nevelsteen et al., 1991).

5.2 Age

Nine out of 17 studies reported a statistical evaluation of the association between age and AAA (table 3). Only 2 did not find an association (Dupont et al., 2010; Poon et al., 2010). Age was associated with AAA by multivariate analysis after adjustment for other known risk factors in 4 studies (table 3). In Nemati et al., ROC curve analysis showed that age of patients with CAD (67 years) predicted the presence of AAA with a sensitivity and specificity of 75% and 80%, respectively (Nemati et al., 2009). Although most guidelines contain recommendations that favour one time AAA screening for male patients 65 years or older in the general population, one can note that 6 out of the 17 studies gave data about AAA detection in men younger than 65 years (table 4).

Reference	AAA age
Dupont et al., 2010	67.1 (9.8), [54-85]
Goessens et al., 2006	68.8 (11,5), [45-79]
Long et al., 2010	69 (11), [51-86]
Calderwood et al., 2004	64.8, [60-72]
Benzaquen et al., 2001	67.2 (5.4), [58-76]
Abela et al., 2009	68.8 (11,5), [45-79]
Nemati et al., 2009	68.2 (7,09)

Table 4. Age distribution of abdominal aortic aneurysm (AAA) patients among coronary artery disease patients (mean (SD), [min-max])

Only the AAA that are vulnerable to rupture contribute to the benefit of screening at an earlier age (Ferket et al., 2011). As an example, in Dupont et al., 7 out of 15 AAA were detected in men aged 50 to 65 years with one of them exceeding 50 mm requiring surgical correction (Dupont et al., 2010). In Long et al., 7 out of 20 AAA were detected in CAD patients aged 50 to 60 years (Long et al., 2010).

5.3 Smoking

Over 90% of all AAA patients have a history of smoking, and nearly half are active smokers at the time of diagnosis (Powell et al., 1996). In population – based studies, smoking may be

more strongly associated with AAA than with CAD (3 fold) or with cerebrovascular disease (5 fold) (Lederle et al., 2003). It also was strongly associated with AAA progression and rupture (Badger et al., 2009) and the strength of its association with AAA persisted independently of the extent of atherosclerotic disease (coronary, peripheral artery disease) (Lee et al., 1997). Five out of the 17 studies on AAA prevalence in CAD patients showed smoking to be significantly associated with AAA by univariate analysis, 3 of them confirming this association by multivariate analysis (table 3). In Shirani et al., even more important was the duration of smoking as 8.6% of CAD patients with a history of smoking ≥ 40 years had AAA compared to an AAA prevalence of 2.6% in their whole CAD population (Odd Ratio (OR): 3.49, p=0.0001) (Shirani et al., 2009). Similar results were found in population based studies (Singh et al., 2001). The effect of smoking cessation has been investigated as well, and showed a slow decrease in risk for AAA of 4% per year (95% confidence interval 2 to 6) (Wilmink et al., 1999). However, when adjusting for smoking duration, the risk of AAA even 20 years after cessation of smoking was not statistically different from the risk of current smokers (Singh et al., 2001). Nontheless, the recent AAA clinical practice guidelines of the European Society for Vascular Surgery recommend smoking cessation to reduce the risk of AAA growth (Moll et al., 2011). This relative slow decline in risk, after cessation of smoking, differs strongly between AAA and CAD. It would be interesting to evaluate the impact of smoking cessation on AAA prevalence and progression among CAD patients.

5.4 Diabetes mellitus

Among the 17 studies on AAA prevalence in CAD patients, only 7 did focus on the association between Diabetes Mellitus (DM) and AAA prevalence (table 3). Five out of these 7 studies reported no association, while one showed an association by univariate analysis which was no more significant by multivariate analysis (Madaric et al. 2005). Shirani et al. reported a significantly higher frequency of AAA in diabetic patients compared with non diabetic ones (3.2% versus 1.4%, p=0.033) (Shirani et al., 2009). Of importance, Guijarro et al. studied 159 patients with CAD and found that microalbuminuria, but not DM, was a potent and independent predictor of AAA (OR: 7.56, 95% Confidence interval: 1.8-31.9) (Guijarro et al., 2006). DM, a strong coronary atherosclerosis risk factor, may therefore lack an association with AAA prevalence in CAD patients.

5.5 Arterial hypertension

Seven out of the 17 papers on AAA prevalence in CAD patients evaluated the association between AAA and arterial hypertension. Only Shirani et al. and Monney et al. confirmed a significant association (table 3) (Monney et al., 2004; Shirani et al., 2009). Arterial hypertension seems to be more positively associated with coronary heart disease and cerebrovascular disease than with aneurysm formation. These findings indicate that a history of hypertension should not be held as a significant risk factor for AAA among CAD patients.

5.6 Lipid profile and obesity

Most CAD patients receive a lipid modifying therapy including statins, fibrates and cholestyramine. In such populations, few studies did evaluate the association between serum lipoproteins levels or history of dyslipidemia and AAA prevalence (Dupont et al.,

2010; Monney et al., 2004; Shirani et al., 2009). None found a statistically significant association. Moreover, in view of current guidelines on atherosclerosis treatment, one cannot construct a study on association between basal lipid profile and AAA prevalence in CAD patients without lipid modifying therapy prescription. We can, therefore, not expect to withdraw conclusions in such a selective population.
As far as obesity is concerned, 3 studies reported on the lack of association between AAA and BMI and/or body weight in CAD patients (Dupont at al., 2010; Long et al., 2010; Monney et al., 2004). A potential association between obesity and AAA or infrarenal aortic diameter in CAD patients requires evaluation by further studies.
To date, in a CAD population, all evaluated potential AAA risk factors are also well – known CAD risk factors. Among these, only age and smoking seem to have a specific impact on AAA prevalence among CAD patients. Of importance, no known specific circulating biomarker of AAA in CAD patients is available.

6. Atherosclerosis and abdominal aortic aneurysm

6.1 Pathophysiology

The pathogenesis of AAA is poorly understood. AAA has traditionally been thought to be caused by atherosclerosis. Recently, this atherosclerosis theory has been challenged on the basis of epidemiologic, genetic and biochemical information, questioning whether atherosclerosis is a "bystander" condition or an active participant in the development and progression of AAA disease (Golledge & Norman, 2010; Johnsen et al., 2010; Lee et al., 1997; Reed et al., 1992; Trollope & Golledge, 2011). As seen in previously described studies on AAA prevalence in CAD patients, not all patients with atherosclerotic disease do present an AAA. On the opposite, several studies reported many AAA patients lacking concomitant atherosclerotic vascular disease. The link between AAA formation and atherosclerosis is also not strong in animal models. Animals developing atherosclerosis by dietary or genetic means scarcely develop an AAA. Conversely, animal models of AAA, by intraluminal elastase infusion or adventitial application of calcium chloride, do not require the presence of atherosclerosis. There are both similarities and differences in the pathogenesis of AAA and atherosclerotic lesions whether coronary, carotid or peripheral arterial diseases. Both involve inflammation, macrophage infiltration, increased vascular smooth muscle cells turnover and thrombus formation. Whereas proliferation of vascular smooth muscle cells (VSMCs) is a typical feature of atherosclerosis affecting vascular media and intima, the density of these cells is low in media and adventitia of aneurismal wall due to apoptosis. Atherosclerosis is also characterized by migrating VSMCs and macrophages, foam cell formation, lipid deposition, leading to endothelial dysfunction and increased intima – media thickness (Palazzuoli et al., 2008). On the other hand, AAA involves dilation of all layers of the aortic wall, destructive remodeling of medial elastin and collagen fibers by matrix metalloproteinases released by activated aortic wall macrophages (Wassef et al., 2007). These different pathological features of CAD and AAA are further emphasized by the results of above mentioned observational studies. Indeed, some of the risk factors for CAD did emerge as being independently associated with AAA in severe CAD populations such as cigarette smoking and age. However, it is not possible to determine from these studies whether these risk factors did so through a pathway of promoting atherosclerosis, in turn increasing the risk of AAA, or if they promoted AAA further leading to CAD development. A third theory could be that both pathways act to some extent, subsequently stimulating the

development of the other. New integrative, hypothesis – driven, carefully designed human and animal studies should shed a light on the sequential development of AAA and coronary atherosclerosis.

6.2 Severity of CAD and AAA

Severity of CAD has been differently described in the aforementioned studies. Long et al. described a significant positive association between AAA and previous coronary events (previous acute coronary syndromes with proven coronary stenosis of 50% or greater, CABG or percutaneous coronary intervention), but not with the number of stenosed coronary vessels (Long et al., 2010). Nemati et al. as well as Shirani al. reported no association between AAA and number of stenosed coronary vessels or left main coronary vessel stenosis (Nemati et al., 2009; Shirani et al., 2009). Monney et al. confirmed these results regarding the lack of association between AAA and number of stenosed coronary vessels, NYHA classification of Angina Pectoris and number of bypass (Monney et al., 2004). Nevertheless, there was a reduced risk among patients with a single coronary vessel affection as compared to patients with CAD involving two or three vessels. Likewise, Dupont et al. did not detect an association between AAA and history of unstable/ stable angina, myocardial infarction, coronary angioplasty, and number of diseased coronary vessels (Dupont et al., 2010). Such an association or lack thereof between AAA and CAD severity has not been evaluated in population – based studies. It would also be important to assess the relationship between extent of coronary stenosis and infrarenal aortic diameter and/or risk of AAA rupture.

6.3 Concomitant vascular disease to abdominal aortic aneurysm and coronary artery disease

Atherosclerosis is a systemic inflammatory vascular disorder involving multiple arterial beds, so it makes sense to evaluate AAA prevalence among patients when Peripheral Arterial Disease (PAD) and/or Carotid Artery Stenosis (CAS) coexist with CAD. Patients with PAD seem to be at particularly high risk for AAA development with an overall prevalence greater than 10%, twice that of the general population (Barba et al., 2005; Galland, et al., 1991). In Barba et al., patients with tibial disease had a significantly higher AAA prevalence than those patients with aortoiliac or femoro-popliteal diseases. A systematic review of population based screening studies has shown a positive association of PAD with AAA (OR 2.5) (Palazzzuoli et al., 2008). The relationship between AAA and CAS is more difficult to apprehend. In patients aged above 65 years with severe CAD awaiting CABG, a recent study showed the presence of an AAA to be a significant predictor of ≥ 70% internal carotid artery stenosis by univariate analysis (Kiernan et al., 2009). Furthermore, a higher prevalence of AAA has been established in patients with CAS (Gratama et al., 2010; Kang et al., 1999; Karanjia et al., 1994; Kurverts et al., 2003). However, recent case control studies did not find any evidence for more carotid atherosclerosis in AAA patients (Cheuk et al., 2007; Palazzzuoli et al., 2008). In an attempt to better elucidate this relationship, Johnsen et al. reported significantly more carotid atherosclerosis in abdominal aortic aneurysm diameter ≥ 27 mm and in AAA (Johnsen et al., 2010).

Among CAD patients, 5 studies appraised an association between AAA and PAD, while the association between AAA and CAS was analyzed in only 4 studies (table 5). Regarding PAD, Benzaquen et al. and Dupont et al. reported a significant association (Benzaquen et al.,

2001; Dupont et al., 2010). This was further confirmed by Guijarro et al. in 157 patients with CAD (angina, acute coronary syndromes, or myocardial infarction) out of a cohort of 269 patients with symptomatic atherosclerosis (Guijarro et al., 2006). PAD was a potent and independent predictor of AAA (Odd Ratio: 6.0, 95% CI: 1.4-26.6). Of importance, in Benzaquen et al., difficulty advancing the catheter into the aorta during coronary catheterization was the only independent predictor of AAA presence by multivariate analysis (Odd Ratio: 11.1, 95% CI: 4.6-26.6) (Benzaquen et al., 2001). The association of AAA with concomitant lower extremity PAD may be due to the strong pathophysiologic association of both AAA and PAD with smoking. Both the aorta and lower extremity arteries are especially susceptible to injury by exposure to all forms of tobacco and cigarette smoking in particular (Baumgartner et al., 2008). As for CAS, its presence was associated with an increased risk of AAA in 3 out of 4 studies (table 5). In Shirani et al., AAA frequency was 10.8% in patients older than 65 years and CAS >50% (Shirani et al., 2009). In Dupont et al., severe CAD male patients aged below 75 years with a smoking history had an AAA prevalence of 24% when they also had PAD and/or CAS, versus 4.4% in the absence of either condition (p=0.007) (Dupont et al., 2010).

Reference	Carotid stenosis	Peripheral arterial disease
Benzaquen et al., 2001		4.7 (2.1-10.3)*
Bonamigo & Siqueira, 2003		0,66 (0,21-2,1)
Monney et al., 2004	0,9 (0,36-2,24)	1,88 (0,78-4,56)
Madaric et al., 2005	3,11 (1,02-9,46)*	3,07 (0,91-10,38)
Shirani et al., 2009	4,72*	
Dupont et al., 2010	4,88 (1,37-17,33)*	5,45 (1,77-16,78)*

Table 5. Odds ratio (95% confidence interval) obtained for association studies between abdominal aortic aneurysm presence and carotid artery stenosis or peripheral arterial disease, among coronary artery disease patients. *: $p < 0.05$ by univariate analysis

7. AAA screening

AAA appears to meet many of the classic criteria of disease screening (Wilson & Jungner, 1968). First, AAA is an important health problem disease with life – threatening consequences when rupture occurs. Its prevalence in cross sectional studies is on the rise, not only because of better case – finding by abdominal ultrasonography, but also due to ageing of the population. In carefully designed randomized controlled trials, it has been well established that AAA screening in men aged 65 to 74 years is effective and decreases the risk of aneurysm rupture by almost 50%. In this group, after a single abdominal ultrasonographic evaluation, death from aortic rupture is rare within the subsequent 10 years (Ashton et al., 2002; Lindholt et al., 2002; Lindholt et al., 2005; Thompson et al., 2009; Wilmink et al., 2003). The evidence of clinical effectiveness was reinforced by a subsequent Cochrane Review—which estimated a 40% relative risk reduction in aortic rupture (absolute risk reduction from 0.27% to 0.16%)—and then by results from MASS after 7 years of follow-up (Cosford & Leng, 2007; Kim et al., 2007). A second point is that abdominal

ultrasonography is an ideal method for AAA screening as it is safe, non – invasive, cheap, lasting only few minutes, with a high sensitivity and specificity (Lederle et al., 1988; Lindholt et al., 1999). Thirdly, the best therapy is pre-symptomatic elective surgery in appropriately selected individuals, with a mortality of 5% for elective surgery, one tenth the mortality of emergency interventions (Golledge & Norman, 2009). Accordingly, population-based screening is currently being implemented in several countries (Scott et al., 2008; Wannheinen et al., 2005; Swedish council on technology assessment in health care, 2008). Most clinical practice guidelines contain recommendations in favor of one – time AAA screening for men 65 – 75 years old with a history of smoking using ultrasonographic scans (Ferket et al., 2011). However, this recommendation is poorly followed up in this target population, partly due to a lack of patients' compliance with an acceptance rate around 65% (Boll et al., 1998; Collin et al., 1988; Lederle et al., 1997; Lindholt et al., 1997; Simoni et al., 1995). Moreover, a recent study estimates that about half the patients with AAA were not eligible for screening under current guidelines and would have been missed (Kent et al., 2010). A different approach, with screening of specific high-risk groups has been suggested (Derubertis et al., 2007) and is implemented within the Medicare programme in the United States (Lederle, 2008). No specific guidelines for AAA screening in CAD patients are available. In those articles dealing with AAA prevalence among CAD patients, we found a higher AAA prevalence among Caucasian patients (between 3.7 and 18.2%) compared to population – based studies, with a high prevalence of AAA above 50 mm, independently of CAD severity. Such prevalence seems to be higher, according to our review, when CAD patients have a smoking history and symptomatic atherosclerotic affection of other vascular beds (CAS and PAD). These data lend support to further urgent controlled randomized studies, dealing with AAA ultrasonographic screening in this specific subpopulation, with a longer follow up of included subjects. End goals would include cost effectiveness, AAA operability, long term survival, sufficiency of one – time screening and quality of life. The impact of cardiovascular co – morbidities has been implicated, by predictive scoring systems, to influence AAA prevalence in the subgroups of women and middle – aged men (50 to 65 years old) (Kent et al., 2010; Wanhainen et al., 2008). The screening of hospitalized CAD patients would be easily organized without adding administrative burden and of high efficiency, as evidenced by full attendance rates in studies of Monney et al. and Dupont et al.; as abdominal ultrasonography was proposed during hospitalization (Monney et al., 2004; Dupont et al., 2010).

8. Conclusion

This review of literature shows, despite the limited number of studies, that CAD patients present with a higher AAA prevalence compared to population – based studies. Some classic atherosclerosis risk factors (history of smoking, age, associated atherosclerotic affection of other vascular beds) maintain an association with AAA in such CAD populations. This has a two-fold consequence: first, AAA may not simply be an atherosclerotic complication, as suggested by a recent work based on TROMSO study, warranting further studies in AAA pathogenesis (Johnsen et al., 2010). Secondly, specific CAD subgroups (those showing the above mentioned common risk factors) may be at risk for a higher AAA burden, strongly justifying the need for further studies to evaluate the impact of AAA screening in such patients subgroups.

9. References

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7

Treatment of Ruptured Abdominal Aortic Aneurysms

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1. Introduction

The incidence of Abdominal Aortic Aneurysms (AAA) has persistently increased over the past decades (Best et al., 2003). This is partly attributed to increased ageing of the population, improved diagnostic tools and the introduction of screening programmes (Sakalihasan et al., 2005). To date, AAAs are responsible for 1.3% of all deaths among men aged between 65-85 years in developed countries (Sakalihasan et al., 2005). This percentage is probably even higher due to underestimation of AAA related mortality, since AAAs generally exist without symptoms (Acosta et al., 2006).

In patients with an identified AAA and abdominal and/or back pain in combination with pain at palpation of the aneurysm (a so called symptomatic AAA), pending rupture of the AAA is assumed. However, evidence for a symptomatic AAA representing pending rupture is lacking (Scott et al., 2005). When rupture occurs, the mortality rate is as high as 80% (Semmens et al., 2000; Veith et al., 2003; Gorham et al., 2004). Forty percent of the patients with a ruptured AAA do not reach the hospital alive (Semmens et al., 2000) and in patients reaching the hospital and undergoing surgery, the mortality rate is approximately 50% (Sayers et al., 1997). Despite progression in surgical techniques, anaesthetical management, vascular prostheses and perioperative care, there is only a gradual decline in operative mortality rate over the past decades (Heller et al., 2000; Bown et al., 2002).

In 1991, a new minimally invasive technique was described by Parodi et al. to treat AAA, endovascular aneurysm repair (EVAR) (Parodi et al., 1991). In the elective setting, EVAR showed an absolute and relative mortality risk reduction of approximately 3 and 75%, respectively (Prinssen et al., 2004; EVAR-trial-participants 2005). In the acute setting, emergency EVAR (eEVAR) is a strategy that might allow for improvement in above mentioned poor prognosis. Since 1994 an increasing amount of publications of eEVAR to treat acute AAAs is published. Currently, eEVAR has become an accepted treatment option which is increasingly being performed to treat acute AAA. However, the potential reduction in peri-operative mortality of eEVAR compared to conventional open repair in patients with an acute AAA is still open to debate.

in this chapter, we will discuss the role of endovascular AAA repair in patients with a ruptured AAA.

2. Treatment options

In patients presenting with a ruptured AAA, a choice can be made whether or not to offer treatment at all (selective treatment policy). When decided to perform an intervention, two treatment options are available; conventional "open" AAA repair or the minimally invasive EndoVascular Aneurysm Repair (EVAR).

2.1 No intervention

In order to identify patients with an unrealistic expectation of a successful outcome after surgery, operative risk predictors, comorbidities and estimated quality of life can be assessed. However, excluding selected patients from treatment is an awkward consideration (Hardman et al., 1996; Tambyraja et al., 2008), which is signified by the number of prediction models generated for risk stratification to support improvement of patient selection for surgical intervention (Samy et al., 1994; Hardman et al., 1996; Prytherch et al., 2001). The 'Hardman Index' and 'Glasgow Aneurysm Score' are the most commonly used prognostic scoring systems. The Hardman Index identifies five independent preoperative factors associated with mortality; age, blood creatinine level, loss of consciousness after arrival, blood haemoglobin level and electrocardiographic ischemia (Hardman et al., 1996). The Glasgow Aneurysm Score uses the following factors: age, shock, myocardial disease, cerebrovascular disease and renal disease (Samy et al., 1994). The validity of both scoring systems has been assessed using 82 patients in the study of Tambyraja et al. from the year 2005 (Tambyraja et al., 2005). Unfortunately, both scoring systems seemed to be poor predictors for postoperative mortality in patients with a ruptured AAA. Two years later, Tambyraja et al. identified three risk factors which might form the basis of a new scoring system to predict the outcome of rAAA, the 'Edinburgh Ruptured Aneurysm Score' (Tambyraja et al., 2007). Risk factors were: blood haemoglobin level, blood pressure, and Glasgow Coma Scale. Until this moment validation studies are still needed in order to assess its predictive value and clinical applicability.

Due to modest validity and clinical applicability of present prognostic scoring systems, selecting patients for intervention remains a subjective consideration. Whenever possible, patients' and families' opinion as well as the opinion of the responsible medical doctor has to be included in the decision.

2.2 Conventional 'open' ruptured AAA repair

Conventional open repair of an AAA was performed for the first time in 1951, replacing the abdominal aortic aneurysm by a homograft (Dubost et al., 1951). Two years later, open repair was performed using synthetic grafts (DeBakey & Cooley 1953). The open procedure to treat ruptured as well as unruptured AAA has almost been consistent over time and known as being an invasive, but generally durable procedure. In patients who are often suffering from considerable hypovolemic shock, a laparotomy is performed immediately after induction of general anaesthesia. Subsequently, the aorta and/or iliacal arteries are clamped proximally and distally from the aneurysm. After clamping, the aneurysm is opened in order to provide access for placement of a polyester tube or bifurcated graft. The aneurysm sac is left in situ and secured around the graft in order to cover it.

This major operation carries a significant mortality and morbidity, due to the combined effects of general anaesthesia, surgical exposure, haemorrhage, and aortic clamping with related lower torso ischaemia-reperfusion injury (Dillon et al., 2007). General anaesthesia is required which might lead to acute haemodynamical changes as a result of associated

inhibition of sympathetic arterial tone. The hypotension and subsequent inadequate oxygenation might induce or accelerate cerebral en cardiac ischemia, resulting in a poor clinical prognosis. Furthermore, loss of abdominal muscle tone can occur during the induction of general anaesthesia which might cause free rupture of the retroperitoneal haematoma with related haemodynamical consequences (Lachat et al., 2002). During surgical exposure, blood loss is generally extensive (Sadat et al., 2008). Hypotension and subsequent inadequate oxygenation might induce or accelerate cerebral en cardiac ischemia, resulting in poor clinical prognosis. Furthermore, after removing the clamps, considerable ischemia-reperfusion injury of the lower extremities and the intra-abdominal organs might occur (Bown et al., 2003).

2.3 Minimally invasive endovascular ruptured AAA repair

In 1991, Parodi et al described a less invasive alternative to conventional 'open' aneurysm repair for the treatment of AAA, Endovascular Aneurysm Repair (EVAR) (Parodi et al., 1991). EVAR involves groin incisions in order to expose the femoral arteries. Using a catheter and guidewire a synthetic stentgraft is fed through the artery up to the AAA neck until positioned correctly just below the renal arteries and subsequently unfolded, excluding the aneurysm sac from blood flow and pressure. Control angiography is performed to assure correct placement of the endovascular stentgraft. Aorto-uni-iliac stentgrafts, reaching one of the common iliac arteries as well as bifurcated stentgrafts, reaching both iliac arteries are available. In case of aorto-uni-iliac stentgrafting, femoro-femoral bypass graft surgery has to be performed in order to restore blood flow to the contralateral leg. A controlateral endovascular occluder is used to stop retrograde bleeding up into the iliac artery into the aneurysm sac. Due to increasing expertise and continuous improvement of both stentgrafts and their delivery systems, increasing success rates and decreasing complications and reintervention rates are observed (Lovegrove et al., 2008).

After several years of experience in EVAR for unruptured AAAs this technique has gradually extended its indication and is currently used to treat feasible patients with a ruptured AAA (Yusuf et al., 1994). However, the applicability for EVAR depends on several anatomical and logistic conditions. Anatomical suitability for EVAR is assessed on a preoperative CTA scan and evaluated for infrarenal aortic neck length, neck angulation and iliac and femoral access arteries that need to be large enough to accommodate the introducer system (Kapma et al., 2005). Approximately half of the ruptured AAAs is considered anatomically suitable for eEVAR according to the preoperative CTA scan (Hoornweg et al., 2007). However, logistic problems are often reported which frequently led to the exclusion of EVAR-suitable patients for undergoing endovascular repair (Yilmaz et al., 2002; Reichart et al., 2003; Kapma et al., 2005; Franks et al., 2006; Peppelenbosch et al., 2006; Visser et al., 2006; Acosta et al., 2007). Logistic criteria for EVAR in patients with a ruptured AAA are the instant availability of a CT-scanner, the 24/7 availability of an operating room that is adequately equipped to perform endovascular procedures as well as an endovascular trained staff. Financial burden is sometimes the availability of a large variety of 'off-the-shelf' stent-grafts (Mehta et al., 2006).

3. EVAR versus open surgery

In a recent systematic review of 61 controlled and uncontrolled clinical studies of patients with an unruptured AAA, EVAR is described as a feasible and safe technique, showing

decreased mortality and morbidity rates compared to a conventional open procedure (Drury et al., 2005). Considering these benefits, EVAR has been generally accepted as the preferred treatment option.

Since its first description in 1994 by Yusuf et al (Yusuf et al., 1994), over 400 reports of EVAR for patients with a ruptured AAA are available. The minimal invasive approach implies the opportunity to use local anaesthesia, which has been proven to be feasible and effective in EVAR (Henretta et al., 1999; Bettex et al., 2001). As described by Lachat et al in 2002, local anaesthesia is not attended with the acute haemodynamical changes which are normally seen during induction of general anaesthesia (Lachat et al., 2002). However, these benefits did not lead to standard application of local anaesthesia, since 19 comparative observational studies show considerable variation in the percentages of patients undergoing local anaesthesia (0-97%). Furthermore, eEVAR involves no crossclamping and minor surgical exposition compared to open surgery.

The above mentioned advantageous consequences of the minimally invasive endovascular approach of acute AAA might reflect on perioperative mortality. Approximately 26 studies comparing EVAR with conventional open surgery in patients with a ruptured AAA can be identified (Ohki & Veith 2000; van Sambeek et al., 2002; Verhoeven et al., 2002; Yilmaz et al., 2002; Reichart et al., 2003; Resch et al., 2003; Lee et al., 2004; Alsac et al., 2005; Brandt et al., 2005; Kapma et al., 2005; Larzon et al., 2005; Vaddineni et al., 2005; Arya et al., 2006; Coppi et al., 2006; Dalainas et al., 2006; Dillavou et al., 2006; Franks et al., 2006; Greco et al., 2006; Hinchliffe et al., 2006; Peppelenbosch et al., 2006; Visser et al., 2006; Acosta et al., 2007; Anain et al., 2007; Moore et al., 2007; Ockert et al., 2007; Egorova et al., 2008). Twenty-four of these studies compared early mortality of EVAR compared to open surgery (Ohki & Veith 2000; van Sambeek et al., 2002; Verhoeven et al., 2002; Yilmaz et al., 2002; Reichart et al., 2003; Resch et al., 2003; Lee et al., 2004; Alsac et al., 2005; Brandt et al., 2005; Kapma et al., 2005; Larzon et al., 2005; Vaddineni et al., 2005; Arya et al., 2006; Coppi et al., 2006; Dalainas et al., 2006; Franks et al., 2006; Greco et al., 2006; Hinchliffe et al., 2006; Peppelenbosch et al., 2006; Visser et al., 2006; Acosta et al., 2007; Anain et al., 2007; Moore et al., 2007; Ockert et al., 2007). One of these studies is a prospective randomised trial by Hinchliffe et al, which showed identical 30-day mortality rates in both treatment groups (9/17 in the open surgery group versus 8/15 in the EVAR group) (Hinchliffe et al., 2006). However, the study is underpowered and served as a pilot study for future randomised studies. The remaining 23 studies are observational studies of which 4 showed no reduction in early mortality compared to open surgery (Ohki & Veith 2000; van Sambeek et al., 2002; Hinchliffe et al., 2006; Ockert et al., 2007). Using Review Manager 4.2.10, provided by the Nordic Cochrane centre, a forest-plots can be created (Figure 1). The overall effect of EVAR compared to open surgery, taking 1 randomised controlled trial and 23 available observational studies into account, showed a 38% decrease in 30-day or hospital mortality rate (peto-odds ratio 0.62; 95% CI 0.52 to 0.74).

Additionally, the 30-day, or hospital mortality is reported in five recent systematic reviews (Table 1) (Harkin et al., 2007; Visser et al., 2007; Mastracci et al., 2008; Rayt et al., 2008; Sadat et al., 2008). Two reviews only discuss the results of the endovascular procedure (Mastracci et al., 2008; Rayt et al., 2008) and three reviews compared the endovascular with the open procedure (Harkin et al., 2007; Visser et al., 2007; Sadat et al., 2008). The first review showed a pooled mortality rate after EVAR of 24% (95% CI 20-28%) across 31 studies concerning 982 patients (Rayt et al., 2008). In 18 observational studies describing 436 people who underwent EVAR, the second review found a pooled mortality of 21% (95% CI 13-29%) (Mastracci et al., 2008). According to two reviews comparing both treatment groups, pooled mortality is 18%

(Harkin et al., 2007) and 22% (Visser et al., 2007) in the EVAR group compared to 34% (Harkin et al., 2007) and 38% (Visser et al., 2007) in the open surgery group. In the fifth review, Sadat et al showed that EVAR is associated with a significant reduction in mortality with a pooled odds ratio of 0.62 (95% CI 0.52-0.75) (Sadat et al., 2008). Visser et al found similar results with an odds ratio of 0.45 (95% BI 0.28-0.72) (Visser et al., 2007). However, after adjustment for patients' hemodynamic condition, the odds ratio was 0.67 (95% CI 0.31-1.44) and therefore no longer significant.

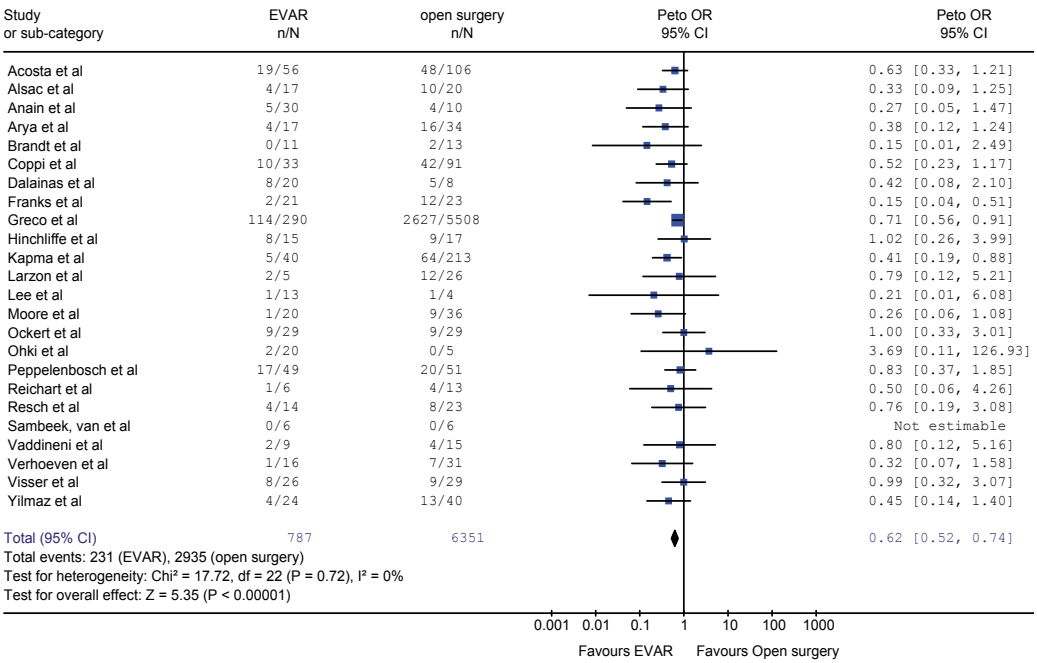

Fig. 1. Forest plot of 30-day or hospital mortality in 24 studies comparing EVAR and open surgery in patients with a ruptured AAA.

Review	**Studies**	**Patients**	**30-day/in-hospital mortality**		
	n	n	EVAR % (95% CI)	Open % (95% CI)	Odds ratio EVAR vs Open
Rayt et al., 2008	31	982	24% (20-28)	-	-
Mastracci et al., 2008	18	436	21% (13-29)	-	-
Harkin et al., 2007	34	891	18% (0-53) *	34% (0-70) *	-
Visser et al., 2007	10	478	22% (16-29)	38% (32-45)	0.45 (0.28-0.78)
Sadat et al., 2008	23	7040	-	-	0.62 (0.52-0.75)

CI = confidence interval, vs = versus, * = % (range of included studies)

Table 1. 30-day or in-hospital mortality in patients treated with open or endovascular repair according to five systematic reviews.

In addition, the systematic reviews showed that EVAR is associated with significant reduction in blood loss, reduced procedure time, reduction in systemical complications and

reduced intensive care and hospital stay compared to open surgery (Harkin et al., 2007; Visser et al., 2007; Mastracci et al., 2008; Sadat et al., 2008).

4. Discussion

Theoretically, both the endovascular and the conventional open technique have benefits. During open repair the aorta is clamped short after the initiation of the procedure, ceasing the blood loss. During endovascular repair on the other hand, the ruptured aneurysm remains part of the circulation until the entire endograft is deployed and correctly positioned without major endoleak.

Reported results of reduced early mortality after EVAR for the treatment of a ruptured AAA compared to open surgery seems conclusive (table 1). However, the currently available, mainly observational, studies are small and add considerable heterogeneity and methodological limitations (Yilmaz et al., 2002; Reichart et al., 2003; Resch et al., 2003; Lee et al., 2004; Alsac et al., 2005; Brandt et al., 2005; Castelli et al., 2005; Hechelhammer et al., 2005; Kapma et al., 2005; Larzon et al., 2005; Vaddineni et al., 2005; Arya et al., 2006; Coppi et al., 2006; Franks et al., 2006; Hinchliffe et al., 2006; Peppelenbosch et al., 2006; Visser et al., 2006; Acosta et al., 2007; Ockert et al., 2007). Heterogeneity is signified by the broad range in percentages of patients treated with EVAR (15-50%) and in percentage of haemodynamical unstable patients (33-73% in the eEVAR group). Even the definition of haemodynamical instability varied between the studies from a systolic blood pressure below 50 mmHg to 100 mmHg. Furthermore, the comparative studies reported so far are flawed by methodological inadequacies such as high potential of selection bias and lack of randomisation (Dillon et al., 2007). Selection bias is created by selecting patients for EVAR constituting a lower-risk category, presuming they need to be haemodynamically more stable for preoperative imaging and have a more favourable (EVAR-suitable) anatomic configuration. In a previous report, though not randomized, we eliminated selection bias due to inadequate patient matching by reporting a comparison of EVAR and open surgery in patients who all had the same preoperative imaging protocol, irrespective of haemodynamic condition, and who were all anatomically suitable for EVAR (Ten Bosch et al., 2010). This study showed a significant reduction in 30-day and 6-month mortality of EVAR compared to open ruptured AAA repair. However, a larger conducted prospective randomised trial such as the Amsterdam Acute Aneurysm Trial, which is currently performed in the Netherlands, is needed to identify possible benefits of EVAR over open surgery in patients with a ruptured AAA. The pilot study of Hinchliffe et al showed the possibility to recruit patients with a ruptured AAA to a randomised trial of open surgery and EVAR (Hinchliffe et al., 2006). However, a RCT might give ethical concerns, given the accumulation of superior results with EVAR based on the available observational studies. In addition, a RCT in an acute, severe condition like a ruptured AAA, appears difficult to perform (Hinchliffe et al., 2006). Furthermore, long term effects on outcome still need further investigation.

In case randomised trials demonstrate a clinically relevant reduction in mortality and morbidity for endovascular repair, consequences for care organisation will be major. Treatment of ruptured AAAs has to be performed in hospitals that are able to guarantee permanent availability of endovascular trained staff, implicating regionalisation and centralisation of acute AAA care.

5. Conclusion

The minimally invasive endovascular procedure (EVAR) is theoretically likely to reduce early mortality in patients with a ruptured AAA. The majority of observational studies show a clear trend toward an improved short term effect of EVAR and a significant reduction in early mortality compared to conventional open surgery. Therefore, EVAR has become a generally accepted treatment option for ruptured AAAs. However, studies comparing EVAR with conventional open surgery have to be interpreted with caution due to the likelihood of methodological inadequacies such as selection bias, heterogeneity, and lack of randomisation. Can endovascular repair of the ruptured AAA be considered as the treatment option of first choice? This question has not been answered yet. Further research in terms of randomised controlled trials with adequate follow-up will be required in order to clarify the role of endovascular repair as treatment option for ruptured abdominal aortic aneurysms.

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8

Magnetic Resonance Imaging of the Thoracic Aorta: A Review of Technical and Clinical Aspects, Including Its Use in the Evaluation of Aneurysms and Acute Vascular Conditions

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1. Introduction

Recent advances in non-invasive cross sectional imaging methods, such as CT and MRI have replaced most of invasive angiographic procedures with less cost and morbidity. Magnetic Resonance angiography (MRA) has gained broad acceptance and is fast becoming a routine in evaluation of the thoracic aorta. Latest developments in gradient hardware, pulse sequences, multiarray receiver coils and parallel imaging techniques as well as improved sequence performance of both 1.5T and 3T allows for detailed and comprehensive evaluation of the thoracic aorta and great vessels without exposure to ionizing radiation or iodinated contrast agents. Because MRA does not require the use of ionizing radiation, it can be performed more safely as repeat studies in the follow-up of thoracic aortic disease. Also, contrast-enhanced MRA uses a lesser volume of intravenous contrast agents, and is much less likely to result in contrast-induced in nephropathy compared with CT with iodine contrast, which may be particularly relevant since patients with aortic disease are often old, and frequently suffer from some extent of renal insufficiency. Another benefit that is intrinsic to MRI is the exquisite contrast resolution and the ability to perform a variety of techniques based on different physical principles. For example, for patients at risk of nephrogenic systemic fibrosis (NSF), non-contrast-enhanced MRA techniques may be considered, generally with good morphologic assessment. Not every MRA technique yields equivalent results in similar situations, and therefore, it is important to understand the

advantages and limitations of each technique. Furthermore, based on the intrinsic sensitivity to flow and motion, MRI offers the possibility of acquiring functional information that is of incremental value to the morphological MRA study.
The utility of MRA has been further improved by the addition of new intravenous contrast agents and the proliferation of post processing techniques, many of which are largely automated on commercially available workstations.
In this chapter we will discuss the current role of MRI in the assessment of the thoracic aorta; the available imaging techniques, and illustrate the application of these techniques to the diagnosis of acute thoracic syndrome related to the aorta.

2. MRA techniques

Magnetic resonance imaging (MRI) can use several different techniques for the evaluation of the aorta, each with advantages and disadvantages. Therefore examinations often require different and complementary approaches, according to the patient and clinical condition.
Magnetic resonance imaging of the aorta and pulmonary arteries is mainly dependent on a morphological evaluation, either alone or combined with a functional evaluation. The goals of the morphological evaluation are to provide information on the vessel location, diameter, wall characteristics, lumen patency and anatomical relations, including adjacent tissues and vessel branches. Unlike CT, MR can additionally provide vascular functional assessment, which can be useful in selected clinical settings. Many advanced practices are converging toward a subset of techniques that are fast, reliable, and reproducible. In the subheadings below, the authors will describe in more detail the different imaging approaches that can be used in the study of the thoracic aorta.

2.1 Gadolinium-enhanced MR angiography techniques

The use of gadolinium-based contrast agents (GBCA) has dramatically expanded the clinical utility of MRA. Gadolinium-enhanced MR angiography techniques can be highly spatially resolved, usually called contrast enhanced-MRA (CE-MRA), or highly temporally resolved, also called Time-resolved MRA (TR-MRA).
Many of the important advances in vascular MR imaging have involved evolution of CE-MRA, resulting in high-quality images in a single breath-hold (Sodickson, 2000; Lohan 2008). The most commonly used approach for CE-MRA is a 3D gradient echo (3D-GRE), allowing thin contiguous image partitions to be obtained during a single breath-hold. CE-MRA using a heavily T1-weighted 3D-GRE technique has become the mainstay of MR study of the vascular abnormalities of the thoracic aorta (Prince, 1993, 1996; Krinsky 1996, 1997; Sakamoto, 2010) (Fig1).
After the intravenous injection of a bolus of a GBCA, there is a T1-shortening of blood so that the blood appears bright irrespective of flow patterns or velocities. Usually, a standard dose (0.1 mL/kg bodyweight) of a GBCA is administered at a flow rate of 2-5 mL per second, followed by a saline flush of 20 mL injected at the same flow rate immediately after contrast administration, to achieve a compact bolus. Because signal enhancement and overall image quality of CE-MRA depends on the intra-arterial concentration of the GBCA, the correct timing of imaging after contrast material injection is fundamental (Sakamoto, 2010). Nevertheless, gadolinium has a larger window of visibility than iodine on CT images, which renders timing of data acquisition less critical than on CT.

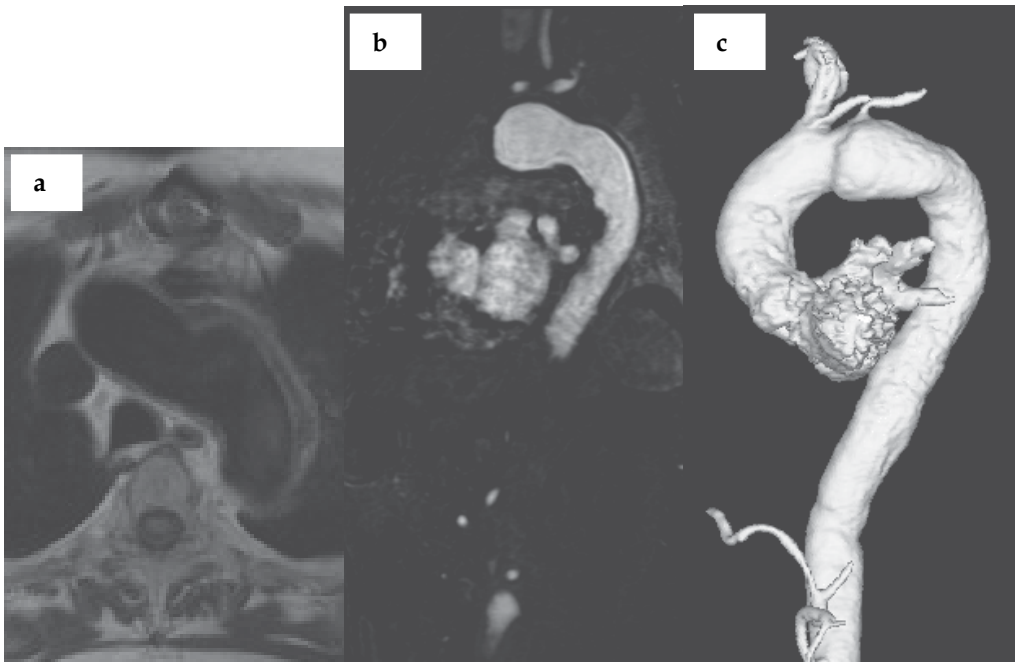


Fig. 1. A 6cm x 4cm saccular aneurysm at the aortic arch is depicted using the black blood technique (a). Black-blood imaging allows visualization of the involved aortic wall, facilitating accurate luminal and wall-to-wall diameter measurement. Source image of 3D parasagital CE-MRA acquisition (b) did not allow confident depiction of the aneurysm. Note the reduced signal from background (stationary) tissue, as there is insufficient time for recovery of longitudinal magnetization. Post processing MRA techniques like volume rendering (c) with multiple projections allowed a confidant diagnosis of this process.

Several methods are used to determine the optimal delay between the start of intravenous contrast material injection and the start of image acquisition, including injection of a test bolus using a small amount of contrast material, automatic triggering, and MR fluoroscopy (Sakamoto, 2010; Hany, 1997; Foo, 1997; Riederer, 2000). More recently, all major MRI system vendors have introduced real-time bolus monitoring software packages and these are now considered the state-of-the art for CE-MRA. Real-time bolus monitoring allows the operator to inject the total volume of contrast material, and to proceed with the 3D CE-MRA acquisition when the desired signal enhancement in the arterial bed of interest has been detected by the MR system, or by visual feedback by the operating technologist. Real-time MR fluoroscopic technique also integrates a monitoring phase and an imaging phase into a single pulse sequence. With the MR fluoroscopic method, monitoring is performed by using a continuous fast two-dimensional (2D) gradient-echo pulse sequence with imaging centered over the vascular bed.

The dose of contrast necessary to perform thoracic aorta CE-MRA varies by scanner, type of gadolinium-based contrast agent and operator experience. Thoracic aorta CE-MRA can be adequately performed with approximately 20mL or less of GBCA. MultiHance® (gadobenate dimeglumine) has greater T1 shortening than the purely extracellular GBCAs currently available, leading some centers like ours, to use this agent at a lower dose (half-dose or 0.5mmol/KG) than would be used with typical extracellular agents. An additional attractive feature of Multihance is mild protein-binding that increases intravascular dwell time.

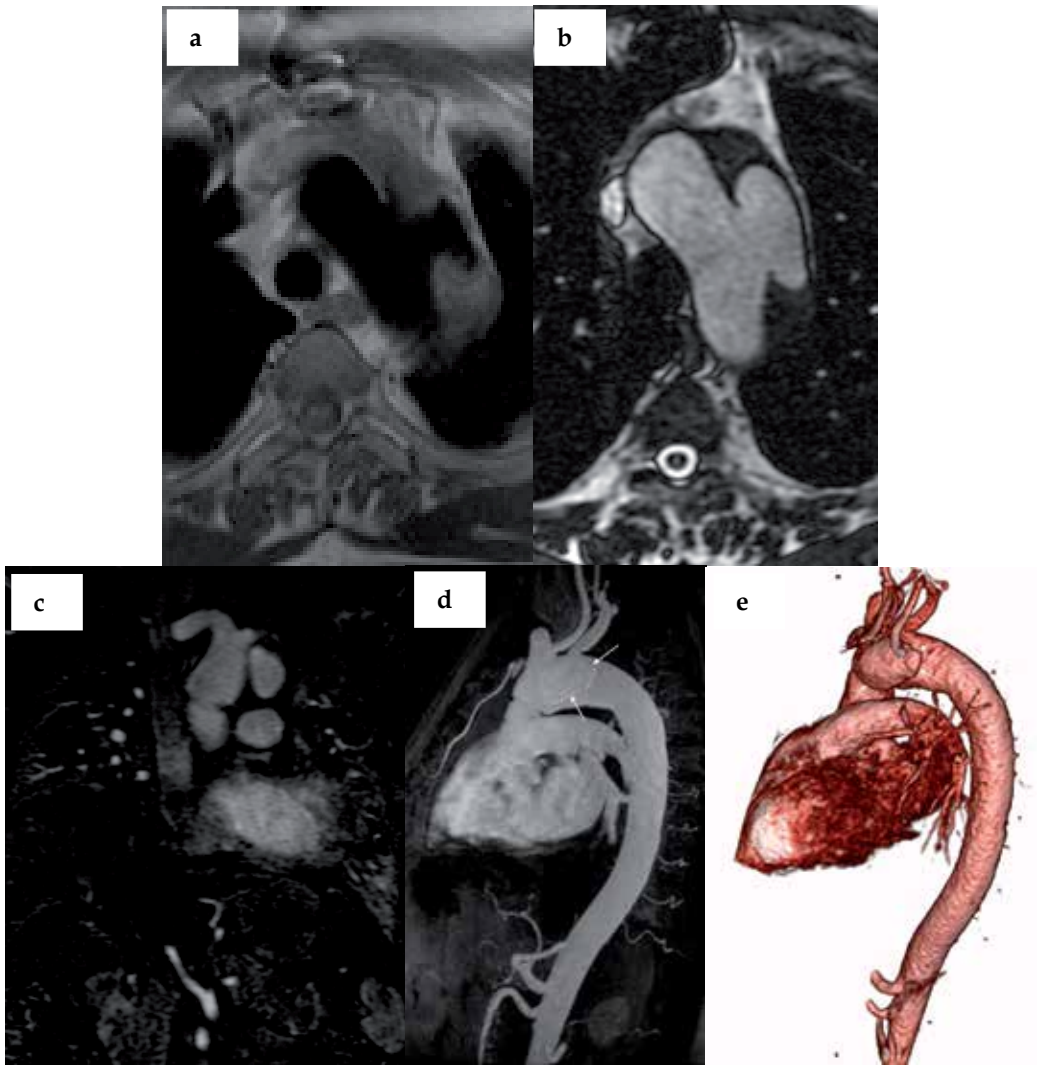


Fig. 2. Aortic pseudoaneurysm in a 48 year-old man, a complication of a previous repair of an aortic aneurysm. Axial black-blood spin-echo (a) and single-shot SSFP (b) images showed a left pseudoaneurysm at the level of the aortic arch. Coronal MPR showed direct communication with the true aortic lumen (c). MIP and volume-rendered full-thickness from CE-MRA examination (d, e) displays the morphology and location of the pseudoaneurysm.

2.1.1 Steady-state contrast enhanced MRA and blood pool contrast agents

Besides dynamic imaging of the arterial-dominant phase after single bolus injection of an extracellular GBCA (first-pass MRA), extended imaging during the steady state of the contrast agent can be performed: this is called steady-state contrast enhanced MRA (Klessen, 2007; Hartmann, 2006; Nissen, 2009). With this technique, specific contrast agents may be

used, blood-pool agents, allowing imaging acquisition up to one hour after contrast administration (Hartmann, 2006).

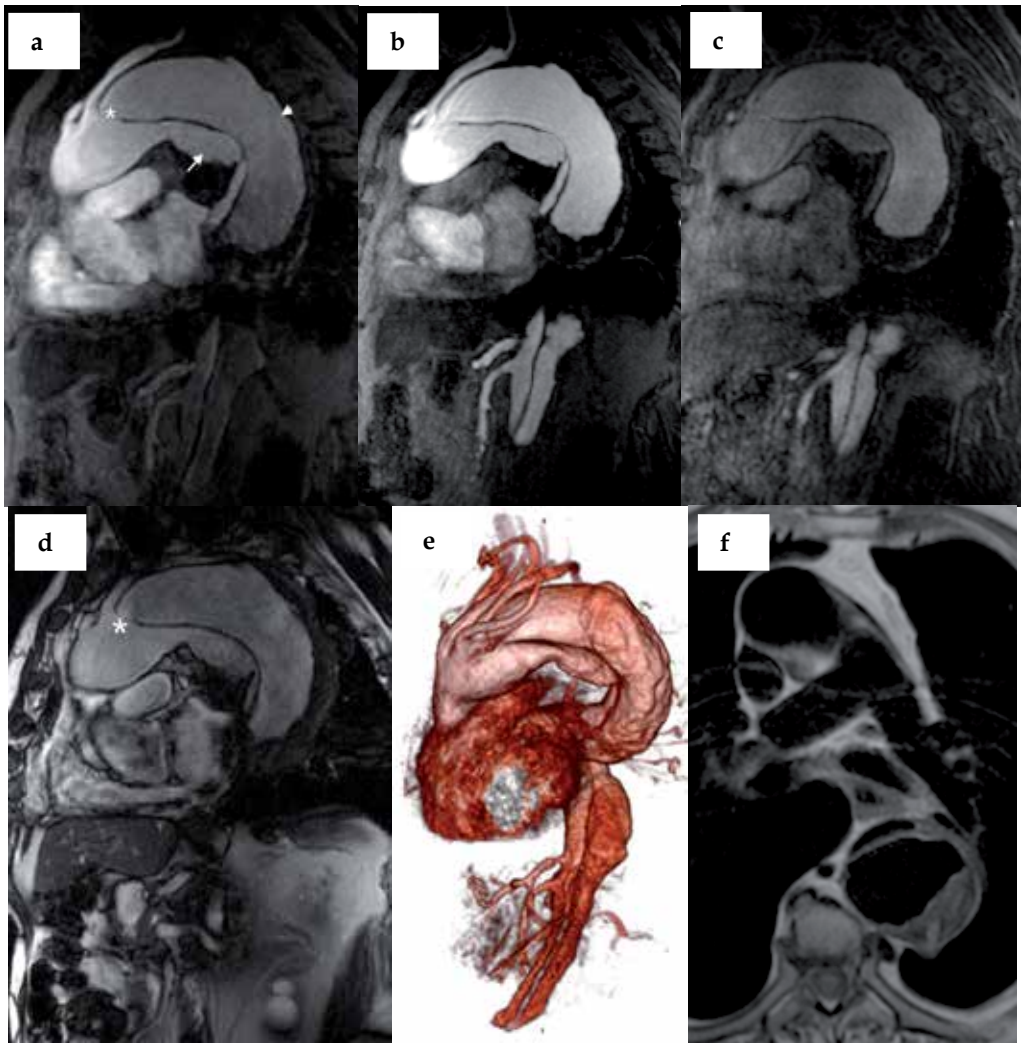


Fig. 3. Oblique sagittal images from a time-resolved MRA of the chest in a 83 year-old male with a Stanford type B aortic dissection. Using a TR-MRA technique it is possible to demonstrate delayed filling of the false lumen (a). There is a dissection flap originating in the aortic arch distal to the origin of the left subclavian artery. Arch vessels that arise from the true lumen and are not involved by dissection. Delayed phases show the distal extent of the false lumen (b, c), with late higher overall enhancement compared to the true lumen (c). The anatomic details of the dissected aorta are somewhat difficult to recognize on volume rendered images (e). Parasagittal reformatted TR-MRA and bSSFP (asterisk, a, d) images clearly depict the intimal flap and also the entry site. Black-blood images (f) show a compressed true lumen due to a dilated false lumen.

Blood pool contrast agents have a prolonged intravascular phase, which means that a wide window of opportunity exists for imaging the blood vessels after contrast agent administration. Gadofosveset trisodium (Ablavar®, Vasovist®) is the first blood pool contrast agent FDA approved for routine clinical use. Gadofosveset is characterized by a lipophilic side chain, which leads to a transient, reversible and non-covalent binding to serum albumin (Lauffer, 1998). The transient protein interaction increases T1-relaxtivity four to five times compared to standard extracellular gadolinium chelates at 1.5 T (Nissen, 2009; Rohrer, 2005; Caravan, 2007), resulting in prolonged blood pool enhancement, which is particularly beneficial for vascular imaging. This can be utilized for higher spatial resolution scanning and greater anatomic coverage. Maximum signal enhancement using this contrast agent on MRA is independent of the injection rate used (Nissen, 2009). Nevertheless, first-pass arterial phase imaging should be performed when possible to avoid interference from venous structures, with steady-state CE-MRA used as a complementary acquisition. Gadofosveset can be used for these two types of CE-MRA with a single dose. It remains longer in the intravascular compartment, allowing several repetitions of the CE-MRA sequences after the initiation of contrast injection. It is possible then to choose the acquisition (both in time and imaging plane) that best displays the vessels of interest for image interpretation.

2.1.2 MRA Post-processing and imaging planes

Interpretation of MR images usually is done with the aid of a computer workstation on which individual source images are analyzed and postprocessing techniques, such as maximum intensity projection (MIP) reformation, volume rendering and multiplanar reformation of the images are performed (Fig 2). MIP images can be obtained quickly, and permit a 3D appreciation of anatomy, which can be useful both for the radiologist and for the clinician, as these resemble catheter angiograms, and are therefore the most widely used post-processing technique. MIP reconstruction involves display of the highest signal intensity voxels within each projection ray to create pixels on the final image. These images must be viewed in multiple projections to detect findings that might be otherwise obscured by overlapping structures with higher signal intensity. Volume rendering uses the entire volume of data for image reconstruction. Volume rendering assigns groups of voxels an opacity score from 0% (transparent) to 100% (completely opaque).

Multiplanar (MPR) and curved reformations allow rapid assessment of MRA data in any plane avoiding problems with vessel overlap and background projection. MPR compresses the full volume of data in a single plane.

Comprehensive thoracic aortic evaluation necessitates that images are acquired in several complementary planes, such that the entire course is fully evaluated. Direct coronal and sagittal images may address shortcomings of true axial views, a parasagittal oblique plane to the ascending, transverse, and descending aorta, is recommended such that subtle abnormalities of the arch may be confidently excluded. This imaging plane also is beneficial in aortic dissection, demonstrating the extent of intimal dissection flaps and their relationship to the origins of the supra-aortic branch vessels. In the presence of aortic dissection or aneurysmal dilatation, particularly when involving the ascending portion of the thoracic aorta, cine imaging of the left ventricular outflow tract represents an essential component to the evaluation of the effect of such pathology on ventricular function.

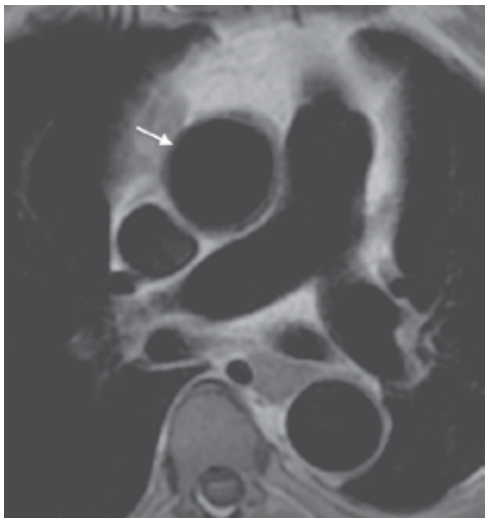


Fig. 4. Ascending aortic aneurysm. Axial black-blood imaging of the aorta through the upper mediastinum at the level of the right pulmonary artery (a). There is homogeneous suppression of luminal blood signal, increasing the conspicuity of the vessel wall.

2.1.3 Time-resolved MR angiography (TR-MRA)

If dynamic information related to direction or rate of vascular enhancement is considered necessary, Time-resolved MR angiography (TR-MRA) techniques can provide this temporal resolution during the vascular phases of enhancement, with a compromise regarding spatial resolution. These techniques are widely available on modern equipments and have become routinely used in many medical centers; TR-MRA can have a complementary or alternative role to conventional CE-MRA and has been advocated by some authors when a comprehensive evaluation of the thoracic vasculature is warranted (Lohan, 2008b).

Dedicated time-resolved MRA sequences such as TRICKS (time-resolved imaging of contrast kinetics), TWIST (time-resolved angiography with stochastic trajectories), or 4D Track (4D time-resolved MRA with Keyhole), can be used to collect data continuously after GBCA injection during a single breath-hold. TR-MRA represents a powerful complement to conventional 3-D CE-MRA. A complementary TR-MRA allows dynamic evaluation of circulatory patency, confidant separation of the arterial and venous phases of luminal enhancement (Lohan, 2008). Patients who have severe respiratory disease and very limited breath-hold capabilities can be examined (Lohan, 2008; Griffin, 2009). Time-resolved CE-MRA is independent of the bolus timing, because the contrast injection and the MR imaging sequence are started simultaneously. TR-MRA may be of particular value in the evaluation of inhomogeneous aortic flow and dissections, showing the opacification of true and false lumens on multiple phases of enhancement (Fig3) (Lohan, 2008; Schoenberg, 1999).

2.1.4 Patient preparation for contrast-enhanced MRA

Patient preparation used has been described elsewhere (Schneider, 2005): In addition to screening for the usual contraindications for MR scanning (e.g. pacemakers) and for the use of GBCA (e.g. pregnancy), patients scheduled for a CE-MRA examination should also be asked about underlying pulmonary disease and their ability to hold their breath. If

necessary, proper coaching is performed in advance and breath holding is optimized by the use of supplemental oxygen and hyperventilation (Marks, 1997). Patients should also be asked about prior interventions, especially vascular or endovascular procedures. Knowledge of extra-anatomic bypass grafts or stent grafts will ensure proper scan prescription and planning.

Patients are checked for venous access. Ideally, for CE-MRA, the intravenous catheter is placed in the antecubital fossa and should be sufficiently large (i.e. at least 22 gauge) to support a bolus rate of at least 2 mL/sec. When imaging the aortic arch and great vessel origins, it is preferable to place the intravenous catheter in the right arm, as left sided venous contrast administration can cause T2* artifacts due to the high concentration of the GBCA within the left brachiocephalic vein en route to the right heart. This can be mistaken for a proximal great vessel stenosis (Lee, 2000).

2.2 Gadolinium-based contrast agents and nephrogenic systemic fibrosis (NSF)

MRA using a GBCA has become the mainstay of high-quality MR imaging of the thoracic vasculature. This reflects its high spatial and temporal resolution, and avoidance of ionizing radiation and of nephrotoxicity related to iodine-based contrast agents, which are utilized in CT. There are however, specific safety conditions that are related to the use of GBCA, such as high-risk patients for nephrogenic systemic fibrosis (NSF), or pregnant patients. Limited intravenous access also may obviate contrast use. Considering NSF and gadolinium, it has been shown that not all agents have the same risk for NSF, and that volume of contrast and cumulative dose influenced the presence and severity of NSF. The use of stable GBCAs are recommended such as macrocyclic agents (eg: Prohance, Gadovist, Dotarem) or ionic Linear with partial hepatobiliary elimination and high T1 relaxation (Gadofosveset or Gadobenate dimeglumine) at risk patients (Wertman, 2008; Altun, 2009a, 2009b; Martin, 2009). Reducing the dose, while maintaining diagnostic information, is also important (Altun, 2009b). Half-dose (0,5mmol/Kg) Gadobenate dimeglumine has been shown to provide diagnostic quality examinations in abdominal studies, including vascular imaging. It is the authors' experience that the same diagnostic results can be achieved in thoracic imaging, when higher doses are not recommended for safety concerns.

Recently, the use of quarter-dose (0,025mmol/Kg) Gadobenate dimeglumine at 3T has been associated with diagnostic images in the abdomen (De Campos, 2011). It is likely that this can also be achieved in thoracic vascular imaging, providing vascular diagnostic imaging of the thorax, either alone or in combination with other techniques, such as TR-MRA and/or noncontrast-enhanced MRA, in selected cases. It should be noted that the relative risk for developing contrast induced nephropathy with iodinated contrast agents in patients with chronic renal failure generally far exceeds the risk of NSF. There is no measurable risk of NSF occurring in patients with mild to moderate (stage 3) chronic renal failure using GBCAs, whereas these patients are at risk for contrast induced nephropathy (Altun, 2009b, Martin 2009).

2.3 Noncontrast-enhanced MR angiography

Over the last decade, contrast-enhanced MR angiography (CE-MRA) techniques (Prince, 1996; Krinsky, 1999; Korosec, 1996) have largely replaced unenhanced MRA techniques for the evaluation of the thoracic aorta because of their high spatial resolution and reliability. In recent years, with the concern about NSF, along with concerns about ionizing radiation and nephrotoxicity of iodinated contrast agents, non-contrast MRA, have re-emerged as important techniques, especially bright blood steady state free precession techniques.

2.3.1 "Bright blood" MR angiography

Non-contrast enhanced "bright blood" vascular imaging includes Steady-state free-precession (SSFP), Time-of-flight (TOF) and Phase-contrast (PC) MR angiography.

Steady-state free-precession (SSFP) sequence (TrueFISP, balanced FFE, FIESTA) is a bright blood technique, with short TE and TR sequences, that has become widely available (Sakamoto, 2010;Earls, 2002; Pereles, 2002). With SSFP, intraluminal signal generally is very high and homogenous even in cases of turbulent flow because this sequence depends mainly on a function of the T2/T1 ratio (Sakamoto, 2010).

SSFP images can be acquired in both breath-hold and free-breathing manners, either with or without ECG-gate and Navigator/ respiratory triggered (Bi, 2005; Amano, 2008). SSFP can provide rapid bright-blood images with high-contrast resolution, free-breathing real-time steady-state free precession techniques allow for a fast non-ECG gated, non–contrast enhanced MRA that may be useful in critically ill patients (Pereles, 2002; Gebker, 2007; Kluge, 2004). A rapid morphologic assessment can be achieved in urgent situations, such as demonstrating aortic abnormalities in unstable patients, for example intimal flaps and false lumens in aortic dissection (Pereles, 2002; Gebker, 2007). Free-breathing cardiac and respiratory-gated 3D SSFP MRA has also been shown valuable in the evaluation of thoracic vessels (Fuchs, 2003; Tomasian, 2008; Krishnam, 2008, 2010), and represents an alternative for free-breathing SSFP MRA.

SSFP sequences can also be acquired in a cine mode, and have become the foundation for cine imaging. Advantages are the higher SNR, shorter imaging duration, and freedom from the reliance on inflow effects for signal generation (Carr, 2001; Lohan, 2008). This sequence has benefited from the application of parallel imaging techniques, allowing high temporal resolution, large FOV imaging of the thoracic aorta, and left ventricular outflow during acceptable breath-holds as low as 5 to 6 seconds. The inherently high blood signal achieved using SSFP throughout a cine acquisition period has been shown to aid evaluation of aortic mural and valvular characteristics and allowing exclusion of the presence of aortic dissection, (Pereles, 2002; Kunz, 2004). SSFP is the most promising of the "bright-blood" non-contrast enhanced MR angiography techniques (Fig2 and 3).

Other techniques, such as time-of-flight (TOF) and phase-contrast (PC) are seldom use for non–contrast-enhanced MR angiography of the thorax because of sensitivity to respiratory and cardiac motions, in-plane saturation, and the need for wide coverage (Prince, 1993;Amano, 2008; McCauley, 1994). These sequences are also time- consuming and susceptible to artifacts. Possible applications exist when vascular flow quantification is warranted.

PC-MRA is an inherently quantitative technique, unlike TOF or CE MRA., allowing for the calculation of flow velocity. With PC-MRA, the signal intensity of blood is proportional to its flow velocity and the direction of flow can be determined on the basis of the direction of the phase shift (Schneider, 2005).

2.3.2 "Black-blood" MR

These techniques are termed black-blood because signal void is created in flowing blood. They consist of either conventional or echo-train spin-echo techniques, usually with ECG-gating, exploiting the contrast between rapidly flowing blood and the aortic wall (Sakamoto, 2010; Czum, 2005; Fattori, 1999; Russo, 2006; Bradley, 1985). Black-blood MRA may be useful for the depiction of intraluminal abnormalities such as dissection flaps and tumor

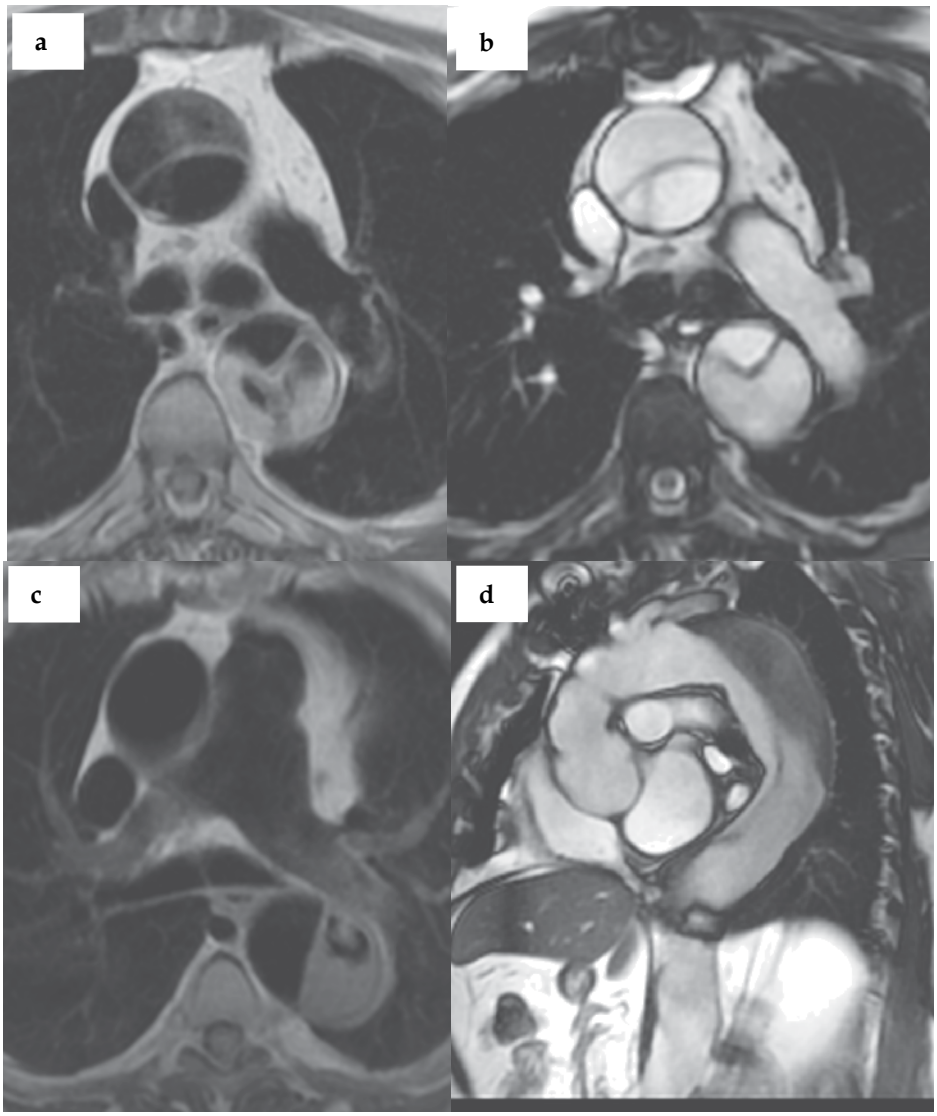


Fig. 5. Two patients with type A dissection. Slow/ turbulent flow may produce high signal in the aortic lumen, artificially simulating wall disease. A simple method of reducing errors is to compare with other sequences. In the first case (a) there is moderate high signal intensity in the false lumen, which correlates with high signal intensity on the bSSFP images (b), associated with slow flow. On the other example (c), the higher signal intensity saw on the spin-echo sequence (black-blood image) correlates with a partial thrombus in the false lumen as low signal intensity on the bSSFP images (d). A simple method of reducing intravascular signal on a black-blood technique is to increase the TE, allowing more time for intravoxel dephasing and for moving excited protons to exit the slice before the refocusing pulse.

thrombus. When vessel wall analysis is desirable, as in aortic conditions such as mural hematoma, black-blood techniques may at times provide a better wall depiction than CE-MRA (Potthast, 2010; Litmanovich, 2009). The goal of black-blood techniques is to eliminate

as much signal as possible from flowing blood in the vessels lumen (Fig4). Luminal signal void occurs because intravascular protons only produce signal if they are exposed to both a 90-degree excitation pulse and subsequent refocusing pulse while travelling through the image slice. Therefore, low flow and entry/exit slice phenomena may produce high signal in the aortic lumen (Fig5), artificially simulating wall disease (Sakamoto, 2010). Echo-train spin-echo techniques are favoured, because of rapid data acquisition (usually in a single breath hold) and improved image resolution (Matsunaga, 2003). T2-weighted single-shot echo-train spin-echo sequences can be obtained as a black blood technique, which may be useful in patients who cannot comply with the necessary breath-holds for alternative imaging (Stehling, 1996; Winterer, 1999).
Usually, black-blood techniques are used in combination with other imaging sequences, most often CE-MRA and/or non-contrast enhanced "bright-blood techniques".

3. Comprehensive thoracic evaluation on vascular MR studies

Although the above-described techniques, especially CE-MRA, can achieve high-quality diagnostic imaging of the thoracic vessels, evaluation of comprehensive chest structures may be necessary. If clinically necessary, the complementary use of T2 weighted single-shot echo-train spin echo and pre-contrast 3D-GRE sequences in axial and coronal planes will provide such information with minimally added time (Fig 6). A basic MRA protocol can be supplemented with additional sequences, based on the suspected clinical condition or pathologic process. Post contrast 3D-GRE MRI visualizes not only the aorta, but also the lungs and other organs and structures in the chest (Bader, 2002; Karabulut, 2002; Altun, 2010) and is usually acquired after the MRA. Blood-pool contrast agents can be beneficial in this setting, allowing for persistently high signal in vessels on delayed acquisition.

4. Clinical conditions

An increasing number of clinical indications for gadolinium-enhanced MRA/MRI have been described, including congenital syndromes, functional imaging of flow and direction, and acquired disease of the aorta. A detailed description of all these indications is beyond the scope of this chapter, and can be found elsewhere (Schneider, 2005). In this review, the authors will focus on some common indications for MRA/MRI imaging of the aorta, aortic aneurysms, and acute aortic syndrome will be discussed. Usually, in these settings, CT is more commonly used than MR, due to its high spatial resolution rapid acquisition, resistance to patient motion, adequate diagnostic capability, and availability of the technique (Bhargavan, 2010; Jha, 2010). Nevertheless, in selected cases, MR may be preferred, such as in young patients, pregnant patients, renal failure, allergy to iodine contrast, or lack of adequate intravenous access. Another setting in which MR is recommended, is in studying patients that will undergo sequential follow up examinations, as a follow-up to initial CT or MR studies, as in the follow-up of aneurysms. In specific conditions, MR can be superior to CT, for example when differentiating false from true lumen in an aortic dissection, using cine-imaging if needed, or when differentiating acute aortic hematoma from atherosclerotic plaque and chronic thrombus (Yucel, 1990).
A combination of morphological assessment techniques and vascular patency techniques is sufficient for most acute conditions. In selected cases, dynamic imaging, usually using TR-

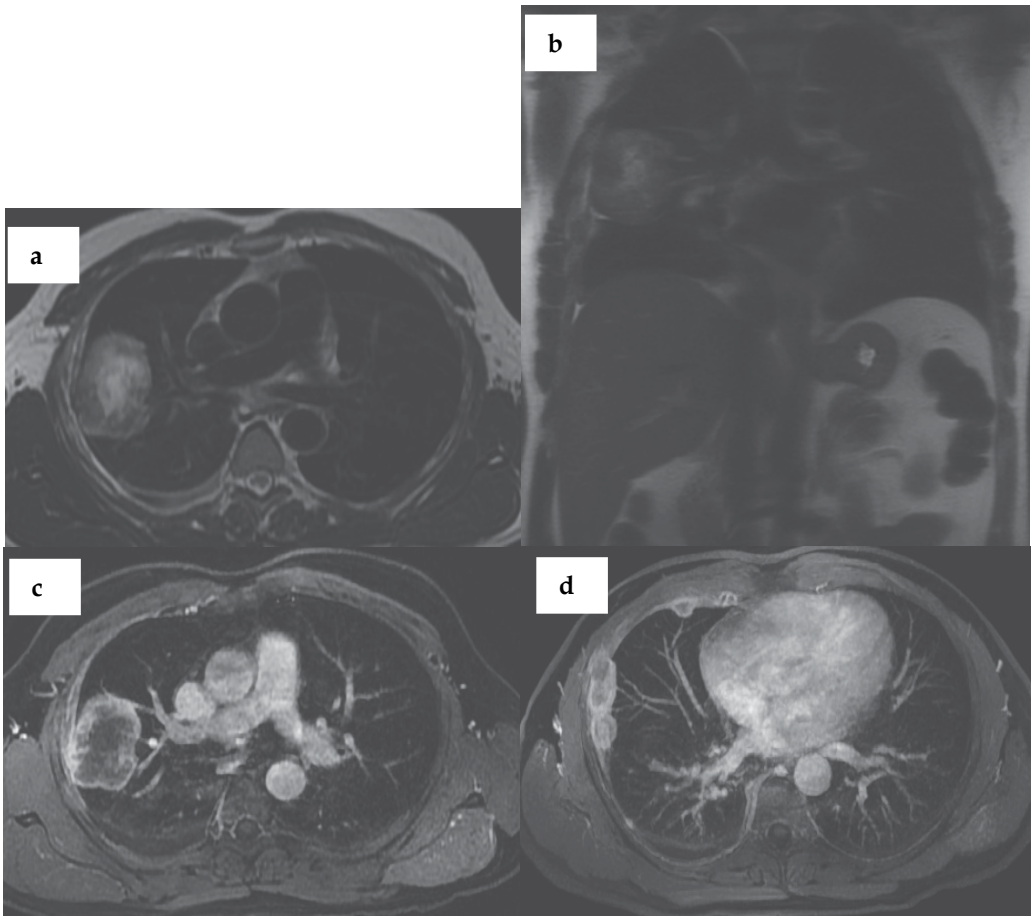


Fig. 6. A 62 year-old male with small cell lung cancer with pleural involvement. Axial double IR black-blood spin-echo MR (a) and coronal T2-weighted single-shot fast spin-echo (b) images clearly showed a pulmonary mass in the right upper lobe. Post contrast T1-weighted 3D-GRE images (c, d) defined the lesion's vascular characteristics and as well as pleural involvement.

MRI or Cine-SSFP can be added to the study, as described below. Using comprehensive imaging protocols provides information, not only on the disease process in question, but other diseases as well. For example, a comprehensive protocol evaluating suspected acute pulmonary embolism can also detect aortic dissection.

4.1 Aortic aneurysm

The normal dimensions of the aorta have been defined based on normative measurements performed in large patient populations (Litmanovich, 2009). An ascending aortic diameter equal to or greater than 4 cm (in individuals younger than 60 years old) and a descending aortic diameter larger than 3 cm is usually considered to indicate dilatation and a diameter equalling or exceeding 1.5 times the expected normal diameter is considered an aneurysm (Litmanovich, 2009). The prevalence of thoracic aortic aneurysms increases with age, with an overall incidence approximating 450 per 100,000 and a 3:1 male predominance

(Bickerstaff, 1982; Litmanovich, 2009). In up to one third of cases, the abdominal aorta is also involved (Bickerstaff, 1982; Litmanovich, 2009) (Fig7). Most thoracic aneurysms are

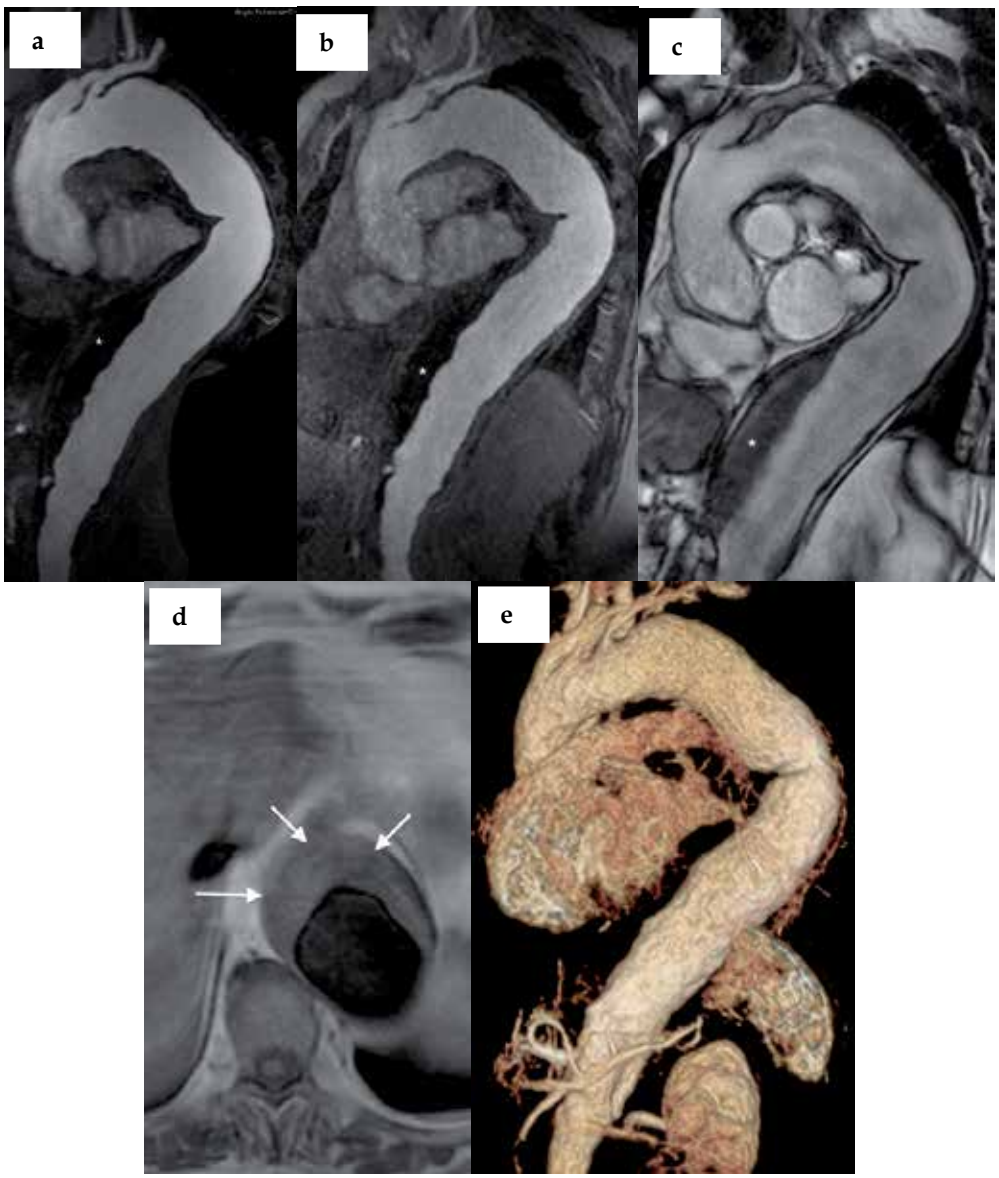


Fig. 7. A 77-year-old male with diffuse long-standing atherosclerotic thoraco-abdominal aneurysm. MIP CE-MRA (a) and TR-MRA (b) images clearly depict the diffuse thoracic aorta dilatation with mural thrombus in the descending aorta (asterisk, A, B) and irregular contour due to severe atherosclerosis. These features are also well appreciated in the bSSFP images (c). Characterization of the aortic wall and thrombus is better preformed with a black-blood sequence (d) like a double inversion spin-echo techniques. With volume rendering (e) the entire volume of data is used in data reconstruction.

atherosclerotic (Tatli, 2004; Litmanovich, 2009). Infection, inflammation, syphilis, and cystic medial necrosis are other causes for aortic aneurysms, the last being the most common cause of an aneurysm isolated to the ascending aorta. Cystic medial necrosis is usually associated with Marfan syndrome but can also be idiopathic (Litmanovich, 2009). In Marfan syndrome, the classic imaging features include a pear-shaped aneurysmal ascending aorta with smooth tapering to a normal aortic arch (Litmanovich, 2009) (Fig 8). Thoracic aortic aneurysms can also be divided into true and false (or pseudoaneurysms), according to their pathologic

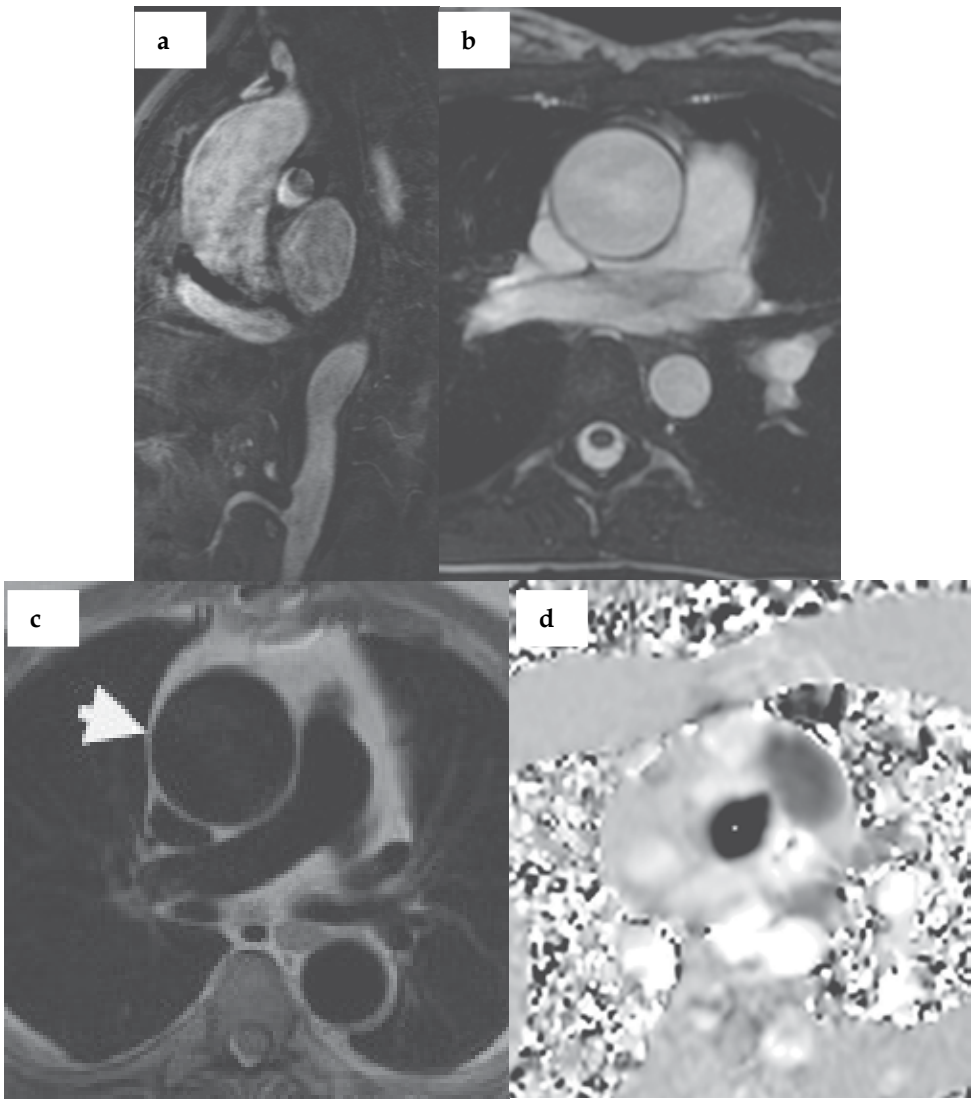


Fig. 8. Fusiform ascending aortic aneurysm in a patient with Marfan syndrome, depicted on CE-MRA (a), bSSFP (b) and on black blood (c) images. Phase contrast flow quantification at the level of the aortic valve (d) shows the characteristic fish-mouth appearance of bicuspid aortic valve, a common addition of aortic aneurysm.

features. In true aneurysms, all layers of the aortic wall are involved. A pseudoaneurysm represents enlargement of the artery resulting from blood accumulating beyond the intimal layer and typically trapped within the serosa or outer layer of the arterial wall (Fig2). Aetiology may be related to ruptured atheroma, dissection, or trauma. When resulting from trauma, the aortic isthmus is more frequently affected by pseudoaneurysms, whereas penetrating aortic ulcer usually occurs in the descending aorta (Litmanovich, 2009; Boiselle, 2007).

True aortic aneurysms are usually fusiform in shape, involving the entire circumference of the aorta, and often extend over a significant length of the vessel, although saccular aneurysms can occasionally be found (Fig1). Pseudoaneurysms are usually saccular, with a narrow neck at the origin in the aorta. The presence of a wide neck in a saccular aneurysm suggests a mycotic origin. These aneurysms have a tendency to involve the ascending aorta, likely because of its proximity to the heart and suspected extension from endocarditis (Boiselle, 2007).

It is important to evaluate eventual extension of thoracic aortic aneurysms to the abdominal aorta, as there are therapeutic implications (Yu, 2007). Thoraco-abdominal aneurysms include Type I (involving the descending thoracic aorta below the origin of the left subclavian artery and the upper abdominal aorta); Type II (involving both the thoracic descending aorta and most of the abdominal aorta); Type III (lower portion of the thoracic aorta) and Type IV (begins at the diaphragm and extends caudally) (Crawford, 1986; Litmanovich, 2009).

When imaging an aortic aneurysm, it is important to exactly evaluate the maximal diameter, the length of the aneurysm, and involvement of major branch vessels (Bonser, 2000). Also, the most frequent complications of aortic aneurysm - mass effect, dissection, and rupture - are related to size. The mean rate of dilatation for thoracic aortic aneurysm is 0.12 cm per year (Coady, 1997). The risk of rupture increases with increasing aortic diameter, with a high risk of complications (rupture and dissection) at 6 cm for the ascending and 7 cm for the descending thoracic aorta (Elefteriades, 2002, 2005). CE-MRA/MRI is generally suitable for this evaluation. It allows the study of the extent of an aneurysm and its relationship to the aortic branches, with reproducible results (Prince, 1996; Krinsky, 1997; Debatin, 1998; Neimatallah, 1999). Breath-hold non ECG-gated CE-MRA is nevertheless more prone to motion artifacts and blurring at the aortic root, with potential implications for treatment planning (Potthast, 2010; Cigarroa, 1993). Non-contrast enhanced ECG-gated 3D-SSFP has shown good results in aneurysm imaging, providing good assessment of diameter, lumen patency and topographic evaluation, including the aortic root (Krishnam, 2008; Potthast, 2010). It can also be used as a cine technique allowing for evaluation of the aortic valve in patients with ascending aortic aneurysms, providing crucial information for treatment planning (Sakamoto, 2010).

Use of the sagittal or oblique sagittal plane allows accurate assessment of the location and extent of the aneurysm and avoids partial volume effects. With CE-MRA, aneurysm measurements should be obtained from source images where the vessel wall is visible, because MIP images represent a cast of the lumen alone, and therefore, underestimates aneurysm dimensions (Sakamoto, 2010). Standard spin echo images and precontrast 3D-GRE also are helpful in evaluating changes in the aortic wall and periaortic structures. Areas of high signal intensity on spin echo images within the thrombus and aortic wall may indicate instability of the aneurysm (Sakamoto, 2010; Russo, 2006b). High signal is

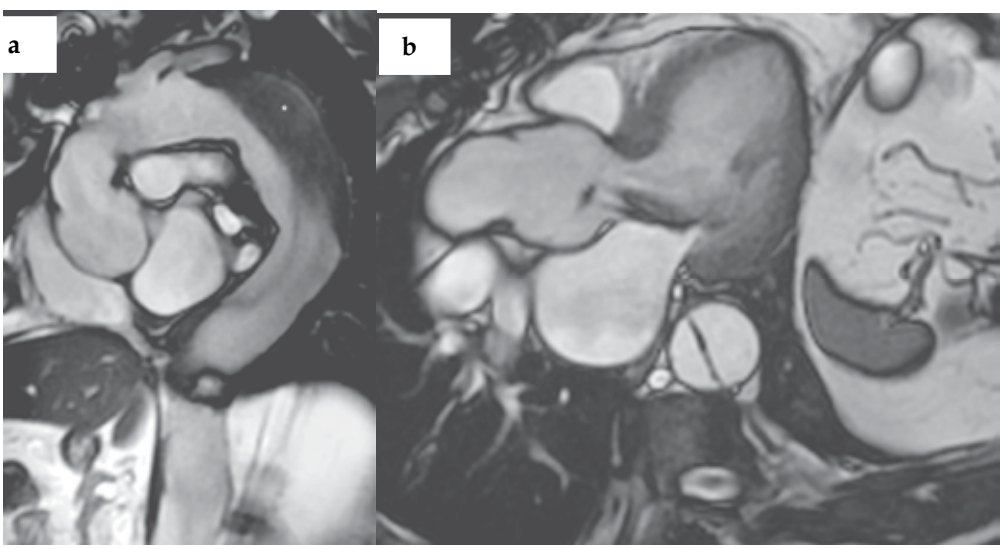
emphasized by using fat suppressed T1-weighted sequences. Also, contrast enhanced MRA, using time resolved techniques, allows visualization of the Adamkiewicz artery (Bley, 2010), providing information that is important in planning the surgical repair of an aneurysm, thus avoiding postoperative neurologic deficit secondary to spinal cord ischemia (Nijenhuis, 2006; Yoshioka, 2006).

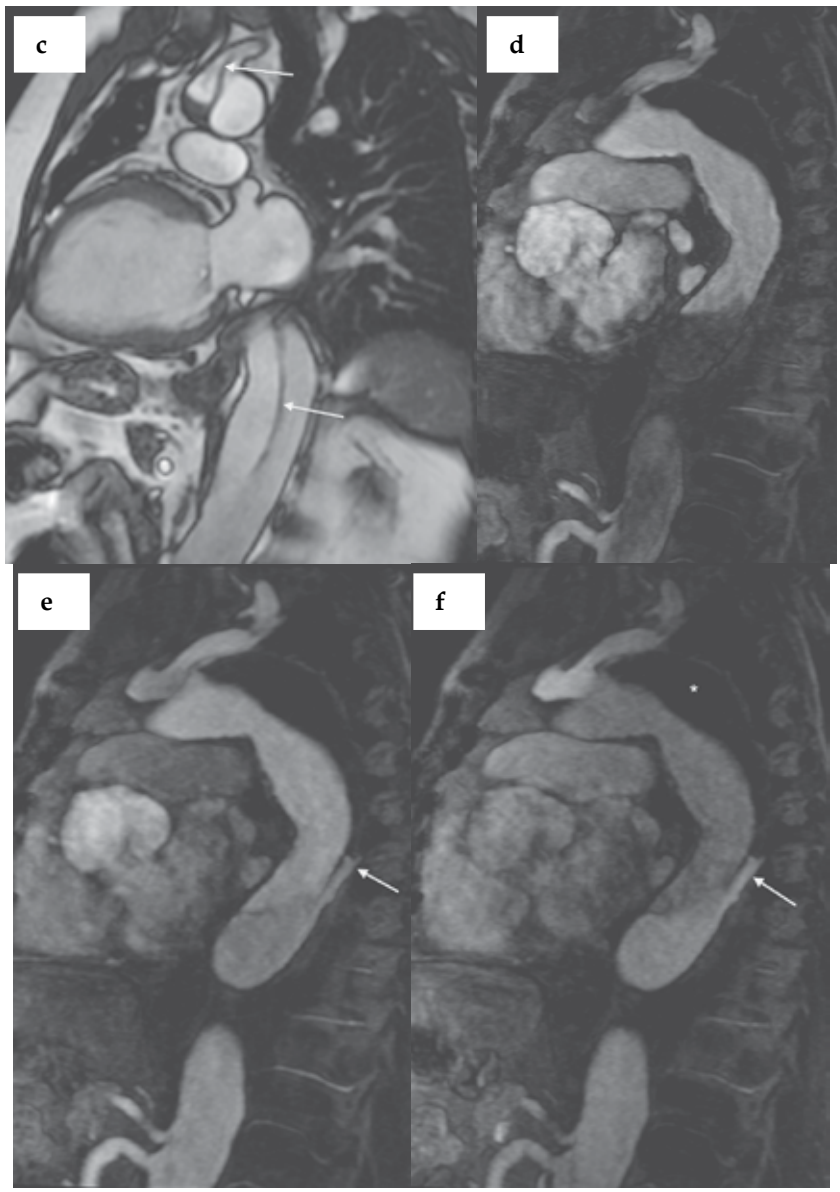
4.2 Acute aortic syndrome

Acute Aortic Syndrome includes dissection, intramural hematoma, and penetrating ulcer. In all three conditions, MRI may have a role with similar diagnostic capability or advantages over CT.

4.2.1 Aortic dissection

Aortic dissection is a life-threatening condition requiring prompt diagnosis and treatment. This condition occurs when blood dissects into the media of the aortic wall through an intimal tear. Classification of aortic dissections has been based traditionally on anatomic location and time from onset. The 14-day period after onset has been designated as the acute phase, because morbidity and mortality rates are highest (15%–25%), and surviving patients typically stabilize during this period. The Stanford classification distinguishes aortic dissection into type A or B, whether the ascending aorta is involved or spared, respectively. This classification is based fundamentally on prognostic factors: type A dissection necessitates urgent surgical repair, but most type B dissections can be managed conservatively. Hence, accurate recognition with imaging of anatomic details of the dissection is essential for successful management (Cigarroa, 1993). The diagnostic goals of imaging are a clear anatomic delineation of the intimal flap and its extension and the detection of the entry and re-entry sites and branch vessel involvement (Fig9).





Aortic root dilatation with severe aortic insufficiency (50%) is noted (b) on axial heart three chambers view bSSFP images. This sentence belongs to figure 9 legend.

Fig. 9. ECG gated bSSFP (a, b, c) and 3D contrast-enhanced MR angiography of aortic dissection (d, e, f). Sequelae of prior surgical repair of the ascending aorta with stable type A aortic dissection with thrombosis of the false lumen (asterisk, a, f) at the level of the arch and with a persistent but unchanged dissection flap originating in the aortic arch near to the left subclavian takeoff. The arch vessels arise from the true lumen and the left subclavian artery is involved by dissection. The distal arch and thoracic aorta are dilated and retrograde fill of the false lumen is depicted on CE-MRA (d, e). The dissection flap extends throughout the thoracic and abdominal aorta and into the right common and external iliac arteries.

With current technology, MR imaging is the most accurate tool for detection of these features of the dissection (Prince, 1993; LaRoy, 1989; Roberts, 2001; Shiga, 2006). Occasionally MR can also demonstrate "aortic cobwebs", which are fibroelastic bands formed during the dissection process that project from the false lumen wall (Williams, 1994). Detection of these bands facilitates the distinction of the false from the true lumen, as they are located in the false lumen. On spin-echo images, flow in the true lumen is usually signal void, whereas flow in the false lumen can be signal void or high in signal intensity depending upon the velocity of blood flow. Slow flow in the false lumen of a dissection may be difficult to differentiate from thrombosis on spin-echo images (Fig5).
The role of conventional spin-echo imaging is limited because CE MRA/MRI imaging are all fast, accurate, and reproducible techniques for the demonstration of dissection. CE-MRA/MRI techniques reliably differentiate slow flow, which is high in signal intensity on these images, from thrombus, which is low to intermediate in signal intensity. Breath - hold CE-MRA images provide sharp detail and demonstrate the full extent of dissection, the entry site, the location of the intimal flap. The entry site, intimal flap, and branch vessel origins are better shown on individual sections than on 3D MIP reconstructions. The serial acquisition of two data sets provides dynamic flow information, which often demonstrates lack of opacification on early post contrast images followed by delayed enhancement of the false lumen, which is apparent in cases with slow flow. TR-MRA can also be used. Its temporal resolution allows a confident distinction between the true and false lumen (Fig3).

4.2.2 Penetrating aortic ulcers and intramural dissecting hematoma

Penetrating aortic ulcers result from ulcerated atherosclerotic plaques that penetrate the internal elastic lamina and may lead to hematoma formation within the media of the aortic wall, false aneurysm, and may progress to transmural rupture of the aorta.
Intramural hematoma (Fig10) usually results from spontaneous rupture of the aortic wall vasa vasorum, from a penetrating atherosclerotic ulcer. Extensive atherosclerotic changes are usually present in the aorta in the latter condition (Welch, 1990). The diagnostic MR imaging findings in penetrating atherosclerotic ulcer is a craterlike outpouching extending beyond the contour of the aortic lumen (Yucel, 1990; Hayashi, 2000; Macura, 2003). Mural thickening with high or intermediate signal intensity T1-weighted fat suppressed gradient- or on spin-echo sequences indicates the formation of intramural hematoma. Intramural hematoma most frequently involves the ascending or proximal descending aorta. The clinical presentation is similar to dissection: severe chest pain radiating to the back. Because of the similarity between the two entities, intramural hematoma is classified in the same way as aortic dissection: type A when the ascending aorta is involved and type B when involvement is limited to the descending aorta. (Litmanovich, 2009; Nienaber, 1995). The importance of intramural hematoma is that it can be a precursor of aortic dissection, representing either an early stage or a variant of dissection (Litmanovich, 2009; Nienaber, 1995; Cho, 2004). Complete resolution of the aortic hematoma is seen occasionally, but complications such as fluid extravasation with pericardial, pleural, and periaortic hematoma or aortic rupture may occur at the time of the onset or during the follow-up period. Progression of intramural hematoma to overt dissection and rupture has been reported in 32% of the cases, particularly when the ascending aorta is involved (Sakamoto, 2010).
Intramural hematoma can be identified as crescentic thickening of the aortic wall with abnormal signal intensity. Intramural hematoma is high in signal intensity on both T1 - and T2-weighted images and can be differentiated from chronic mural thrombus, which is low in

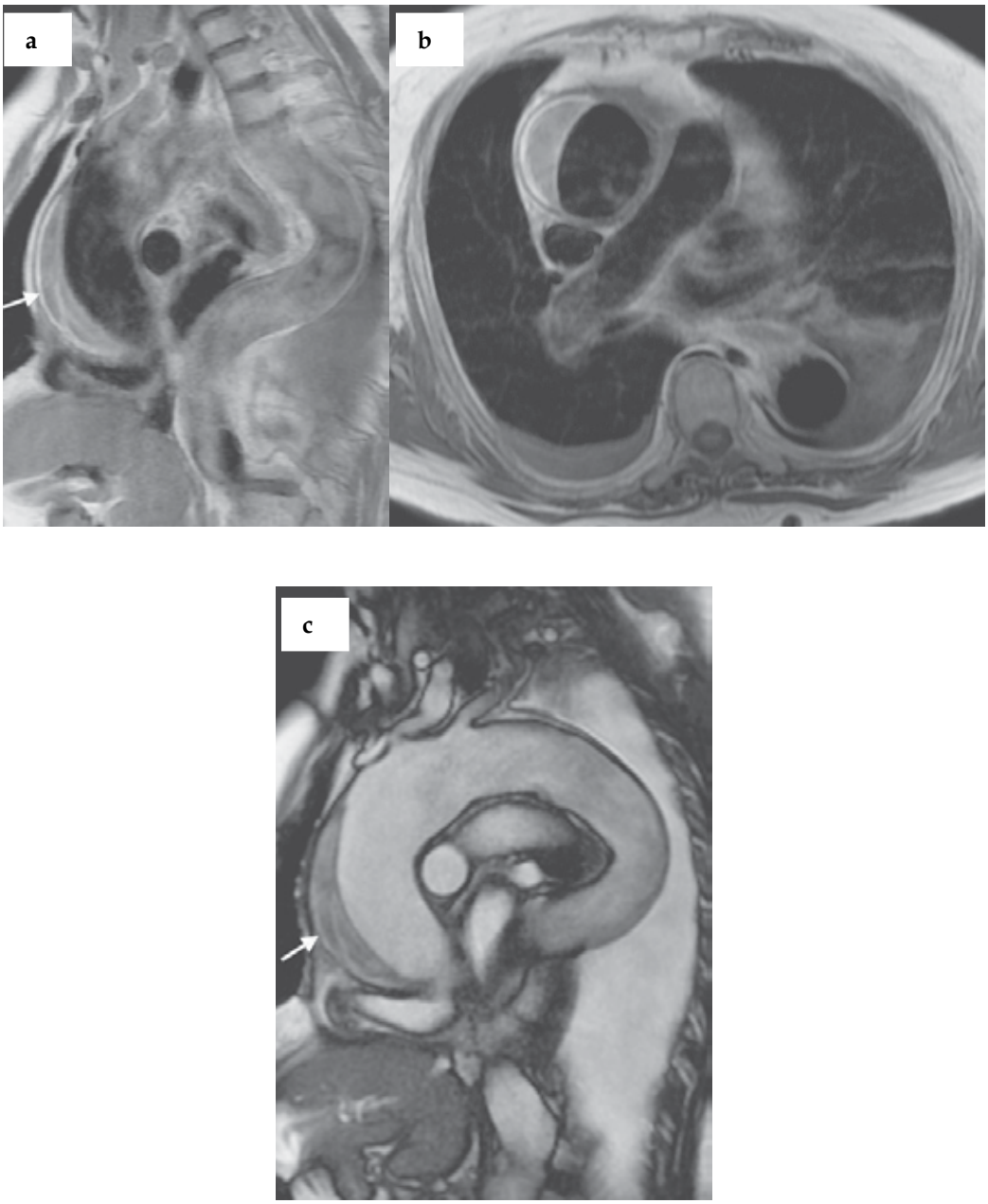


Fig. 10. Double inversion recovery spin echo MR imaging of intramural hematoma (a, b). On a T1-weighted spin echo MR image, intramural hematoma of the ascending thoracic aorta shows a crescentic local wall thickening with high signal intensity (arrow, a) caused by the presence of methemoglobin (subacute stage). Two-chamber view oblique sagittal bSSFP (c) shows in the same topography, a crescentic low signal intensity area.

signal intensity (Yucel, 1990). The combination of CE-MRA images to define the aortic lumen and 3D-GRE images to demonstrate the wall thickness in deep aortic ulcers may be the most effective means for evaluating this entity. Fat suppression images can be helpful in differentiating high-signal intramural hematoma from surrounding mediastinal fat. T1-weighted spin echo MR imaging (black blood techniques), can also be used to evaluate the aortic wall (Sakamoto, 2010; Litmanovich, 2009).

5. Future perspectives and challenges

There is growing concern among clinicians for the necessity of diagnostic, cost effective and safe imaging, with ionizing radiation being a major concern in some patients (Picano, 2007). At present, the routine use of MR angiography/MRI in the emergency setting for acute aortic syndrome is not established, reflecting lesser availability than CT and greater problems with motion artifacts compromising some studies. Nevertheless, there are increasing indications of MRI, such as young individuals, pregnant patients, and high-risk to iodinated contrast agent nephropathy. CE-MRA and 3D-GRE MRI with gadolinium have been shown to be a reliable and safe method for imaging the aorta. Motion artifacts remain the major cause for study compromise if patients are not able to comply with breathholding. Recent developments, such as 3D-GRE with a radial K-space acquisition (Azevedo, 2011), have been shown to provide adequate motion resistant imaging in the abdomen. This sequence may also provide diagnostic images in the chest, in combination with a blood contrast agent such as gadofosveset trisodium, probably allowing motion-resistant steady-state contrast enhanced MRA of the chest. Other techniques, such as non-contrast enhanced real-time SSFP can also provide rapid acquisition, motion resistant images in critically ill patients. Newer scanner with greater numbers of channels will also permit higher parallel imaging acquisition sequences with considerably shorter acquisition, in general important for patients who are critically ill.

6. Conclusion

In conclusion, MRI can provide a comprehensive evaluation of the aorta, using different and often complementary approaches, with protocols tailored individually to the clinical question, including morphological and functional evaluation. It is the authors' opinion that the recent development of MRI hardware and software facilitating faster imaging with the growing concern of safety, regarding ionizing radiation will further increase the importance of MRI in the study of vascular thoracic pathology, in the emergency department setting.

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9

Combined Surgical and Endovascular Approach for the Treatment of Complex Thoracic Aortic Pathologies

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1. Introduction

Extensive pathologies of the aorta are a major challenge in terms of its surgical treatment. In principle, complex pathologies of the aorta are divided into type A aortic dissection according to the Stanford classification, and aneurysmatic changes involving the aortic arch.
The first successful operations in the ascending aorta and the aortic arch were described by Denton Cooley, Michael DeBakey and Stanley Crawford (DeBakey et al. 1955, Cooley et al. 1956, Cooley et al. 1955). Several advancements made since this time have led to improvements in the surgical treatment of the ascending aorta (Bentall &De Bono 1968, Starr et al. 1963, David & Feindel 1992, Yacoub et al. 1998).
Surgical procedures focused on dissections of the proximal portion of the descending aorta and the distal aortic arch have received increasing attention in the last few years and been subjected to several modifications. Especially the development of interventional radiological endovascular techniques that reduce the invasive nature of surgery as well as complication rates led to rapid advancements.
In the following, a combined surgical and endovascular procedure for the treatment of complex aortic diseases will be presented. It is advancement on the methods used thus far. The development and performance of the method and results obtained by its application in patients at the Department of Cardiovascular Surgery, Hietzing Hospital -Vienna, as well as with reference to the European register will be summarised.

2. Background

Type A aortic dissection and aneurysms in the ascending aorta involving the aortic arch and the descending aorta are diseases that pose a major challenge for the surgeon. The classical approach of two-step surgery involves, as the first step, replacement of the ascending aorta and the aortic arch through a median sternotomy, which is then concluded after an interval of a few weeks by performing the second step. The latter consisted of replacement of the descending aorta through a left-lateral thoracotomy and connection with the vascular prosthesis inserted at the first session.
However, this procedure is associated with a high risk of morbidity and mortality; the cumulative risk may be as high as 20%. A further important aspect is the waiting period of

several weeks between the two surgical steps, which is associated with a mortality risk of 10% due to rupture. Restrictions for this laborious procedure are the patient's age and comorbidities. In fact, up to 30% of the patients do not live long enough to undergo the second step of the procedure (Kouchoukos, 2001). The aim of the method presented here is to render this complex treatment procedure simpler and safer.

Based on Borst's (Borst et al. 1983) description, the first part of the classical approach is named the "*elephant trunk*" operation and was developed further because of the setbacks reported after its application. The combination of open surgery and implantation of a stent graft opened new perspectives in the treatment of extensive changes in this sensitive portion of the aorta (Fleck et al. 2002, Mizuno et al. 2002, Jazayeri et al. 2003, Karck et al. 2005).

This combination of surgery and a stent-assisted procedure, which is partly performed simultaneously, may avoid or simplify further interventions. Besides, the occurrence of type I endoleaks can be avoided by this approach. A type I endoleak in cases of implanted endoprostheses is defined as a leak at the proximal docking site.

The results of this modified and combined surgical procedure have been analysed in the studies published thus far. In patients who underwent aortic dissection, the behaviour of the false lumen during the postoperative observation period was also analysed.

3. Material and methods

3.1 Patients

3.1.1 Primary analysis

Between August 2005 and December 2006, the first seven patients were treated at the Department of Cardiovascular Surgery, Hietzing Hospital Vienna (5 were men and 2 were women). Five patients had an aortic dissection; two of these were acute type A dissections and two were extensive complex chronic aneurysms of the aorta. The patients' median age was 62 years (Gorlitzer et al. 2007).

Thirty-one patients were treated with this combined method in our department until December 2010. After primary analysis all consecutive patients were included into the international E-vita Open Register.

3.1.2 E-vita open register

One hundred and twenty-eight patients were included in the international E-vita Open Register (IEOR) between January 2005 and March 2009. Five European centres (Hietzing Hospital Vienna, Western Germany Heart Centre Essen, University of Bologna, Na Homolce Hospital in Prague, and the University of Barcelona) participated in this multicentre trial (Tsagakis et al. 2011). Fifty-five of them had been operated on for an acute type A dissection, 51 for a chronic dissection, and 22 because of extensive aneurysms. Of these, nine patients had a Marfan syndrome (Tsagakis et al. 2010).

3.1.3 Follow-up: transformation of the false lumen

Our own series of patients were evaluated between August 2005 and February 2009 as regards transformation of the false lumen after treatment of aortic dissection. The mean observation period was 43 months. A control CT-angiography was performed immediately post-surgery, after 3, 6, and 12 months, and thereafter at yearly intervals. In all, 14 type A dissections were followed. The combined surgical and interventional procedure had been used in all 14 patients (Gorlitzer et al., 2010).

Ninety-three patients were followed in the course of the IEOR investigation: 49 after acute dissection and 44 after chronic dissection (Tsagakis et al., 2010).

3.2 Hybrid stent graft

Replacement of the ascending aorta, the aortic arch, and the proximal portion of the descending aorta can be performed by the use of the E-vita open prosthesis in a single-stage operation. This recently developed prosthesis consists of a 70-mm-long woven "classical" Dacron portion which is directly connected to a polytetrafluoroethylene-covered stent prosthesis via Z-shaped nitinol rings. (Figure 1) The rings are not connected to each other. Thus, two things are ensured: optimal flexibility of the stent graft, and ideal adaptation to the course of the proximal descending aorta (Gorlitzer et al., 2007). Self-expandable stents measuring 13 cm in length and 32mm, 34 mm or 36 mm in diameter were used. A spiral CT angiography of the thoracic aorta was performed preoperatively to assess the extent of the aneurysm and /or dissection and to determine the appropriate size of the stent graft in each case.

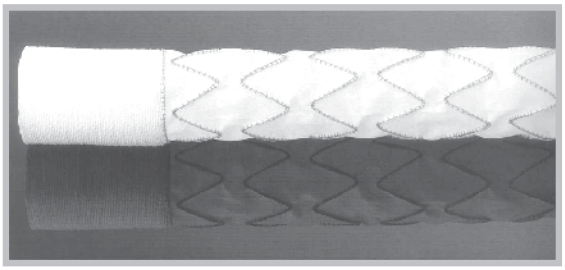


Fig. 1. E vita open graft

3.3 Surgical technique

For cerebral protection and extracorporeal circulation we use a classical heart-lung machine with alternative arterial cannulation via the axillary artery, moderate hypothermic circulatory arrest, and selective antegrade bilateral cerebral perfusion. The arterial cannula is introduced via a short 8-mm Dacron prosthesis, which is anastomosed to the right axillary artery. This permits the surgeon to subsequently perform a safe sternotomy on the one hand, and a means of achieving antegrade cerebral perfusion during circulatory arrest on the other (Strauch et al. 2005, Shimazaki et al. 2004, Numata et al. 2003, Okita et al. 2001).(Figure 2)

After median sternotomy, a venous two-step cannula is placed in the right atrium and the patient is cooled to 25°C at the heart-lung machine in order to achieve moderate hypothermia (Minatoya et al. 2008, Pacini et al. 2007). In contrast to deep hypothermia, moderate cooling offers the advantages of a lower risk of haemorrhage, shorter operating times, and a lower likelihood of inflammatory signs secondary to haemostasis (Kamiya et al. 2007).

During the cooling phase, the left ventricle has to be vented via the right upper pulmonary vein or the apex of the heart. Once the core temperature of 25° C has been achieved, the ascending aorta and the concave portion of the aortic arch are resected in a state of circulatory arrest. Selective antegrade cerebral perfusion with 10 ml/kg/min cold blood is achieved via a catheter in the left carotid artery and the cannula in the right axillary artery

after clamping the brachiocephalic artery (Mazzola et al. 2002). Oxygen saturation is measured by infrared spectroscopy during cerebral perfusion (Harrer et al. 2010).

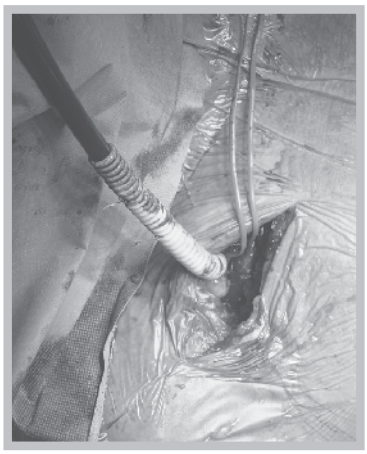


Fig. 2. Arterial cannulation of axillary artery

In cases of aortic dissection, the true lumen is identified by insertion of a stiff transfemoral guidewire which can be placed prior to commencement of the operation.
The E-vita open stent graft is introduced into the descending aorta via the open aortic arch, and is then adapted. The point of orientation for placement of the stent is the site of origin of the subclavian artery. (Figure 3)

Fig. 3. Insertion if combined stentgraft

The proximal part of the stent lies one centimetre distal to this point of origin. To avoid potential endoleaks - as initial experience in the use of this procedure showed - the integrated Dacron prosthesis is pulled out slightly and fixed to the proximal descending aorta by the use of sutures supported with Teflon strips. (Figure 4)

Fig. 4. Replacement the ascending aorta and hemiarch with a separate prosthesis

Two methods were used for replacement of the aortic arch: complete aortic arch replacement with reinsertion of the supra-aortic branches (Di Eusanio et al. 2004), or reconstruction of the aortic arch with preservation of the convex portion by way of "*light arch replacement*" (Gorlitzer et al. 2007). When using the latter approach, the supra-aortic branches are not isolated and need not be reimplanted individually. (Figure 5)

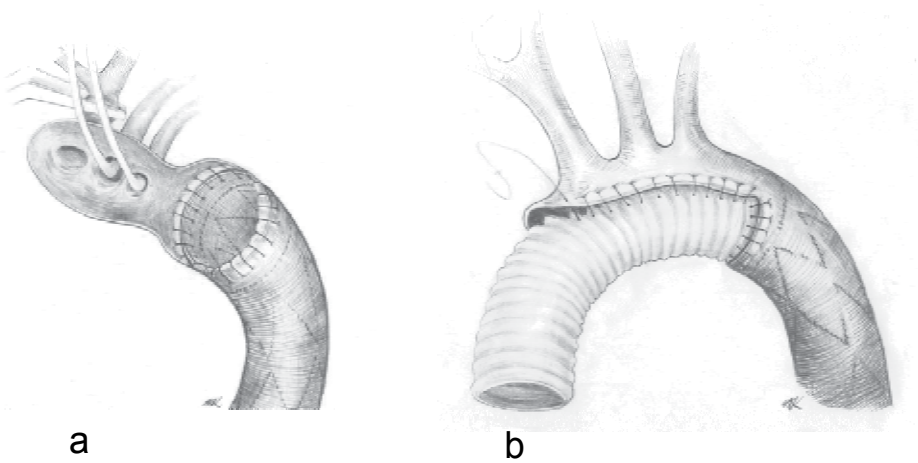


Fig. 5. Replacement of the aortic arch with preservation of its convexity

The ascending aorta and the concave portion of the aortic arch are replaced with an additional coated Dacron prosthesis, and anastomosed to the reconstructed descending aorta. Additionally - if necessary - this access may be used to replace the aortic valve or create aortocoronary bypasses.

4. Results

4.1 Results of hospital hietzing

In our own series, implantations of the antegrade stent in the descending aorta as well as replacement of the ascending aorta and the aortic arch were successfully achieved in all patients. All patients survived the intervention. The duration of time on the heart-lung machine (HLM) was 197±29.9 minutes, that of hypothermic circulatory arrest 60±15.5 minutes, and aortic clamping 88±33.2 minutes. Implantation of the stent in the descending aorta took 10 minutes (range, 8 to 12 minutes). The duration of stay at the intensive care unit was 6.8 days (range, 2 to 21 days) while the overall hospital stay had a duration of 20 days (range, 8 to 35 days).

One patient had a transient neurological deficit postoperatively. Another patient had to be drained on the 11th postoperative day because of a pericardial effusion.

In one patient with a Marfan syndrome, thoraco-abdominal replacement of the aorta had to be performed five months later. At this operation, a direct proximal anastomosis to the stent graft could be performed. In a further patient, the stent had to be lengthened into the distal descending aorta. These operations involved no complications and did not require circulatory arrest (Gorlitzer et al. 2007).

4.2 Results of international E-vita open registry

In the course of the investigation of the International E-vita Open Registry (IEOR), 106 patients with acute (n=55) and chronic (n=51) aortic dissection were evaluated (see Table 1). The duration of time on the HLM, aortic clamping and hypothermic circulatory arrest were 242±64, 144±44 and 75±23 minutes, respectively.

Clinical status preoperatively of Aortic dissections

Aortic disease *no (%)*	Overall (n=106)	Acute AD-IEOR (n=55)	Chronic AD-IEOR (n=51)
Emergency < 24h	49 (46)	47 (86)	2 (4)
Inotropics preoperatively	23 (22)	21 (38)	2 (4)
Cardiac tamponade	13 (12)	13 (24)	0
Intubated prior to admission	14 (13)	12 (22)	2 (4)
Malperfusion			
Cardiac	9 (9)	9 (16)	0
Cerebral	13 (12)	13 (24)	0
Spinal cord	4 (4)	4 (7)	0
Visceral	7 (7)	7 (13)	0
Renal	9 (9)	8 (15)	1 (2)
Peripheral	9 (9)	8 (15)	1 (2)
Aortic valve regurgitation	57 (54)	37 (67)	20 (39)

AD= Aortic dissection; IEOR= International E-vita Open Registry

Table 1. Clinical status of patients of the International E-vita Open Register

The techniques of reconstruction of the aortic arch and associated procedures, such as replacement of the aortic valve and the mitral valve or aortocoronary bypass, are summarised in Table 2. Stent implantation was successful in 99% of cases. In one case the distal end of the stent was in the false lumen.

Intraoperative variables (mean±SD; no (%)			
Aortic disease	Overall (n=106)	Acute AD-IEOR (n=55)	Chronic AD-IEOR (n=51)
Cannulation site (n)			
Axillary artery	70 (66)	34 (62)	36 (71)
Proximal aorta	22 (21)	17 (31)	5 (10)
Femoral artery	1 (1)	1 (2)	0
Previous prosthesis	11 (10)	1 (2)	10 (20)
Others	2 (2)	2 (4)	0
Intraoperative values (min)			
CPB-time	242±64	239±59	246±70
Cross-clamp Time	144±44	139±40	150±47
SACP time	75±23	67±19	83±24
HCA-time	8±6	9±7	7±6
Antegrade stent grafting (n)			
Stent-graft size (mm)	29±5	28±4	30±5
Oversizing > 10%	17 (16)	10 (18)	7 (14)
Use of guidewire	71 (67)	30 (55)	41 (80)
Arch replacement			
Total	95 (90)	48 (87)	47 (92)
Subtotal	11 (10)	7 (13)	4 (8)
Supra-aortic vessels (n)			
Island	67 (63)	42 (76)	25 (49)
Separate	39 (37)	13 (24)	26 (51)
Ascending aorta replacement			
E-vita open prosthesis	9 (9)	3 (5)	6 (12)
Other prosthesis	82 (77)	51 (93)	31 (61)
Aortic valve intervention			
Bentall	14 (13)	6 (11)	8 (16)
Isolated valve replacement	10 (9)	3 (5)	7 (14)
Resuspension	20 (19)	20 (36)	0
Repair	5 (5)	5 (9)	0
Mitral valve repair	2 (2)	0	2 (4)
CABG	17 (16)	12 (22)	5 (10)

AD= Aortic dissection; IEOR= International E-vita Open Registry; CPB= cardiopulmonary bypass;
SACP= selective antegrade cerebral perfusion; CABG= coronary artery bypass grafting

Table 2. Intraoperative variables of the International E-vita Open Register

The median duration of stay at the intensive care unit was 6 days while that of the entire hospital stay was 21 days.
Mortality rates were 11% /6/55) for acute dissection and 14% (7/51) for chronic dissection; p=0.77. Of these, one patient died due to rupture of the abdominal aorta. Other causes of death were heart failure (n=3), visceral malperfusion (n=2), haemorrhage (n=2), sepsis (n=2), cerebrovascular accident (n=1) and lung failure (n=2). The incidence of postoperative cerebrovascular accident was 5%. Damage to the spinal cord occurred in three patients (3%). Of these, one had paraplegia and two had paraparesis (see Table 3).

Aortic disease, *no (%)*	Overall (n=106)	Acute AD (n=55)	Chronic AD (n=51)	p-value
In-hospital mortality	13 (12)	6 (11)	7 (14)	0.77
Intubation time 72 h	36 (34)	22 (40)	14 (28)	0.21
Re-exploration	20 (19)	11 (20)	9 (18)	0.80
LOS	9 (9)	6 (11)	2 (6)	0.49
Visceral ischemia	4 (4)	3 (5)	1 (2)	0.61
Stroke	5 (5)	4 (7)	1 (2)	0.36
Spinal cord injury	3 (3)	0	3 (6)	0.10

AD= Aortic dissection; LOS= low output syndrome

Table 3. Postoperative results of the Evita open Registry

Eleven patients (10%) had to undergo a second intervention in the aorta during their hospital stay: 10 stent elongations (acute dissection 4/55, 7% vs. chronic dissection 6/51, 12%; p= 0.52). Open replacement of the descending aorta was performed in one patient.
Ten patients (11%) died in the observation period of 20±11 months. As regards overall survival after 36 months, no significant difference was registered between acute and chronic dissections (79% vs. 87%; p=0.69) (Figure 6).

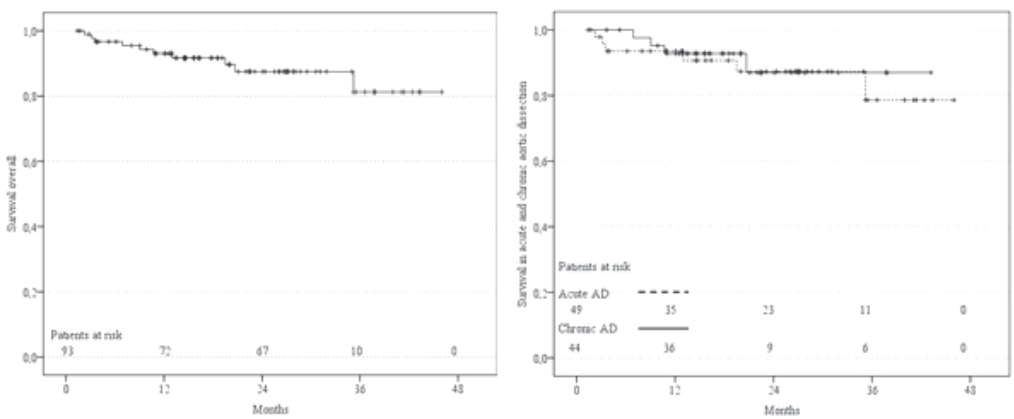


Fig. 6. Survival rates after the hybrid operation (left: all patients; right: after acute and chronic aortic dissection)

An additional intervention in the aorta could be avoided in 91% of patients after 12 months, and in 87% after 36 months (Figure 7) (Tsagakis et al. 2011).

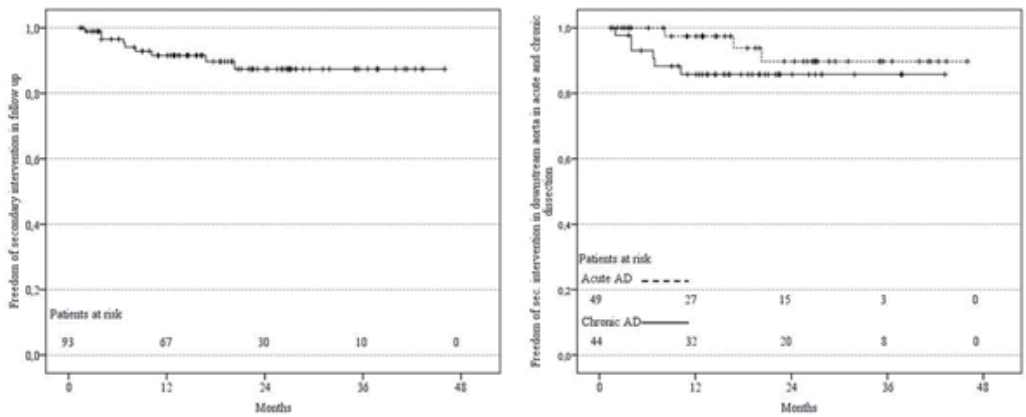


Fig. 7. Avoidance of additional surgery in the aorta (left: all patients; right: after acute and chronic aortic dissection)

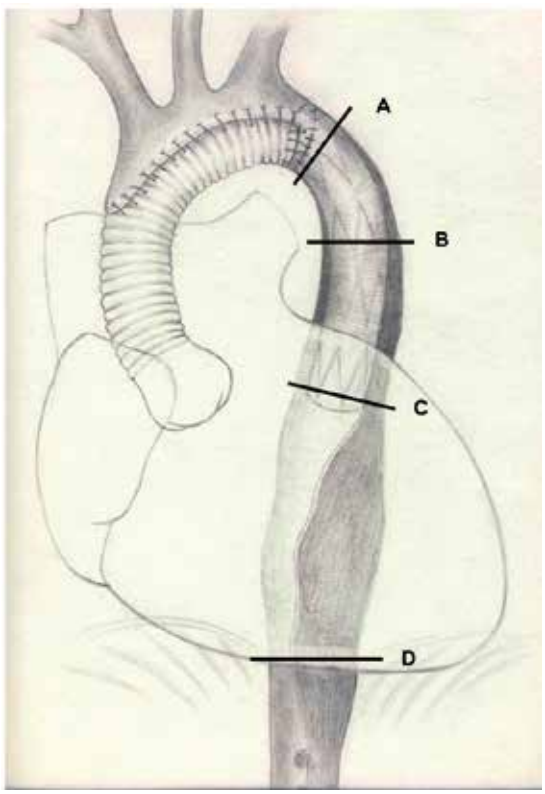
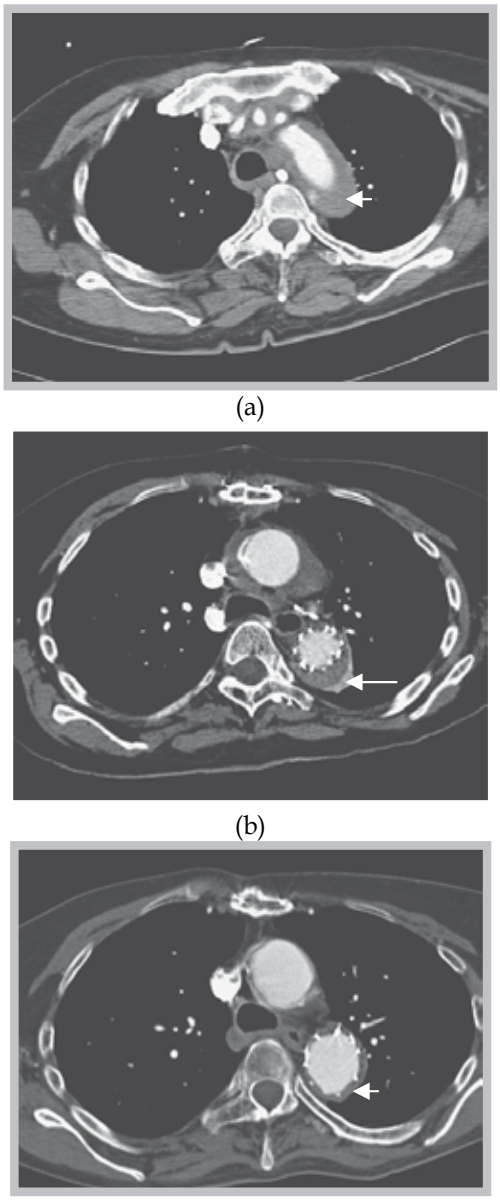


Fig. 8. The points measured in the aorta: A= Point of origin of the left subclavian artery, B= Pulmonary arteries, C= End of the stent, D= Diaphragm

4.3 Fate of the false lumen

In our own series of patients, the false lumen thrombosed completely at the level of the stent graft within two weeks in 86% of patients, while complete thrombosis at the level of the stent graft was observed after three months in all patients. The diameter of the aorta was measured at four points: the point of origin of the left subclavian artery, the level of the pulmonary artery, the end of the stent, and in the region of the diaphragm (Figure 8).



(a)

(b)

(c)

Fig. 9. CT scans preoperatively (a), 10 days (b) and 6 months postoperatively (c) (false lumen marked with arrow)

A significant reduction in the overall diameter of the aorta was observed at the level of the subclavian artery (3.9±0.45 cm vs. 3.6±0.39 cm; p=0.011), and a significant reduction in the diameter of the false lumen was noted in all portions of the stent graft.
No significant changes were observed in the untreated part of the aorta at the diaphragm (Gorlitzer et al 2010).
These observations concur with those of the IEOR, according to which 93% of patients developed a complete thrombosis in the region of the stent (Tsagakis et al. 2011). (Figure 9).

5. Conclusion

The treatment of complex aortic diseases by the use of the combined surgical and endovascular procedure is of a single-step operation which can be performed safely and is associated with a low rate of complications. Preservation of the convexity of the aortic arch (so-called *light arch replacement*) permits shorter, more visible suture line and reduces the duration of circulatory arrest.
Thrombosis of the false lumen in the region of the stent graft causes re-structuring of the descending aorta in its proximal portion. Our results are confirmed by those of the multicenter trial of the International E-vita Open Register.
Subsequent operations can be avoided or markedly reduced by this method without increasing the risk for the patient.

6. Acknowledgment

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10

Endovascular Repair of Thoracic Aortic Emergencies

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1. Introduction

The thoracic aorta begins at the lower border of the fourth thoracic vertebra, descends from the aortic arch, and ends at the level of the lower border of the twelfth thoracic vertebra. After passing through the aortic hiatus, it becomes the abdominal aorta.

The volume and pressure of blood through the thoracic aorta are greater than those of all other vascular structures. Consequently, diseases and complications of the thoracic aorta are extremely problematic. Emergencies such as aortic dissection, trauma, ruptured thoracic aortic aneurysms, penetrating aortic ulcers, thoracic aortic tears, aortobronchial fistulas, and any other condition where the integrity of the thoracic aorta is disrupted can have fatal consequences.

One of the most difficult emergencies of the thoracic aorta is acute aortic syndrome, which encompasses classic aortic dissection, intramural hematoma, and penetrating aortic ulcers.

Emergency open repair of lesions in the thoracic aorta is associated with very high surgical risk. Even with the use of cardiopulmonary bypass, profound hypothermia, circulatory arrest, spinal cord protection, and intensive care unit support, operative mortality rates for open repair have been reported to range from 8% to 20% for elective cases and from 60% to 70% following aortic rupture or aortic emergencies (Saratzis et al., 2008; Cowley et al.; 1990). Some series report mortality rates to be as high as 40-50% for open surgical repair of the thoracic aorta in emergency situations (Kaya et al., 2009; Schermerhorn et al., 2008).

Other postoperative complications, such as cardiac conditions, paraplegia, pulmonary conditions, or renal failure are observed in 12% to 45% of patients undergoing open surgical repair (Kaya et al., 2009; Schermerhorn et al., 2008; Achneck et al., 2007; Bozinovski & Coselli, 2008; Rousseau et al., 2005; Buz et al., 2008; Demetriades et al., 2008).

Endovascular repair, on the other hand, is associated with lower morbidity and mortality (Schermerhorn et al., 2008). Moreover, patients considered unsuitable for surgery because of severe comorbid conditions may benefit from this less invasive technique.

In this chapter, we present our experience with endovascular approaches to a series of thoracic aortic emergencies: aortic dissection, ruptured thoracic aneurysms, aortobronchial fistula, aortoesophageal fistula, subclavian symptomatic pseudoaneurysm, and blunt aortic disruption. We also review previous publications on this important vascular pathology.

2. Clinical cases

2.1 Material and methods

We present our experience with thoracic aortic emergencies. From May 2003 to September 2010, more than 200 patients were evaluated in our hospital for various emergencies affecting the entire aorta. Many patients required laparotomy or thoracotomy due to hemodynamic instability.

From January 2000 to September 2010, we treated 80 patients using endovascular stent grafting, both in elective and in emergency repair. Endovascular procedures were performed in 25 patients for emergency lesions between May 2003 and September 2010.

In this section, we describe the cases, procedures, and outcome.

At our institution, we divide aortic emergencies into 5 groups:

- Acute aortic syndrome: aortic dissection (5), penetrating aortic ulcer (2), intramural hematoma (2)
- Ruptured thoracic aneurysm (5)
- Symptomatic thoracic aortic pseudoaneurysm (3)
- Traumatic (blunt) aortic disruption (4)
- Aortobronchial fistula (1), aortoesophageal fistula (2)
- Subclavian symptomatic pseudoaneurysm (1)

The indications for treatment were aortic rupture in 5 patients (20%), persistent or recurrent pain in 8 patients (32%), hypotension or shock in 9 patients (36%), hemoptysis in 2 patients (8%), and acute renal failure in 1 patient (4%).

Baseline characteristics and cardiovascular risk factors of our patients are given in Table 1.

Age, years	60 (range, 26-80)
Gender (male: female)	21:4 (84%: 16%)
Hypertension	20 (80%)
Diabetes mellitus	7 (28%)
Dyslipidemia	9 (36%)
Smoking	16 (64%)
Coronary artery disease	4 (16%)
Previous cardiac surgery/coronary intervention	5 (20%)
Renal insufficiency	3 (12%)
Chronic obstructive pulmonary disease	5 (21%)
Aortic disease	
- Aortic dissection	5
- Penetrating aortic ulcer	2
- Intramural hematoma	2
- Ruptured thoracic aneurysm	5
- Symptomatic thoracic aortic pseudoaneurysm	3
- Traumatic (blunt) aortic disruption	4
- Aortobronchial fistula	1
- Aortoesophageal fistula	2
- Subclavian symptomatic pseudoaneurysm	1
	n=25

Table 1. Patient characteristics and comorbidities

Five patients (20%) had already undergone aortic surgery and five (20%) had undergone cardiac surgery. Two patients had undergone open repair of the abdominal aorta for abdominal aortic aneurysm.
The mean diameter of the thoracic aorta in patients with ruptured thoracic aortic aneurysms was 79 ± 18 mm (range, 70-92 mm). Mean diameter including all patients with thoracic aortic aneurysms and pseudoaneurysms (11 patients) was 77 mm (range, 40-110 mm).
The median interval between onset of symptoms and the endovascular procedure was 0.7 days (range, 0- 6).
We used four commercially available thoracic stent-graft prostheses: Talent® (n=12, 48%), Valiant®, (Medtronic Vascular, Santa Rosa, California, USA) (n=6, 24%), Relay® (Bolton Medical, Florida, USA) (n=6, 24%), and AneuRx® (Medtronic AVE, Cupertino, California, USA) (n=1, 4%).
Each endoprosthesis consisted of a self-expanding nitinol stent, covered externally by a Dacron graft. The type of stent graft was selected depending on availability and surgeon preference.
Data were collected on case report forms and checked for inconsistencies by two of the authors (R.L, P. JL).

2.2 Preprocedural diagnosis

Sizing of the endoprosthesis was based on centerline diameter measurements from contrast enhanced computed tomography (CT) angiography and three-dimensional image reconstructions; 10-20% oversizing was applied when selecting the stent graft diameter.
Trans-esophageal echocardiography was used in all cases of acute aortic syndrome (Stanford type B acute aortic dissection, intramural hematoma, penetrating aortic ulcer) and in the patient with an aortobronchial fistula.
Intravascular ultrasound was used in 3 of the patients with aortic dissection and for deployment of the stent graft in the patient with aortobronchial fistula.

2.3 Procedures

All surgical procedures were performed under general anesthesia in an operating room with angiographic and fluoroscopic equipment. Each patient received a single dose of antibiotic therapy (cefazolin) and 5000 units of heparin (except in ruptured aneurysms or head injuries). Cerebrospinal fluid (CSF) was drained in 8 hemodynamically stable patients (n=8). CSF pressure was monitored and maintained at 10 mmHg. CSF drainage was continued for 48 hours after surgery unless complications occurred. Hypotension was induced before device deployment when patients were stable.
Intravascular access was by transfemoral insertion in one groin. An ultrastiff 0.035-inch Amplatz SuperStiff™ guidewire (Boston Scientific, Miami, Florida, USA) or Lunderquist ExtraStiff wire (Cook, Inc., Bloomington, Illinois, USA) was directed into the ascending aorta via a transverse arteriotomy. Using a percutaneous contralateral approach, a soft Terumo guidewire (Terumo Medical, Somerset, New Jersey, USA) and 6-F pigtail catheter (Cordis, Johnson and Johnson, Warren, New Jersey, USA) were directed into the ascending aorta. Intraoperative angiogram was then performed in a left anterior oblique view at 40°-60°. The stent graft delivery system was inserted through the access artery. After marking the left subclavian artery, the endoprosthesis was delivered and deployed. During deployment, systolic blood pressure was usually maintained below 80 mmHg.

A prosthetic conduit was used from the common iliac artery (2 cases) when the diameter of the femoral or iliac vessels was very small (under 7 mm) or the vessels were very calcified or tortuous.

Completion angiography was performed at the end of the procedure to assess accurate placement of the endoprosthesis and exclusion of pathology.

Table 2 shows the diagnosis, patient´s age and endovascular procedure details.

CASES	DIAGNOSIS	AGE (years)	PROCEDURE
1	DISSECTION	67	Thoracic endoprosthesis
2	DISSECTION	39	Thoracic endoprosthesis
3	DISSECTION	65	Thoracic endoprosthesis
4	DISSECTION	74	Thoracic endoprosthesis
5	DISSECTION	33	Thoracic endoprosthesis
6	PENETRATING AORTIC ULCER	61	Thoracic endoprosthesis
7	PENETRATING AORTIC ULCER	66	Thoracic endoprosthesis
8	INTRAMURAL HEMATOMA	64	Thoracic endoprosthesis
9	INTRAMURAL HEMATOMA	69	Thoracic endoprosthesis
10	RUPTURED TAA	80	Thoracic endoprosthesis
11	RUPTURED TAA	56	Thoracic endoprosthesis
12	RUPTURED TAA	69	Thoracic endoprosthesis
13	RUPTURED TAA	72	Thoracic endoprosthesis
14	RUPTURED TAA	76	Thoracic endoprosthesis
15	PSEUDOANEURYSM	74	Thoracic endoprosthesis
16	PSEUDOANEURYSM	44	Thoracic endoprosthesis
17	PSEUDOANEURYSM	46	Thoracic endoprosthesis
18	TRAUMATIC AORTIC DISRUPTION	64	Thoracic endoprosthesis
19	TRAUMATIC AORTIC DISRUPTION	55	Thoracic endoprosthesis
20	TRAUMATIC AORTIC DISRUPTION	30	Thoracic endoprosthesis
21	TRAUMATIC AORTIC DISRUPTION	26	Thoracic endoprosthesis
22	AORTOBRONHCIAL FISTULA	55	Thoracic endoprosthesis
23	AORTOESOPHAGEAL FISTULA	74	Thoracic endoprosthesis
24	AORTOESOPHAGEAL FISTULA	68	Thoracic endoprosthesis
25	SUBCLAVIAN PSEUDOANEURYSM	65	Thoracic endoprosthesis and Amplatzer plug

Table 2. Diagnosis, age and endovascular procedure details.

2.4 Cases

2.4.1 Cases 1-9. Acute aortic syndrome (9)

Five patients were treated during this period for symptomatic type B aortic dissection, 2 for symptomatic penetrating aortic ulcer and 2 for intramural hematoma. Median age was 60 years (range, 33- 74 years).

Seven patients were treated for persistent pain. One patient was treated for uncontrolled hypertension. One patient was treated for onset of acute renal failure (due to the dissection) and persistent pain.

One patient was a 33-year-old male with Marfan syndrome who was treated for a symptomatic huge growth of a distal thoracic aorta dissection (10 cm in diameter) with a postdissection thoracoabdominal aneurysm (Figure 1). He presented at the emergency department with interscapular pain. The patient underwent a hybrid surgical procedure in a 2-stage intervention involving placement of a thoracic endoprosthesis (34 x 34 x 200 mm Valiant-Medtronic®) followed 2 days later by open repair of his visceral aorta using an aorto-aortic bypass Dacron graft with reimplantation of the 4 visceral vessels. He was discharged 32 days after the second procedure.

Another patient was a 60-year-old male who presented with acute-onset intense thoracic interscapular pain and hypertension. CT scan revealed an intramural hematoma complicated with penetrating aortic ulcers (Figure 2). A 46 x 42 x 110-mm Talent® stent-graft was deployed. Four days later, CT scan revealed a type I proximal endoleak. A proximal stent graft (46 x 46 x 130-mm Talent) was successfully delivered and deployed. The patient was discharged 6 days later.

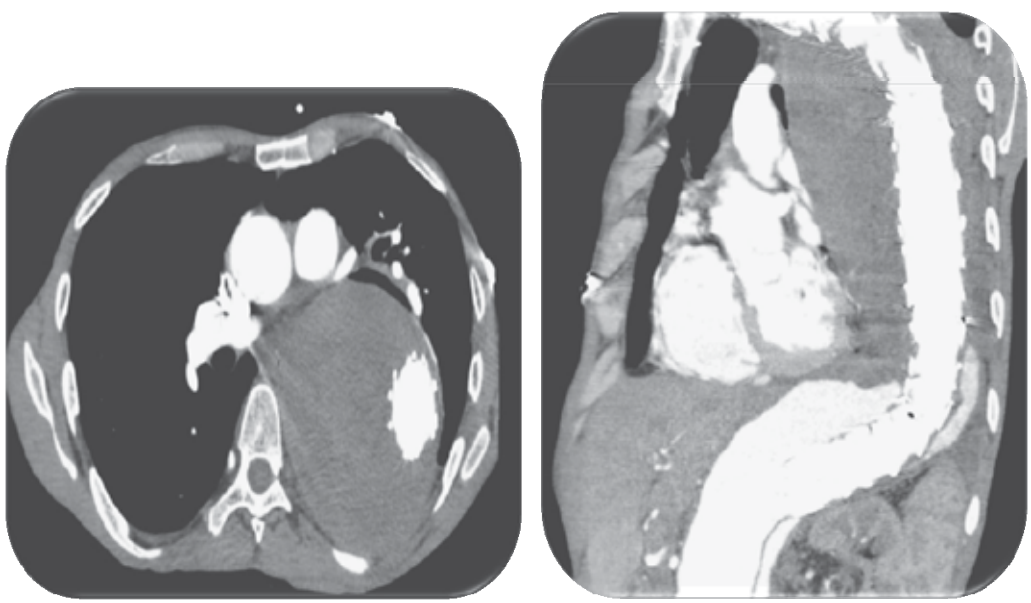

Fig. 1. Case 5. Left: Chest computed tomography scan showing sac growth (11 cm in diameter) in the descending thoracic aorta. Right: Dissection of the distal thoracic aorta and visceral aorta, with a huge thoracic postdissection sac.

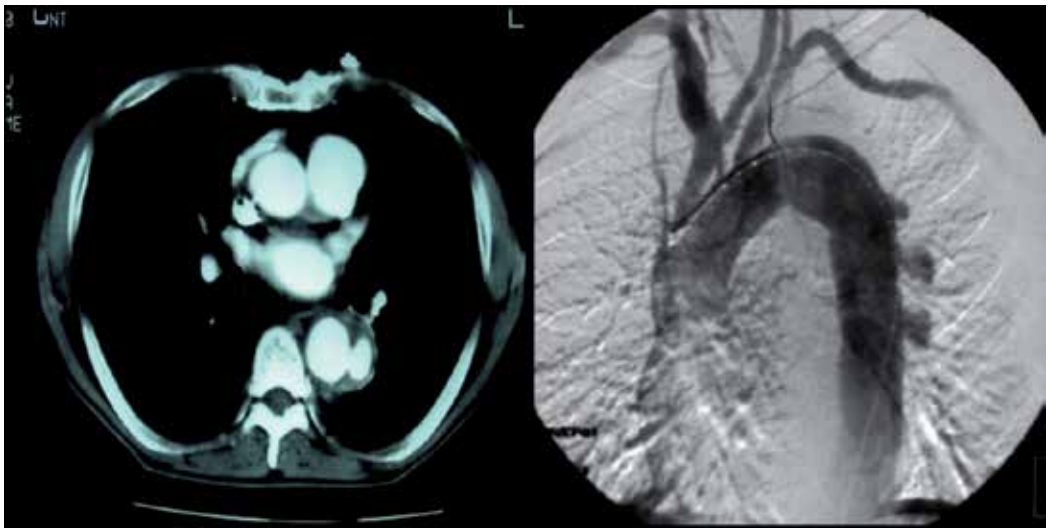

Fig. 2. Case 6. Left: Computed tomography scan revealing a 20 x 10-mm penetrating aortic ulcer with an intramural hematoma. Right: Aortography showing 3 penetrating ulcers in the descending thoracic aorta.

2.4.2 Cases 10-17. Ruptured thoracic aneurysms and symptomatic pseudoaneurysms (8)

Five patients were treated during this period for ruptured thoracic aneurysms and 3 patients for symptomatic thoracic pseudoaneurysms. Median age (all 8 patients) was 65 years (range, 44-80 years). Mean thoracic aorta diameter in patients with ruptured thoracic aortic aneurysms was 79 mm (range, 70- 92 mm) (Figure 3). On admission, 7 patients were hemodynamically unstable. One patient presented with hemoptysis.

As an unusual presentation, we describe the case of a 46-year-old HIV-infected woman (stage B2) coinfected with hepatitis C virus and tuberculosis. She presented with persistent hemoptysis (ongoing for 3 days), interscapular pain, and fever. CT scan revealed a 40-mm upper thoracic pseudoaneurysm in close contact with the left bronchus (Figure 4). The patient became hemodynamically unstable and went into cardiopulmonary arrest. After cardiopulmonary resuscitation and stabilization in the intensive care unit, she underwent successful exclusion of the lesion with a 26 x 26 x 155-mm Relay® endoprosthesis placed distal to the origin of the left common carotid artery and covering the ostium of the left subclavian artery. The postoperative period was uneventful and she was discharged 11 days after surgery.

Follow up was scheduled at 1, 3, 6, and 12 months. Her latest CT scan (36 months) showed patency of the endoprosthesis with no endoleaks. Her latest physical examination revealed no vascular abnormalities.

Mortality in this group was very high (3 of 8 patients). Three of the 5 patients who died during their stay were in this group.

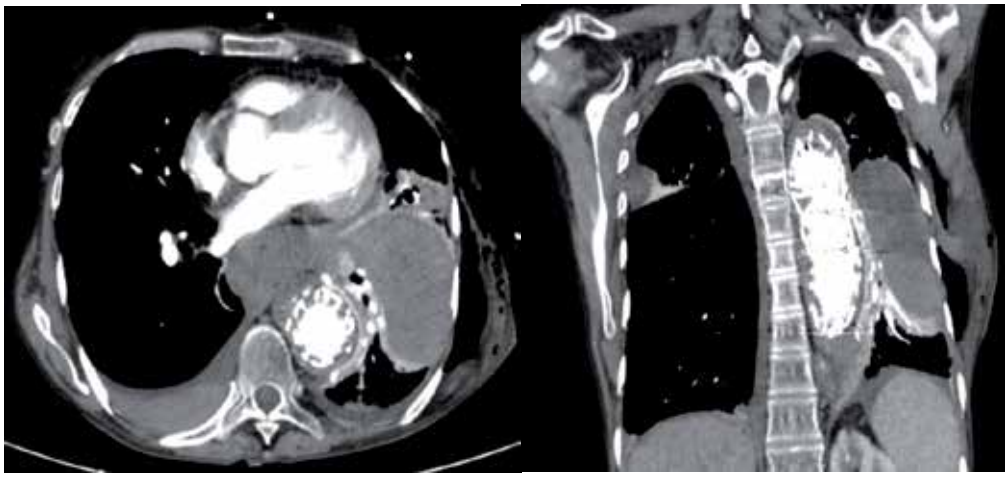

Fig. 3. Case 16. Chest computed tomography scan showing a ruptured (contained) pseudoaneurysm in the descending thoracic aorta at the site of a previous thoracic stent graft.

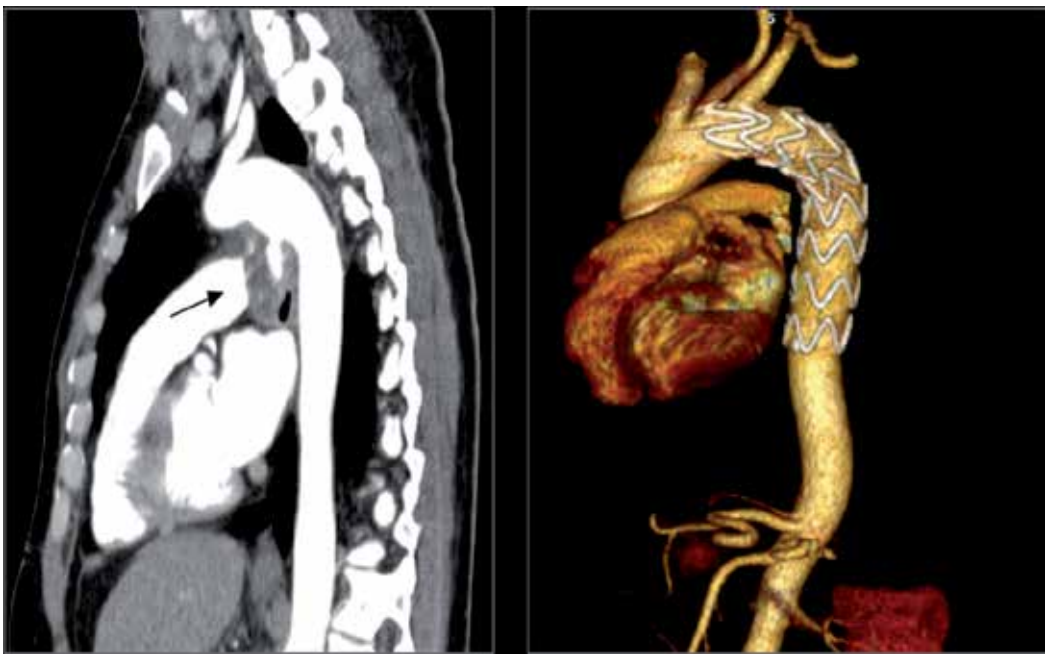

Fig. 4. Case 17. Left: Chest computed tomography scan showing a mycotic pseudoaneurysm (arrow) in the descending thoracic aorta. Right: Computed tomography scan demonstrating correct position of the stent graft.

2.4.3 Cases 18-21. Traumatic (blunt) aortic disruption (4)

In this group, all the patients were young (median age, 40 years [range, 26-58 years]) and were treated for hypotension or shock.

In all cases, the lesion was located at the aortic isthmus.
A 26-year-old woman was admitted after a fall from 15 meters. CT scan revealed a blunt aortic disruption at the level of the proximal thoracic aorta (aortic isthmus), slightly distal to the left subclavian artery. The patient was unstable and therefore immediately transferred to the operating room. She underwent successful endovascular stent grafting (22 x 22 x 150 mm Relay® endoprosthesis) of the ruptured thoracic aorta. The patient had multiple fractures, as well as hemothorax and liver contusion. She was discharged 54 days after surgery.

2.4.4 Cases 22-24: Aortobronchial fistula (1) and aortoesophageal fistula (2)

The patient with the aortobronchial fistula presented with massive (>400 cc) hemoptysis and hypotension. The other 2 patients were evaluated for hematemesis, malaise, and sudden hypotension.
A 55-year-old male was referred to our hospital for evaluation of massive hemoptysis. CT with intravenous contrast revealed a ruptured para-anastomotic pseudo-aneurysm in the descending thoracic aorta. Intra-operative angiography confirmed the presence of an aortobronchial fistula at the site of the pseudo-aneurysm (Figure 5).

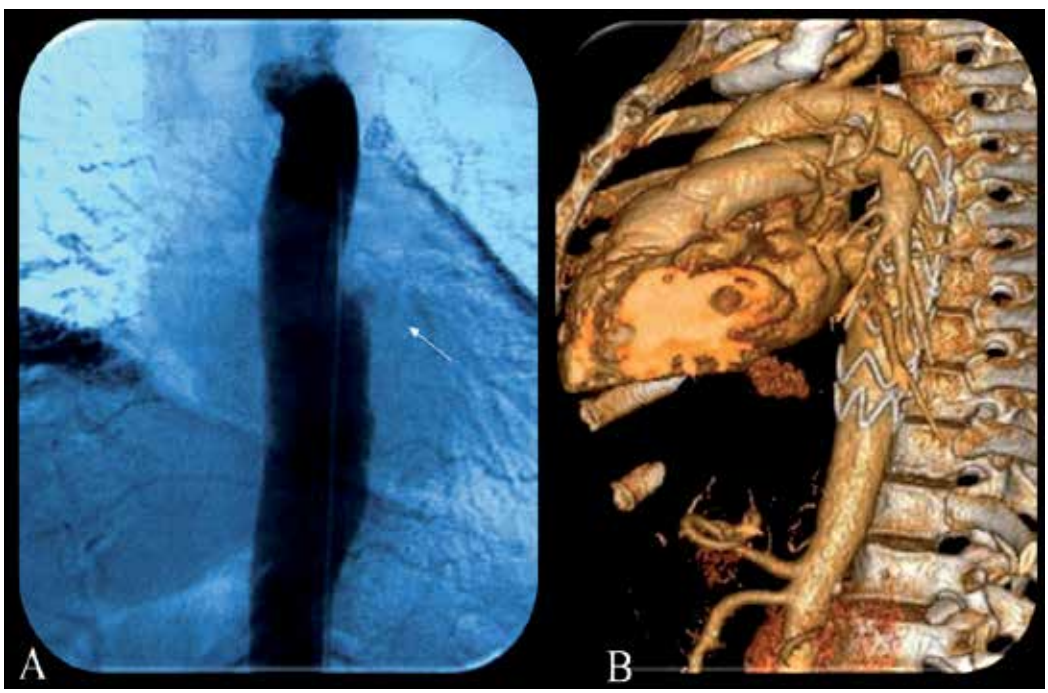

Fig. 5. Case 22. A, Aortography showing an aortobronchial fistula (arrow) at the site of a thoracic pseudoaneurysm. B, Computed tomography scan showing accurate placement of endoprosthesis with successful exclusion of the aortobronchial fistula (B).

A 74-year-old man was referred to our hospital for evaluation of massive hematemesis and hypotension. Preoperative assessment was with blood samples and chest X-ray. A CT scan revealed a descending thoracic aneurysm measuring 100 mm in diameter. This aneurysm was displacing the esophagus (Figures 6 and 7). In the emergency department, the patient

became hemodynamically unstable and was transferred to the operating room. He underwent successful endovascular stent grafting (36 x 36 x 200 and 36 x 36 x 145-mm Relay® endoprostheses). The patient died of a massive myocardial infarction on the third day after surgery.

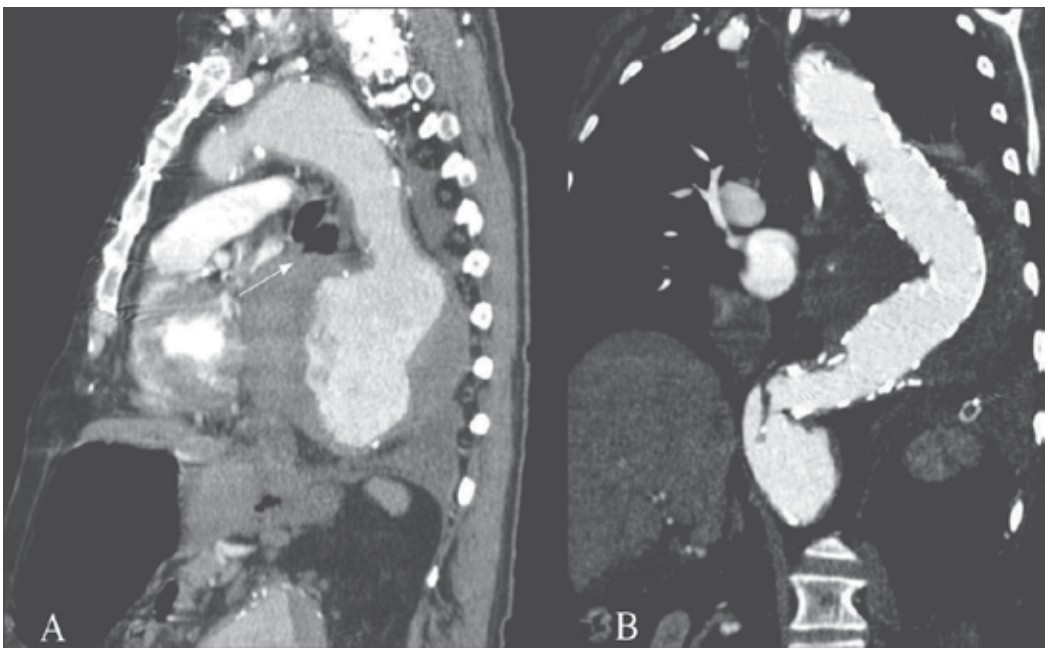

Fig. 6. Case 23. A, Chest computed tomography scan showing complete contact between a thoracic aortic aneurysm (10 cm in diameter) and the esophagus (arrow), causing an aortoesophageal fistula. B, Computed tomography scan showing accurate placement of endoprosthesis (postoperative day 2), with successful exclusion of the aortoesophageal fistula and aneurysm.

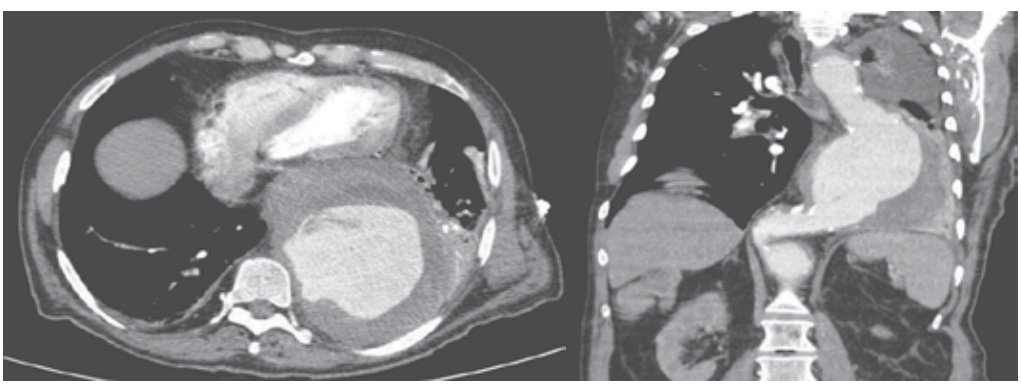

Fig. 7. Case 23. Upper: Chest computed tomography scan (transverse view) showing the thoracic aortic aneurysm measuring 10 cm in diameter. Lower: Computed tomography scan in a coronal view.

2.4.5 Case 25: Subclavian symptomatic pseudoaneurysm (1)

A 70-year-old Chinese man with a significant history of hypertension and smoking was referred to our hospital for evaluation of intermittent hemoptysis. On admission, he presented hemoptysis (>300 cc) and dyspnea. CT scan revealed a pseudoaneurysm measuring 30 mm x 20 mm at the origin of the left subclavian artery and in contact with the left pulmonary apex (Figure 8). The patient experienced 2 new episodes of massive hemoptysis with progressive anemia and was transferred immediately to the operating room. A Relay® covered self-expandable thoracic endoprosthesis (36 mm x 36 mm x 145-mm) was successfully placed distal to the origin of the left common carotid artery and covering the left subclavian artery. A 16-mm Amplatzer® vascular plug (AGA Medical Corporation, Plymouth, Minnesota, USA) was inserted through the left brachial artery to occlude the left subclavian artery without covering the left vertebral artery. Serology and culture studies were negative.

The patient was discharged 13 days after the endovascular procedure. Follow-up was scheduled at 1, 6, and 12 months, and yearly thereafter. His latest examination revealed the recovery of left brachial and distal pulses.

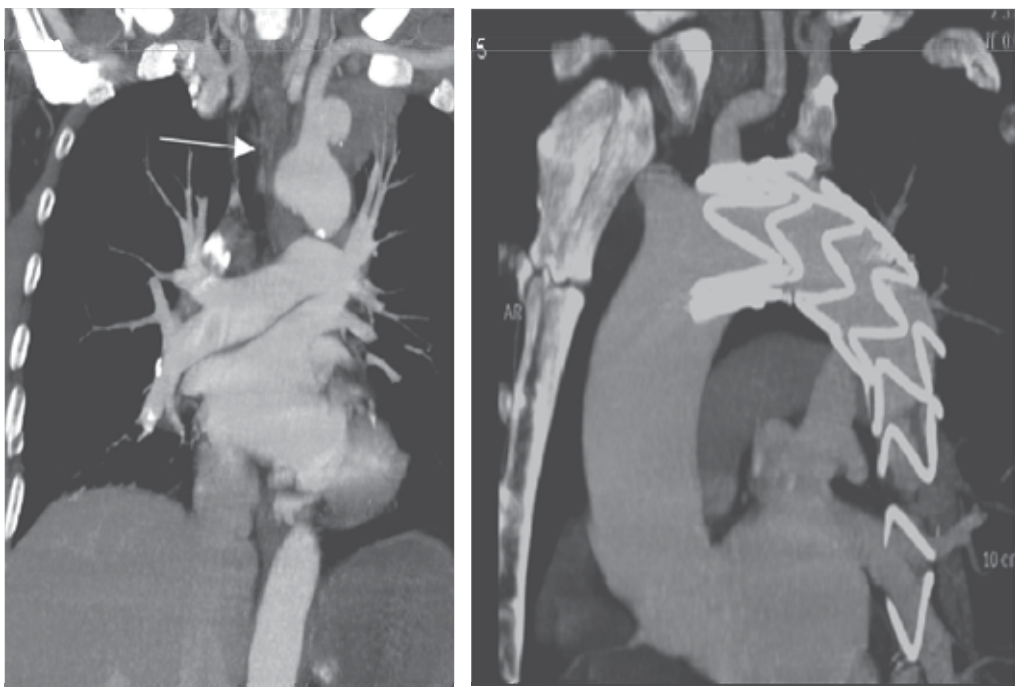

Fig. 8. Case 25. Left: Computed tomography scan revealing a pseudoaneurysm measuring 30 mm x 20 mm (arrow) at the origin of the left subclavian artery. Right: Computed tomography scan revealing accurate placement of endoprosthesis and 16-mm Amplatzer plug, with successful exclusion of the pseudoaneurysm (right).

3. Results

A total of 41 endografts were implanted. Median diameter and length were 36 mm (range, 22-46 mm) and 135 mm (range, 100-200 mm), respectively. The characteristics of the endografts and types of lesion are described in Table 3.

Lesions were excluded by 1 stent graft in 15 patients (60%, table 2), by 2 stent grafts in 4 patients (16%), and 3 stent grafts in 6 patients (24%).
The stent grafts were all deployed at the intended position, which was predominantly in the distal aortic arch or proximal descending aorta, necessitating complete coverage of the ostium of the left subclavian artery in 6 of 25 patients (24%).

Case	Type of stent graft	Size (mm)	Length (mm)	No. of grafts	LSA coverage
1	TALENT	36 x 36	200	1	Yes
2	VALIANT	34 x 34	150	1	Yes
3	TALENT	36 and 34	112 and 115	2	No
4	TALENT	34, 38, and 42	115, 114, 113	3	No
5	VALIANT	30, 32, and 34	200, 150, 120	3	Yes
6	TALENT	46 x 42	110	1	No
7	TALENT	34 x 34	100	1	No
8	TALENT	46 and 42	113	2	No
9	TALENT	36, 38, and 38	115, 115, 115	3	Yes
10	VALIANT	38, 38, and 38	150, 100, 100	3	No
11	VALIANT	36 and 32	150 and 150	2	No
12	RELAY	38, 36, and 32	200, 130, 130	3	No
13	RELAY	34 x 34	200	1	No
14	VALIANT	38 x 38	200	1	No
15	TALENT	34 x 34	130	1	No
16	VALIANT	42, 44, and 46	150, 100, 100	3	No
17	RELAY	26 x 26	155	1	Yes
18	ANEURX	40 x 40	120	1	No
19	TALENT	28 x 24	113	1	No
20	RELAY	22 x 22	150	1	No
21	TALENT	24 x 24	113	1	No
22	TALENT	30 x 30	130	1	No
23	RELAY	36 and 36	200 and 145	2	No
24	TALENT	34 x 34	150	1	No
25	RELAY	36 x 36	145	1	Yes

Table 3. Stent graft and endovascular procedure

LSA: Left subclavian artery.
Technical success, defined as correct stent placement and accurate coverage of the affected site, was achieved in all 25 patients (100%).
One patient required a proximal extension for a proximal type I endoleak 4 days after the procedure. One patient with a traumatic (blunt) aortic disruption required a proximal extension 20 days after the endovascular procedure for a proximal type I endoleak.
Intraoperative mortality was 4% (1 patient who was in severe shock before surgery and died during stent graft implantation from a ruptured thoracic aneurysm).
There was no conversion to open thoracotomy and no incidence of paraplegia after surgery.
Median length of hospital stay was 18 days (range, 6-60 days).

3.1 Mortality

Overall hospital and 30-day mortality was 20% (n = 5). One patient (4%) died during surgery.
Two patients died during their hospital stay due to multiorgan failure (after 17 and 80 days, respectively). One patient died of cardiorespiratory failure (postoperative day 15). One patient (treated for an aortoesophageal fistula) died on the third day after surgery of a massive myocardial infarction.

3.2 Follow-up

Follow-up was scheduled at 1, 6, and 12 months and yearly thereafter. Patients with endoleaks (type II) were followed closely at 3 to 6 months. Mean follow-up was 51 months (range, 4-96 months). Nineteen patients were followed up, 1 was lost to follow-up, and 5 died in hospital.
Two patients (8%) died after discharge from hospital.
One patient died of a cerebral hemorrhage after 8 months, the other died of an aortoesophageal fistula 4 months after discharge.
Overall survival at 1 year was 72%. At the time of writing, 17 patients are still alive, with no evidence of new leaks, device migration, or other complications.
One patient treated for an acute type B dissection required a proximal stent graft extension for a type I endoleak after 12 months. One patient (previously treated for an acute type B dissection) required a left renal angioplasty and stent for renal stenosis and hypertension after 13 months. One patient (treated for an intramural hematoma) required a distal stent graft after 48 months to repair postdissection sac growth.
Although we had to cover the ostium of the left subclavian artery in 6 of 25 patients (24%), it was not necessary to revascularize the left subclavian artery, as no arm ischemia or vertebro-basilar ischemia was detected.
According to the definitions of Chaikof et al. (Chaikof et al, 2002), primary technical success was 80%.
Table 4 shows results in terms of mortality and follow up.

4. Discussion

Vascular lesions and injuries to the thoracic aorta are associated with very high morbidity and mortality. Many patients with severe injuries die at the scene of the accident before being diagnosed or are severely ill on arrival at the emergency department.

CASES	DIAGNOSIS	Intraoperative Mortality	30- day Mortality	FOLLOW UP (months)
1	DISSECTION	No	No	48
2	DISSECTION	No	No	72
3	DISSECTION	No	No	72
4	DISSECTION	No	No	72
5	DISSECTION	No	No	8
6	PENETRATING ULCER	No	No	84
7	PENETRATING ULCER	No	No	72
8	INTRAMURAL HEMATOMA	No	No	72
9	INTRAMURAL HEMATOMA	No	No	60
10	RUPTURED TAA	No	No	60
11	RUPTURED TAA	Yes	Yes	
12	RUPTURED TAA	No	No	4
13	RUPTURED TAA	No	No	12
14	RUPTURED TAA	No	Yes- Day 80	
15	PSEUDOANEURYSM	No	Yes- Day 17	
16	PSEUDOANEURYSM	No	No	36
17	PSEUDOANEURYSM	No	No	36
18	TRAUMATIC DISRUPTION	No	No	84
19	TRAUMATIC DISRUPTION	No	No	72
20	TRAUMATIC DISRUPTION	No	No	36
21	TRAUMATIC DISRUPTION	No	No	6
22	AORTOBRONHCIAL FISTULA	No	No	96
23	AORTOESOPHAGEAL FISTULA	No	Yes- Day 15	
24	AORTOESOPHAGEAL FISTULA	No	Yes- Day 3	
25	SUBCLAVIAN PSEUDOANEURYSM	No	No	20

Table 4. Intra- postoperative mortality and follow up.

Endovascular repair of a ruptured thoracic aorta was initiated in the mid-nineties. Dake et al. presented one of the first series of endovascular stent grafts for the treatment of descending thoracic aortic aneurysms in 1994 (Dake et al., 1994).

Since then, several authors have reported successful endovascular treatment of both chronic and acute lesions of the thoracic aorta (Dake, 2001; Kato et al., 1997; Fujikawa et al., 2001; Lachat et al., 2002; Czermak et al., 2002; Amabile et al., 2004; Dunham et al., 2004; Hoornweg et al., 2006; Alsac et al., 2008; Kaya et al., 2009).

Despite advances in surgical techniques, surgery for acute thoracic aortic rupture is associated with high morbidity and mortality rates (Doss et al., 2003; Dake et al., 1994). Open thoracic aortic repair carries the risk of severe complications affecting the heart, lungs, kidneys, and nervous system (spinal cord ischemia), with frequencies as high as 50%

(Lachat et al., 2002). Mortality rates for elective open surgical repair of descending thoracic aortic aneurysm have been reported at 3-12%. Most reports, however, are from high-volume centers of excellence and national referral centers; therefore, the results may not reflect the actual experience worldwide (Schermerhorn et al., 2008).

Ruptured descending thoracic aortic aneurysm (rDTAA) is a cardiovascular catastrophe, associated with high morbidity and mortality. The vast majority of patients who suffer from rDTAA die before they reach hospital (Johansson et al., 1995). rDTAA is less common than aortic dissection and traumatic aortic rupture, and the treatment of choice in most centers is thoracic endovascular aortic repair (TEVAR) .

Open surgical repair of rDTAA presents very high mortality rates and is only feasible in referral centers. Mortality rates for open surgery vary from 30% to 60% depending on the series (Jonker et al., 2011).

Patients with rDTAA treated with TEVAR present lower mortality rates, although morbidity is also high. Recent reports present 30-day mortality rates of 15%-20%. Only highly specialized centers have reported mortality rates of between 25% and 30% after open repair of rDTAA (Jonker et al., 2010; Estrera et al., 2001). A recent comparative study by Patel and colleagues showed a 30-day mortality of 11.4% after TEVAR compared with 26.5% after open repair of ruptured thoracic aortic dissections and aneurysms (Patel et al., 2009). In endovascular repair of descending thoracic aortic aneurysms, the incidence rates of paraplegia and stroke usually range from 1% to 6% and from 2.5% to 5%, respectively. The risk of neurological complications may increase after endovascular repair of rDTAA, although it is still lower than that of open repair. The incidence of paraplegia and stroke after conventional surgical treatment of rDTAA may be as high as 12.5% and 25% (Jonker et al., 2011; Barbato et al., 2007), providing even greater support for endovascular treatment of rDTAA.

Although TEVAR is currently the most appropriate approach for the management of this often-fatal lesion, endovascular repair of rDTAA is still associated with considerable rates of neurological complications and procedure-related complications such as endoleak.

In our series, mortality for thoracic endovascular aortic repair in the ruptured thoracic aneurysm group was high (2 patients out of 5: 40%). Previous medical comorbidities and severe preoperative shock were determinant factors.

The prevalence of intramural hematoma in patients with acute aortic syndrome is 10%-20%, and approximately 10% of patients with symptomatic intramural hematoma develop aortic rupture. The signs of disease progression include aortic diameter ≥40 mm and thickening of the aortic wall ≥10mm. Close surveillance in these patients is critical (Geisbüsch et al., 2008).

The prevalence of penetrating aortic ulcer among patients presenting with acute aortic syndrome is about 2%-8%. Although frequently causing the same symptoms, penetrating aortic ulcer and classic aortic dissection must be distinguished, as they differ in their natural course. The rupture rate in symptomatic penetrating aortic ulcer is reported to be as high as 40% compared to 4% in Stanford type B dissection. Therefore, urgent repair is required in symptomatic cases (Geisbüsch et al., 2008; Tittle et al., 2002; Coady et al., 1996; Ganaha et al., 2002). Signs of progression of this condition include aortic ulcer diameter >20 mm and ulcer depth >10 mm. Close surveillance is essential.

Early mortality after TEVAR in penetrating aortic ulcer is reported at 0%-11%. Medium-term outcomes have been published, with 1-, 3-, and 5- year survival rates of 85%, 75%, and 60%, respectively (Geisbüsch et al., 2008; Botta et al., 2008; Demers et al., 2004).

In 2007, Estrera et al. published their series of 159 patients treated for acute type B aortic dissection. They concluded that mortality associated with complicated dissection was 17%. In contrast, 53% of patients with uncomplicated dissection were managed medically, with a mortality rate of only 1.2% (Estrera et al., 2007).

TEVAR should now be considered the gold standard for complicated acute type B thoracic dissections and symptomatic penetrating ulcers.

In our series, the acute aortic syndrome group was quite homogeneous as regards age, initial presentation, postoperative period, and outcome. There was no in-hospital mortality, with 90% of patients alive during a mean follow-up of 62 months (range, 8-84 months).

Traumatic aortic injury is the second commonest cause of death in patients after blunt injury; autopsy reveals that 15%-30% of deaths from blunt trauma involve aortic transection (Thompson & Morgan., 2009; Shorr, 1987). Traumatic thoracic aortic rupture is a potentially lethal injury and leads to immediate death in 75%-90% of cases. Only about 10%-20% of victims reach the hospital alive.

The most common site of aortic injury is the isthmus, where the relatively mobile thoracic aorta joins the fixed arch. Aortic rupture occurs at this site in 80% of pathological series and in 90% of the clinical series Thompson & Morgan., 2009).

Despite advances in surgical techniques, in emergency settings, open surgical repair of aortic rupture is still associated with a mortality rate of 18%-67% (Steingruber et al., 2007, Karmy-Jones et al. 2003; Richens et al., 2002; Williams et al., 1994).

Most series report the technical success of TEVAR to be 81.1-100%, with a paraplegia rate of 0%. These series present low mortality and morbidity rates, with accompanying injuries as primary causes of morbidity and mortality (Urgnani et al., 2009, Neuhauser et al., 2004; Rousseau et al., 2005).

Our results revealed considerable age differences between the traumatic (blunt) aortic rupture group and the other groups. This is due to the type of injury, which commonly occurs in young patients after high velocity trauma such as car accidents or falls from great heights. These patients commonly present multiple extremity and other fractures, vertebral or spinal cord injuries, and lung and visceral contusions, thus increasing the already high postoperative mortality.

In spite of the many benefits in the short and medium terms, the long-term results of endovascular repair of traumatic aortic rupture remain a major issue in these relatively young patients. In the future, we expect to see the development and use of stent grafts specifically designed to treat aortic trauma.

We present our experience with endovascular repair of thoracic aortic emergencies. Some of the cases we report are very unusual and therefore challenging, in terms of both diagnosis and treatment.

In several cases the presenting symptom was hemoptysis. In patients with massive hemoptysis, lesions in the intrathoracic large vessels, including the supra-aortic arteries, must be considered in the differential diagnosis. Moreover, in patients with previous aortic surgery and hemoptysis, the physician must have a high index of suspicion (Kopp et al., 2009).

Aortobronchial fistula and aortoesophageal fistula can be difficult to diagnose and extremely complex to treat. These conditions are often devastating, and the results of surgery are usually very poor. Endovascular repair provides an alternative to very complex open surgical repair. Very few series in the literature analyze endovascular repair of these complex lesions, and data are mostly from case reports or small series.

Open surgery entails high morbidity and mortality, and mortality rates range from 25% to 60% (Thompson et al., 2002; Piciche et al., 2003; Liu et al., 2004).
As regards endovascular repair of aortobronchial fistula, a review of the literature revealed less than 60 cases treated using endovascular repair. These were all from small series (Wheatley et al., 2007; Pirrelli et al., 2006; Ribé et al., 2010).
Initial results are encouraging, with 30-day mortality rates below 10%; however, larger series with longer-term follow-up are still required (Pirrelli et al., 2006).
Both our results and those published in the literature indicate that endovascular repair of thoracic aortic emergencies is a promising approach.
In some acute conditions, such as complicated type B thoracic dissections or ruptured thoracic aortic aneurysms, endovascular repair must be considered the treatment of choice. Larger series and longer follow-up are required for future assessment of these conditions.

5. Conclusion

Endovascular therapy may now be considered the first-line treatment for thoracic aortic emergencies, especially for ruptured thoracic aortic aneurysms and acute complicated dissections.
Endovascular procedures reduce morbidity and mortality in patients with acute thoracic aortic lesions, and must therefore be considered the gold standard in these situations.

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11

Ascending Aneurysms in Bicuspid Aortic Valve

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1. Introduction

The bicuspid aortic valve (BAV), the most common congenital cardiac malformation, is associated with ascending thoracic aneurysms and appears to reflect a common developmental defect. (Hahn et al., 1992; Roberts, 1970) The average time of patients with BAV undergoing surgery (of the aortic valve and/or because of complications associated with it) is a decade earlier than patients with a normally developed aortic valve. Accordingly, it is contended that if a diseased BAV must be replaced because of a diseased BAV, the aneurysmal ascending aorta should also be replaced. Valve replacement surgery without replacing the aorta would simplify the surgical intervention and shorten the time of operation. In contrast, an enlarged ascending aorta represents an increased likelihood of the patient undergoing the same surgical procedure after a few years. Replacing the aortic valve in patients with BAV does not prevent the progressive dilation of the aortic root and ascending aorta. (Yasuda et al., 2003)

Cellular and extracellular processes are involved in the pathogenesis of the ascending aortic aneurysms in patients with BAV. (Bonderman et al., 1999; Mohamed et al., 2010; Nataatmadja et al., 2003; Tang et al., 2005) Many studies have demonstrated the abnormalities of matrix metalloproteinases (MMPs) and tissue inhibitors of metalloproteinases (TIMPs) in aneurysmal tissues. (Boyum et al., 2004; Koullias et al., 2004; Longo et al., 2002) Using tissue microarray techniques, Koullias et al. detected a significantly higher MMP-2 and MMP-9 levels in BAV compared with normal tricuspid aortic valves (TAV), and even significantly higher MMP-2, MMP-9 and TIMP-1 levels compared with all other tissues (control and TAV together). LeMaire et al. observed a lack of inflammatory processes and an increased MMP-2 level and normal MMP-9, TIMP-1 and TIMP-2 expression levels in aneurysmal tissues obtained from patients with BAV. In contrast, in aneurysmal tissues obtained from patients with TAV, they observed increased inflammatory processes and MMP-9 levels. (Lemaire et al., 2005) Furthermore, they showed an increased incidence of cultured vascular smooth muscle cell (VSMC) loss in BAV and Marfan syndrome (MFS) compared with control samples and suggested that a link between the up-regulation of MMP-2 and VSMC apoptosis may exist in MFS. Certainly, there are similarities between the histology of the aneurysmal tissue of the aorta in MFS and that BAV. (Longo et al., 2002) In MFS, a mutation in the gene encoding for the extracellular matrix protein fibrillin-1 can be observed; this mutation leads to dysregulation of the transforming growth factor-beta (TGF-b) signaling. (Dietz et al., 2005) In this chapter, we review the present knowledge for elucidating the ascending aortic aneurysm pathogenesis, particularly in patients with BAV.

We will discuss the genetic basis and basic pathology underlying BAV and ascending aortic aneurysms. We used a simultaneous detection system for MMPs and TIMPs in two different areas of aortic aneurysms to quantify protein levels. Light and transmission electron microscopy were performed in some cases.

2. The aorta and its basic structure

The aorta transports oxygenated blood from the heart to the organs of the body. It plays a major role in the biomechanics of the circulatory system. The high velocity pulsatile flow of the ascending aorta changes into a low velocity steady flow when entering the arterioles and capillaries where metabolic processes such as gaseous and nutrient exchange occur. (Lohff, 1999; Olufsen and Nadim, 2004) A healthy aorta has a flexible vasculature and specific size, which correlates with age and gender. Located near the left ventricle, the ascending aorta along with the aortic root forms a unique shape and displays mechanical properties to influence left ventricle workload and coronary blood flow. (Davies et al., 2008; El-Hamamsy and Yacoub, 2009) Similar to all other arterial walls, the ascending aorta comprises three basic layers: the innermost layer, *tunica intima* that adjoins the blood vessel lumen with an endothelial lining; the middle layer, *tunica media* that contains muscular elastic fibers; and the outer layer, *tunica adventitia*. The internal and external elastic laminae (thick elastic fibers) separate these layers from each other. The lamellar unit of the media is the fundamental structural and functional unit of the aortic wall providing viscoelastic properties to the aorta. It is composed of vascular smooth muscle cells between two layers of elastin fibers, which comprise microfibrils and proteoglycans that form the extracellular matrix. (El-Hamamsy and Yacoub, 2009; Wolinsky and Glagov, 1967)

3. Present knowledge of genetics of BAV and thoracic aortic aneurysms

Remodeling, processing, and degradation of extracellular matrix proteins are regulated by MMPs and tissue inhibitors of TIMPs. MMPs are a family of zinc-dependent proteolytic enzymes with five major members categorized according to substrates. These members include collagenases, gelatinases, stromelysins, matrilysins, and membrane-type MMPs. (Brauer, 2006; Folgueras et al., 2004) Imbalances in MMP and/or TIMP synthesis have been linked to changes in the aortic wall and formation of aortic aneurysms. (Coady et al., 1999; Davis et al., 1998; Isselbacher, 2005) Although the involvement of MMPs or TIMPs in the pathogenesis of abdominal aortic aneurysms is clarified to a great extent, MMP or TIMP levels in ascending aortic aneurysms have shown different results. (Davis et al., 1998; Goodall et al., 2001; Raffetto and Khalil, 2008) In particular, the elevation of MMPs and TIMPs occurs in ascending aneurysms in BAV. BAV, which was probably first depicted more than 400 years ago in Leonardo da Vinci's sketches, is a genetic disorder. (Clementi et al., 1996; Cripe et al., 2004; Friedman et al., 2008; Huntington et al., 1997; Roberts, 1970) The high heritability of BAV was estimated to be 0.89. Family-based genome-wide analysis revealed linkage of BAV to the chromosomal regions 5q, 13q, and 18q in an autosomal dominant inheritance with reduced penetrance and a non-Mendelian pattern. (Cripe et al., 2004; Huntington et al., 1997; Ward, 2000) Mutations were detected in the transmembrane receptor *NOTCH1* (gene mapped to a locus on chromosome 9q) in familiar and sporadic cases of BAV. (Garg et al., 2005; McKellar et al., 2007; Mohamed et al., 2006) Moreover,

mutations in the *vascular smooth muscle cell alpha actin* gene (mapped to chromosome 10q) have also been identified in patients with BAV and aortic aneurysms. (Milewicz et al., 2008) The *ubiquitin fusion degradation 1-like* gene (mapped to chromosome 22q), which is highly expressed in the outflow tract during embryogenesis, was down-regulated in the cusps of patients with BAV compared with those of control patients. (Mohamed et al., 2005) Furthermore, BAV can manifest as a type of a group of left ventricular outflow tract abnormalities such as aortic coarctation, arch hypoplasia, and supravalvular and mitral valve stenosis. *The homeobox* gene (mapped to a locus on chromosome 5q in humans) *Nkx2-5* deficient heterozygous mice are at a higher risk of developing BAV. (Biben et al., 2000; Wessels et al., 2005) A male predominance of more than 3:1 has been reported for BAV, and this anomaly is very frequent in the X0 Turner's syndrome, with an incidence rate of 22%–34%, suggesting an X-linked etiology. (Miller et al., 1983; Tadros et al., 2009) Analysis of a subpopulation with Anderson syndrome described 4 members (4/41) with BAV. In Anderson syndrome a mutation in the *potassium inwardly-rectifying channel, subfamily J, member 2* (mapped to chromosome 17q) was observed. (Andelfinger et al., 2002) Endothelial nitric oxide synthase (eNOS; located on chromosome 7q in humans) knockout is associated with the development of BAV in mice. (Lee et al., 2000) Kuhlencordt et al. detected a higher incidence of aortic aneurysms in eNOS/apolipoprotein E double-knockout mice. (Kuhlencordt et al., 2001) Aicher et al. reported a significant decrease in the amount of the eNOS protein in BAV aortic tissue compared with that in TAV aortic tissue. (Aicher et al., 2007) The expression and activity of eNOS in aortic endothelial cells is controlled by hemodynamic wall shear stress. Recent studies have indicated that aortic wall shear stress differs locally between BAV and control patients, when examined by magnetic resonance imaging. (Barker et al., 2010; Weigang et al., 2008) Furthermore, we have provided evidence that VSMCs show different apoptotic behavior in the convex and opposite concave portions of the dilated aorta (Fig. 1). Inhibition of caspase-3 protected cultured cells derived from the tunica media of the concavity to a greater extent than those derived from the convexity of the aorta. (Mohamed et al., 2010) These observations that compare of convex and concave ascending aortic sites are extremely important, not only necessarily from a genetic standpoint but also from the standpoint of differential pressures experienced (or more specifically dP/dt) at every site. Early in development, the growth of the embryonic outflow tract (OFT, descendant of the second heart field) shortens at specific stages according to programmed cell death (apoptosis). (Fisher et al., 2000) During cardiac valve formation, when the heart is a simple tube, invaded the extracellular matrix to build the endocardial cushions in the OFT. Migratory cells from pharyngeal arches, i.e., neural crest cells, participate and differentiate into VSMCs that populate the walls of the ascending aorta, aortic arch, head vessels, and interior of semilunar valves. Transient and moderate activities of caspase-3 promote stem cell differentiation; in OFT, only cells with moderate caspase-3 activity undergo smooth muscle differentiation. (bdul-Ghani and Megeney, 2008) It is also our personal belief that dysregulation of apoptosis during valvulogenesis may lead to failure in separating valve leaflets from each other like in BAV. (Zhang et al., 2010).

This present knowledge of ascending aortic aneurysms in patients with BAV reflects only a part of the complex entity of the pathogenesis. BAV occurs at an incidence rate of 1%–2% in the general population, and almost 50% of the anomaly is associated with ascending aneurysms that can lead to aortic dissection or rupture. (Roberts, 1970b; Siu and Silversides, 2010) Therefore, further investigations to understand the pathogenesis of ascending aneurysms are required.

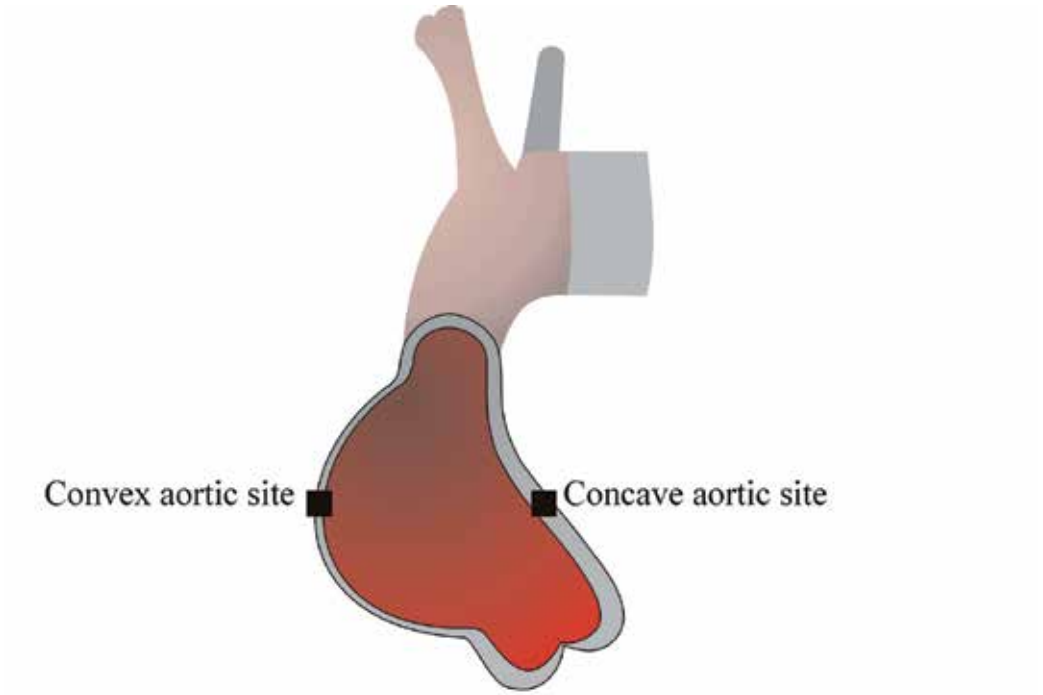

Fig. 1. Schematic representation of ascending aneurysms. Rescted tissue of the concave and convex aortic sites for analysis.

4. Simultaneous detection of MMPs and TIMPs in thoracic aortic aneurysms

The mutiplex system (Bio-Plex, BioRad Laboratories, Hercules, CA, USA)) analyses were used to determine the concentrations of MMP-1, MMP -2, MMP -8, MMP -9, MMP -12, and MMP -13 in pg/ml as well as those of TIMP-1, TIMP -2, TIMP -3, and TIMP -4 in two areas of the dilated aorta ascendens (Fig. 1). The Human MMP Fluorokine MultiAnalyte Profiling (FMAP) Base Kit and the respective kits to this panel of targets obtained from R&D Systems (Minneapolis, MN, USA), applied according to the manufacturer's instructions.

Forty-one patients were included in the analysis, the concave and convex aortic sites were identified from overall cases. The group of 31 patients with BAV consisted of 24 male (77%) and 7 female patients, while 7 of the 10 patients with TAV were male (70%). The distribution of age was considerably different between the two groups. Patients with BAV featured a mean age of 50.9 ± 12.9 years and were therefore significantly younger than patients with TAV having a mean age of 63.2 ± 8.2 years (P = 0.006). On the other hand, the means of aortic diameters are comparable (52.7 ± 4.9 mm vs. 56.7 ± 6.6 mm). There were differences in the aortic valve disease between the two groups. While the BAV group contained 10 patients with aortic valve insufficiency (32%), 3 patients with stenosis (10%), and 18 patients with a combination of both diseases (58%), the TAV group comprised patients who only suffered from aortic valve insufficiency.

The overall detection of MMPs and TIMPs using the multiplex system revealed significantly higher MMP-8 and MMP-9 levels in the convex aortic site than in the opposite area (concave) in all patients (P = 0.001; P =.007). On the other hand, MMP-2 and TIMP-3 levels

were elevated in the concave aortic site (P = 0.04, P = 0.0007; Table 1). Patients with TAV have a higher TIMP-3 level in the concave aortic site than in convex aortic site (P = 0.008).

4.1 Elevation of MMPs and TIMPs with age

Within the BAV group the age group below and including 51 years displayed a significantly lower expression of TIMP-3 in the convex aortic site in contrast to convex aortic site (10.35 ± 3.4 pg/ml; P = 0.01). The convex area of older patients featured significantly higher MMP-8 and TIMP-2 levels than that of the younger group (10.84 ± 13.92 pg/ml, P = 0.02; 141.91 ± 34.29 pg/ml, P = 0.05).

4.2 Elevation of MMPs and TIMPs based on the diameter of aortic aneurysm

To classify patients according to the diameter of aortic aneurysms, the threshold was chosen to be located between 54 and 55 mm, as the mean diameter was 53.7 ± 5.6 mm. Most of the TAV associated aneurysm was larger in diameter than the BAV associated aneurysm. Therefore, all patients with TAV were selected in the group of greater than or equal to 55 mm.

The aortic convex area of patients with BAV suffering from an aneurysm of 54 mm diameter or less, showed a higher MMP-8 and MMP-9 levels compared with the concave area (2.78 ± 2.76 pg/ml, P = 0.04; 9.61 ± 9.78 pg/ml, P = 0.05). The expression of TIMP-3 and TIMP-4 on the other hand is significantly lower in the convex area (11.51 ± 3.81 pg/ml, P = 0.004; 0.25 ± 0.07 pg/ml, P = 0.004). Patients with BAV and an aneurysm with greater than or equal to 55 mm displayed considerably higher MMP-8 and MMP-9 levels in the convex aortic site when compared the concave aortic site (12.30 ± 15.20 pg/ml, P = 0.01, 28.29 ± 41.80 pg/ml, P = 0.04). The TAV group exhibited a higher TIMP-3 expression in the concave when compared with the convex aortic site (10.03 ± 3.50 pg/ml, P = 0.05).

4.3 Elevation of MMPs and TIMPs based on gender

Comparison of male and female patients with BAV resulted in a significantly higher TIMP-1 concentration in area 23II of female patients (P = 0.03).

Analyses of the male BAV group resulted in significantly increased MMP-8 and MMP-9 levels in the convex aortic site than in the concave aortic site (P = 0.005; P = 0.01). The concave aortic site showed an elevated TIMP-3 concentration (P = 0.03).

4.4 Elevation of MMPs and TIMPs based on aortic valve disease

The classification of patients depending on their aortic valve disease was restricted by the low number of patients with isolated stenosis. Therefore, only patients with BAV with aortic valve insufficiency or a combination of insufficiency and stenosis were considered.

The TAV group comprised patients who only suffered from aortic valve insufficiency.

The BAV group with aortic valve insufficiency showed increased TIMP-3 in the convex aortic site in contrast to concave aortic site (P = 0.02).

The BAV group with a combination of aortic valve disease showed significantly elevated MMP-8 and MMP-9 levels in the convex aortic site (P = 0.004; P = 0.007).

5. Light and transmission electron microscopy

In light microscopy, we studied the histopathological features of ascending aortic aneurysms in 15 patients with BAV and 6 with TAV. Convex and concave aortic sites were

graded according to the severity of seven histopathological features: fibrosis, atherosclerosis, medionecrosis, cystic medial necrosis, smooth muscle cell orientation, elastic fiber fragmentation, and inflammation. (de Sa et al., 1999) The most prominent feature is elastic fiber fragmentation (Fig. 2). Aortic ascending abnormalities were more severe in TAV than in BAV. Nonetheless, it became obvious that histological grading of the convex aortic site was generally more severe in BAV, which is associated with the aortic diameter of the convex and not concave aortic sites (Fig. 2). These results correlated with the previous observations of Bechtel et al. (Matthias Bechtel et al., 2003).

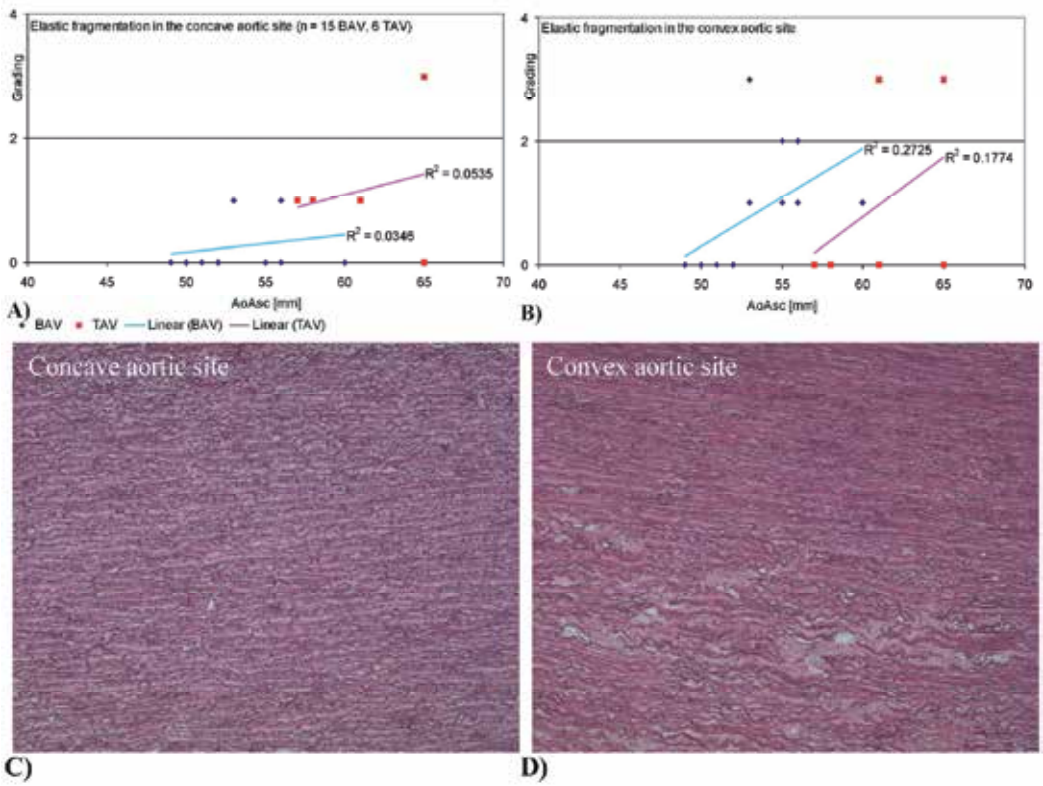

Fig. 2. Elastic fragmentation detected in two sites (concave and convex) of ascending aneurysms of 15 patients with BAV and 6 with TAV. The histopathological evaluation after de SA et al. The histological grading was copared with the aortic diameter (AoAsc; in millimetres) of the concave aortic site in A) and convex aortic site B). Elastica van Gieson staining is demonstrated in paraffin section of aneurysmatic tissue obtained from a 46 year-old-male with BAV thoracic aortic aneurysms (original magnification, x100). In C) the concave aortic site, in D) grade 2 elastic fragmentation of the presence of foci elastic fragmentation in more than five neighboring elastic lamellae of the convex aortic site.

The transmission electron microscopy analysis of the examined slides of aneurysmal tissues obtained from patients with BAV lacks any well known typical structure of the aortic wall. This texture mingles the whole aortic wall as well as the adventitia; the typical build up layer of an aortic wall is not recognisable (Fig. 3A).

In the intima, the endotheliums still possess a single layered consistent coating of plain cells that are aligned parallel to the bloodstream with their longitudinal axis.
The subendothelial layer of the examined specimen exhibits partial extensive differences. This layer contains few cells, at the most long thin stretched processes of fibrocytes, muscle cells are rare. A rather broad layer with a variously running bundle of collagen fibers is attached. The transition to the media is marked through fibrocytes processes, followed by strong bundles of collagen fibers with different orientation. The typical structure of the dense elastic membrane is completely abolished within the media. Bizarre shaped fibrocytes among bundles of collagen fibers, small parts of elastic membranes, and few vascular smooth muscle cells dominate, together with strikingly wide and empty appearing matrix spaces in the TEM. Among all compounds of this series, calcium concrements in all layers of the aortic wall exist as round eosinophilic granules (Fig. 3B).

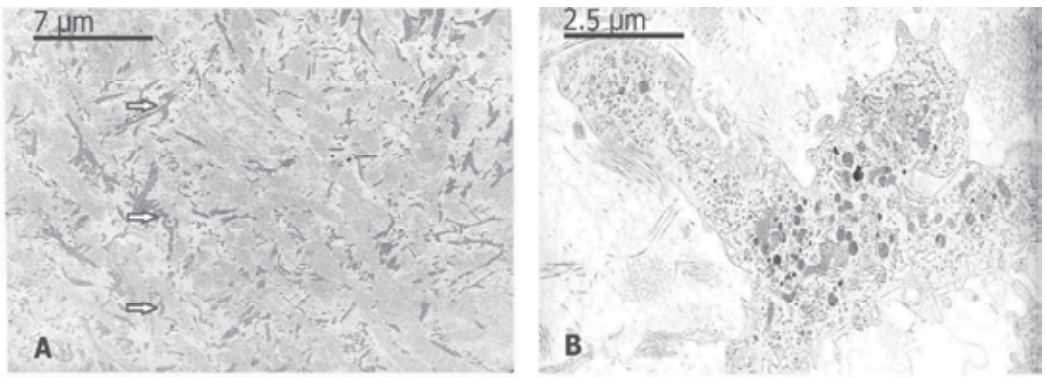

Fig. 3. The transmission electon micropy analysis of the tunica media of the aneurysmal tissue obtained from 15-year-old patient with BAV thoracic aortic aneurysm. In A, the electron micrograph demonstration of the lamellar structure and many broken VSMCs (arrows) with different elongations. In B, a fibaroblast with osmiophilic granules and space vacuoles is demonstrated.

6. Discussion

BAV is associated with ascending aneurysms that can lead to acute aortic dissection. (Januzzi et al., 2004) Acute aortic dissection is a life-threatening condition with high morbidity and mortality rates and is generally an unpredictable event. (Abbara et al., 2007; Januzzi et al., 2004; Mohamed et al., 2008; Mohamed et al., 2009; Park et al., 2004; Wheat, Jr., 1987) People commonly at risk of this disease include those with connective tissue disorders such as Marfan syndrome, Ehlers-Danlos syndrome, Erdheim–Gsell medial necrosis, and BAV. (Beroukhim et al., 2006; Dietz et al., 1994; Silverman et al., 1995) The exact genetic cause of BAV is unknown. Patients with BAV present a wide spectrum of heterogeneous morphological phenotypes of fused cusps. (Sievers and Schmidtke, 2007)
The normal aorta is a large elastic artery with a wall consisting of the intima and a prominent internal elastic lamina between the intima and media. The media has a markedly layered structure, in which fenestrated layers of elastic lamellae alternate with interlamellar

VSMCs, collagen, and fine elastic fibers. This arrangement is regular so that each elastic lamella and adjacent interlamellar zone is reported as a lamellar unit of the media. In addition to collagen and elastic fibers, the adventitia contains flattened fibroblasts with extremely long processes, macrophages and mast cells, nerve bundles, and lymphatic vessels. On examining the tissue samples of ascending aortic aneurysms of patients with BAV, we observed that the spatial structure of the aortic wall is totally destroyed. This structure was also partly observed during immunohistochemical analysis performed for Marfan syndrome. (Guo et al., 2009) The lamellar units of the media were disintegrated, and the VSMCs were atrophied and wrinkled in a bizarre shape. Between these wrinkled muscle cells, existed thick bundles of collagen fibrils. In some cases of the thoracic aortic aneurysms we detected dramatic changes in the distribution of collagen fibrils in the media with different diameters, and fibroblasts with long and thin processes between the enormous collagen bundles. However, the most striking observation was the lack of elastic fibers. In the adventitia, we observed dysplastic collagen fibrils, which had a flower-like appearance in transverse sections. In addition, accumulations of lipid droplets and eosinophilic granules, probably proteoglycan granules or calcium concrements were observed.

In the literature, different reports exist about matrix protein expression in aneurysmal tissues. In accordance with the published data, we observed the profile of six MMPs and their four inhibitors using a simultaneous detection system in two different areas (concave/convex) of ascending aneurysms. Using this method, we detected and quantified the elevation of MMP-2, MMP-8, MMP-9, and TIMP-1, TIMP-2, TIMP-3, and TIMP-4 in aneurysmal tissues obtained from the concave and opposite convex aortic sites. Concentrations of MMP-1, MMP-12, and MMP-13 were extremely low in these tissues and were therefore omitted. The areas of concave and convex aortic sites were combined in 41 patients (31 BAV and 10 TAV). The patients were divided into group on the basis of age, ascending aneurysm diameter, gender, and valve malformation.

When complete patient data were considered, increased MMP-2 and TIMP-3 levels in the area of the concave (inner curves) aortic site became apparent. The convex area (outer curves) of the ascending aortic aneurysm showed significantly raised MMP-8 and MMP-9 levels. Younger patients (≤51 years) revealed an elevated TIMP-3 level in the inner curves. In addition to the TIMP-3 level, older patients (≥52 years) showed an increase in MMP-2 level in the area of the concave aortic site, and an increase in MMP-8 and MMP-9 levels in the area of the convex aortic site.

Patients with an ascending aneurysm diameter of less than or equal to 54 mm were showed elevated TIMP-3 and TIMP-4 levels in the area of the concave aortic site, whereas aneurysmal convexity showed higher MMP-8 and MMP-9 levels. A aneurysm diameter of greater than or equal to 55 mm was associated with elevated MMP-8 and MMP-9 levels in the ascending aortic wall of the dilated convexity. Comparisons of gender and aortic valve disease groups revealed no significant differences.

In patients with Marfan syndrome, a mutation was observed in the gene encoding ECM protein fibrillin-1 (Dietz and Pyeritz, 1995) and further analysis in this regard may facilitate diagnosis and treatment of this syndrome. The situation differs in patients with BAV because haemodynamics can also play a role, and no defect can be detected in the gene encoding fibrillin-1. Although many studies support the genetic origin of BAV, the genetic pathomechanism of BAV is probably far more complicated possibly due to mutations in different genes.

7. Conclusions and future directions

To the best of our knowledge, simultaneous detection of six matrix protein levels was performed for the first time. This method is as accurate as old methods and minimizes the errors that occurred with those methods. Although we did not measure these proteins in blood or body liquids, the results obtained demonstrated that MMPs and matrix proteins can be differently elevated in ascending aortic aneurysms in BAV.

Many factors, such as hemodynamics, environmental factors, and genetic factors (in part) appear to be involved in this process. Other modern technologies such as whole genome screening may identify additional risk factors (single nucleotide polymorphisms); however, these risk factors must also be considered on the basis of their functionality. Another interesting topic for the near future is the microRNAs (miRNAs). miRNAs, small approximately 22 nucleotides in length noncoding nucleotide RNAs, have been shown to modulate mRNA stability and translation. (Cordes and Srivastava, 2009; van and Olson, 2007a; van and Olson, 2007b) In a pervious study, miR-26a was down-regulated in a fused aortic valve. (Nigam et al., 2010) Recently, this miR-26a was also found to be down-regulated in aneurysms. (Leeper et al., 2011)

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12

Reimplantation Valve Sparing Procedure in Type A Aortic Dissection: A Predictive Factor of Mortality and Morbidity?

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1. Introduction

The aim of surgical interventions in type A aortic dissections (TAAD) is to manage the potentially fatal complications associated with it. These are: intra-pericardial rupture and tamponade, malperfusion phenomena (coronary, neurological, visceral) and acute aortic valve regurgitation. Despite excellent results from individual surgeons and expert centres, operative outcomes for TAAD have remained static with mortality rates from large databases that perhaps better reflect "real-world" practice still around 15 to 30% [Ergin et al, 1996, Fann et al, 1991, Hagl et al, 2003, Kouchoukos et al, 1991, Mazzucotelli et al, 1993, Nienaber et al, 2003a, 2003b, von Segesser et al, 1996].

Since the past decade, the reimplantation aortic valve sparing technique (David I) has been proposed as an alternative to supra commissural replacements or to modified Bentall-deBono procedures for repair of TAAD, based upon the principle of totally resecting the aortic root, but leaving in place a macroscopically intact aortic valve [Kallenbach et al, 2004]. Since the sinuses are very frequently involved in the dissection, in opposition to the aortic leaflets, this technique seems to be very appealing. Yet, in most of the cardiac centres, reimplantation valve sparing techniques are done by experienced surgeons, most often in elective ascending aortic aneurysms. These same surgeons are not those who deal routinely with aortic dissections, and it can be easily understandable that young assistants set as a gold standard in aortic dissection surgery a living patient better than an intellectually satisfying surgery.

For all these reasons, we have carried in our department a prospective study over a 5 years period to evaluate whether a reimplantation valve sparing technique could be associated with an increased perioperative morbidity or mortality when done routinely. The aims of this study were multiple: to proof efficacy and feasibility, to confirm long term reliability of the technique, and to demystify this approach still considered for too many surgeons as a technical challenge.

2. Patients

2.1 Preoperative data

Between February 2005 and April 2010, 51 consecutive patients (40 male/11 female) who underwent surgery for TAAD were analyzed prospectively. Mean age was 65±11 years. Mean logistic Euroscore was 23.3±15.3. Past medical history was marked by severe pulmonary disease in 8 patients, multivascular disease in 5, clopidogrel/anti K vitamin treatment in 4, cerebral stroke in 6, alcohol addiction in 1, and pulmonary Rendu-Ossler disease in 1. Cardiovascular risk factors were severe arterial hypertension (88%) and smoking (27%). None of the patients had previous cardiac surgery.

Diagnosis of type A aortic dissection, defined as involvement of the ascending aorta regardless to the distal extension of the lesions, was assessed by echocardiography, and confirmed in 46 cases by CT-scan. All of the diagnoses were done in external hospitals before transfer to our institution. All the patients had tricuspid aortic valve. Preoperative morphologic and hemodynamic data are represented in table 1. In two cases, the patients presented with a preoperative collapse needing intubation, inotropic support and fluid venous filling. Two other patients had an aortic rupture at the onset of the surgery. Eleven patients had one or more preoperative malperfusion syndromes (limbs 8, cerebral 4, digestive 4 and coronary 5). A 38-year-old woman had a complete coronary artery network dissection in association with the TAAD. Among these patients, 45 underwent a reimplantation valve sparing technique, 2 a modified Bentall-DeBono and 4 a supra commissural replacement.

		n	%
Imaging assessement	TEE	51	100
	CT-scan	46	90.2
Anatomical findings	Aortic insufficiency >2/4	9	17.6
	Ascending aortic diameter >50mm	22	43.1
Hemodynamic status	Shock (alone)	4	7.8
	Malperfusion (alone)	11	21.6
	Both	7	13.7

Table 1. Preoperative data TEE: transesophageal echocardiography.

2.2 Surgical technique in case of reimplantation valve sparing technique

All the procedures were performed under general anaesthesia, standard tracheal intubation and transesophageal echocardiography (TEE) monitoring. Two catheters were inserted into the right radial and the left femoral arteries for continuous blood pressure monitoring. Bispectral index was used for cerebral monitoring. After exposition of the heart and the great vessels, venous cannulation was done into the right atrium using a double stage cannula. In twelve cases, arterial cannulation was performed into the right femoral artery before sternotomy. For 38 patients, the arterial cannulation was made directly in the concavity of the aorta, at the junction between the ascending segment and the arch. In one, canulation of the brachiocephalic trunck was performed. After the cardiopulmonary bypass

(CPB) was started, we began general cooling to reach a rectal temperature of 30°C if an arch replacement was planned. The aortic root was dissected free from the pulmonary artery, the right ventricle and the left atrium. After cross clamping, the aorta was opened transversally and cold crystalloid cardioplegia (Celsior®, Imtix Sangstat, Wien, Austria) was infused directly into the coronary ostia and repeated when necessary. The coronary ostia were dissected, leaving two coronary buttons of approximately 1cm diameter, as well as the sinuses, up to a remnant of 3 to 4mm. The tops of the aortic commissures were suspended with one U-stitch of 4-0 polypropylene each. The diameter of the aortic annulus was assessed using a Hegar dilator to determine the size of the Dacron™ tube. Six threads of 2-0 coated polyester fibre were passed in a U-fashion underneath the aortic annulus from inside to outside in a horizontal way. These threads secured a Valsalva shaped Dacron™ Tube (Gelweave Valsalva graft, Vascutek, Ann Harbor, Mi) to the aortic annulus. The tops of the aortic commissures were then attached inside the tube. The aorta remnant layers forming three cuffs were reimplanted into the tube using three 4-0 polypropylene running sutures, without glue. The coaptation of the three cusps was then examined carefully to determine any residual leakage. In this case, additional leaflet plasty was performed by the mean of free margin running suture using CV-7 PTFe.

	With arch replacement (n=36)	Without arch replacement (n=15)	*p*
Age (years)	65±2	64±4	0.73
Cross clamping (min)	109±5	86±8	*0.01*
CPB (min)	136±6	138±24	0.91
Lowest temperature (°C)	29.1±0.5	34.7±0.5	*<0.0001*

Table 2. Comparative data between patients with or without arch replacement

At that moment, rectal temperature usually reached 30°C. In case of aortic arch replacement, a brief circulatory arrest was performed and the aortic arch was resected, totally or partially, in order to remove as much arch tissue as possible. Two manually inflatable retrograde cardioplegia cannulas (Medtronic™, Minneapolis, Mn) mounted on a Y-shaped injection line were inserted into the lumen of the brachiocephalic trunk and the left carotid artery to provide continuous cerebral antegrade perfusion at a temperature of 30°C and a flow rate of 1.2 to 1.6l/min (10 to 15ml/kg). The adequate perfusion was determined regarding to the right arterial radial pressure and to the lateral pressure line on the left carotid artery cannula. Another Dacron™ prosthesis was anastomosed to the aortic isthmus with a 4/0 polypropylene running suture, after instillation of fibrin glue (Tissucol®, Baxter™, Maurepas, France) between the two layers of the descending aorta. An aortic cuff, including the three cerebral trunks, was anastomosed on the top side of the graft. At the end of the suture, the cerebral perfusion cannulas were removed, and a new cannulation was performed directly into the arch tube through a small incision and secured using a snare. The CPB was started slowly in order to de-air the tube before clamping and re warming.
The two coronary buttons (left then right) were anastomosed on the lateral side of the Valsalva tube at the level of the skirt-like segment. Finally, the two Dacron™ tubes (ascending aorta and arch) were anastomosed end-to-end with a 3-0 polypropylene running suture. For the patients without arch replacement, the ascending tube was directly anastomosed underneath the arterial brachiocephelic trunk. The aorta was declamped after

de-airing, and the CPB was weaned in a standard manner. Two temporary epicardial pacing wires were placed on the right ventricle. Pericardial drainage was made using two Ch16 redon catheters with high depression (-700mmHg) [Farhat et al, 2003].

2.3 Follow-up

Postoperative follow-up was done by the surgeon at the hospital, after 1, 6, 12 months and every year. A transthoracic echocardiography (TTE) and a CT-scan were done before each outcome visit. Aortic regurgitation was assessed semi quantitatively between 0 and IV/IV. Thrombosis of the false lumen of the descending aorta was noted as well. Clinically, general dyspnoea was calculated using the New York Heart Association classification (NYHA).

3. Results

3.1 Operative data

We didn't note any intraoperative mortality. Mean cross clamping, cerebral perfusion and CPB times were respectively 102±31, 24±10 and 137±58min. Mean low temperature was 30.7±3.8°C. There was a significant difference in cross clamping times and lowest temperatures between patients with or without arch replacement, but surprisingly not in CPB times (table 2).

	Alive, n=43	Dead, n=8	*p* value
	N=43	N=8	
Age (mean standard deviation)	63 (11)	72 (13)	0.12
Type 1 DeBakey Dissection (%)	32 (74%)	7 (88%)	0.66
Hypertension	38 (88%)	7 (88%)	1
Preoperative malperfusion	14 (33%)	4 (50%)	0.43
Preoperative shoc	8 (19%)	3 (38%)	0.35
Preoperative AI>2	18 (42%)	2 (25%)	0.46
Aorta diameter > 50 mm	19 (44%)	3 (38%)	1
Arch repair	30 (70%)	6 (75%)	1

Table 3. Comparative data between alive and dead patient in the perioperative period AI: aortic insufficiency.

The overall cooling time was less than 20 minutes. The surgical sequence that we used allowed us in each case to reach the ideal temperature at aortic declamping. In two cases, the aortic cannulation was directly made into the false lumen. At the aortic cross clamping, the radial pressure dropped dramatically attesting of the hypoperfusion of the true lumen. A brief CPB arrest was performed in a Trendelenburg position. The aortic clamp was released, and a surgical fenestration of the intimal flap was made in the aortic arch. The CPB was restarted after recalmping the aorta re-establishing a homogenous perfusion within the two lumen. Among all patients, 36 had an arch replacement, including one elephant trunk distal suture.
Five patients had associated coronary artery bypasses during surgery, four for coronary occlusions and one for coronary dissections. Another patient had an extracorporeal life support (ECLS) at the end of the surgical procedure because of biventricular failure (preoperative left main coronary trunk dissection).

3.2 Early postoperative course

3.2.1 Postoperative mortality

Eight patients died in the early postoperative period (15.7%). One patient died on postoperative day (POD) 8 during a tracheal aspiration. No diagnostic autopsy was performed. Two patients presenting with a preoperative coma died respectively on POD 3 and 4. Two patients died from myocardial infarction respectively on POD 1 and 13. One patient died on POD 56 due to severe pneumopathy. One patient died on POD 27 from multiple organ failure. The last patient died one day from discharge without clear reason (non contributive autopsy). There was no statistical difference in between alive and dead patients regarding age, distal extension of the dissection, preoperative hypertension, preoperative malperfusion or shock, preoperative severe aortic insufficiency, aortic diameter or arch repair (table 3).

With malperfusion (4 death)	Survival 78% (95%CI : 61-100)
Without malperfusion (4 death)	Survival 87% (95%CI : 76-100)
Log-rank	p=0.36
With preoperative shock (3 death)	Survival 73% (95%CI : 51-100)
Without preoperative shock (5 death)	Survival 87% (95%CI : 77-99)
Log-rank	p=0.23

Table 4. Survival in patients with or without preoperative malperfusion

Moreover, postoperative survival was not affected by preoperative malperfusion (OR=2.07 [0.45-9.52] p=0.35), shock (OR=2.63 [0.52-13.32] p=0.24, table 4) or age (OR=2.21 [0.96-5.05] p=0.06). To refine the analysis of preoperative risk factors for postoperative mortality, we have defined as severity factor patients presenting with malperfusion, shock or both. In this case, there was no difference in between patients with (5 death) or without (3 death) severity criteria regarding mortality (OR=2.55 [0.54-12.08] p=0.24). After analysing the population of patients over 70 years old, the results were also comparable (OR=5.54 [0.63-48.44] p=0.12).

		Value
Total transfusion		
	RBC	4.4±5.1
	FFP	3.6±3.6
	Platelets	0.6±0.8
Aortic insufficiency		
	Grade 0	43
	Grade 1	2

Table 5. Early postoperative data.

Regarding anatomical findings, preoperative aortic insufficiency >2/4 (2 *vs* 6 deaths, OR=0.46 [0.08-2.56] p=0.38) was not related to increased mortality, neither was an aortic diameter >50mm (3 *vs* 5 deaths, OR=0.76 [0.16-3.58] p=0.72). Patients with a preoperative AI>2/4 had better survival comparably to others but without reaching statistically significant difference (90% *vs* 80%, p=0.32), as well as patients with an aortic diameter >50mm (86% *vs* 82%, p=0.72) when compared with patients with aortic diameter <=50mm.
Finally, survival in case of reimplantation technique (7 deaths) was comparable to other approaches (1 death, respectively 84% *vs* 83%, p=0.94, OR=0.92 [0.09-9.13])

3.2.2 Postoperative morbidity

Eleven patients (21.6%) underwent revision for bleeding. Four were previously treated with clopidogrel, and one was under ECLS. No surgical causes were noted on reintervention. Eight patients (15.7%) had postoperative neurological deficit, completely regressive within 24 hours. Cerebral CT-scan didn't show ischemic signs. One patient with preoperative leg malperfusion presented with postoperative mesenteric ischemia needing surgical abdominal aortic fenestration on POD 1. One patient had on POD 7 an implantation of a descending aortic covered stent graft (Talent™, Medtronic) for a pre-existing penetrating aortic ulcer (PAU) located 10 cm above the celiac trunk. This procedure was done under epidural analgesia because of severe COPD.

Mean troponin I level at 24 hours was 15±20µg/l. Mean bleeding at 24 hours was 846±825ml. Mean intubation and ICU times were respectively 9.2±17.2 and 10.7±14.2 days. Yet, twelve patients with severe preoperative comorbidities (malperfusion, alcohol addiction, pulmonary Rendu-Ossler disease, preoperative shock) had prolonged ventilations (range from 14 to 48 days). Other postoperative data are represented in table 5.

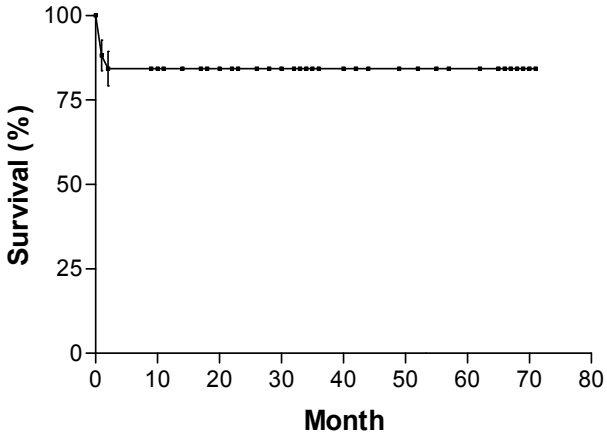
ICU stay was analyzed regarding preoperative risk factors. Malperfusion (13.9 days if malperfusion *vs* 9.0 if not, p=0.33) or preoperative shock (7.14 if shock *vs* 11.7 if not, p=0.13) were not found to be predictive factors of prolonged ICU stay. Analyzing the postoperative neurological deficit, neither arch repair (8/36 *vs* 0/15, p=0.08) nor direct aortic canulation (6/38 *vs* 2/13, p=1) were found to be risk factors.

3.3 Late postoperative course

Mean follow up was of 34±25 months and was completed in all cases. Actuarial survival rate at 1 year was 84.3% (figure 1). We didn't have any reintervention on the aorta during the follow up period. 42 patients presented in NYHA I class while 1 was in NYHA II (COPD). TTE control didn't show any aortic insufficiency greater then grade I. CT-scan control showed neither false aneurysm on the proximal or distal anastomosis, nor malperfusion syndrome. In 6 cases, CT-scan showed a complete thrombosis of the descending aortic false lumen. For all patients, we could note the Valsalva shaped aspect of the aortic root (figure 2) with a non modified geometry of the cusps coaptation.

4. Discussion

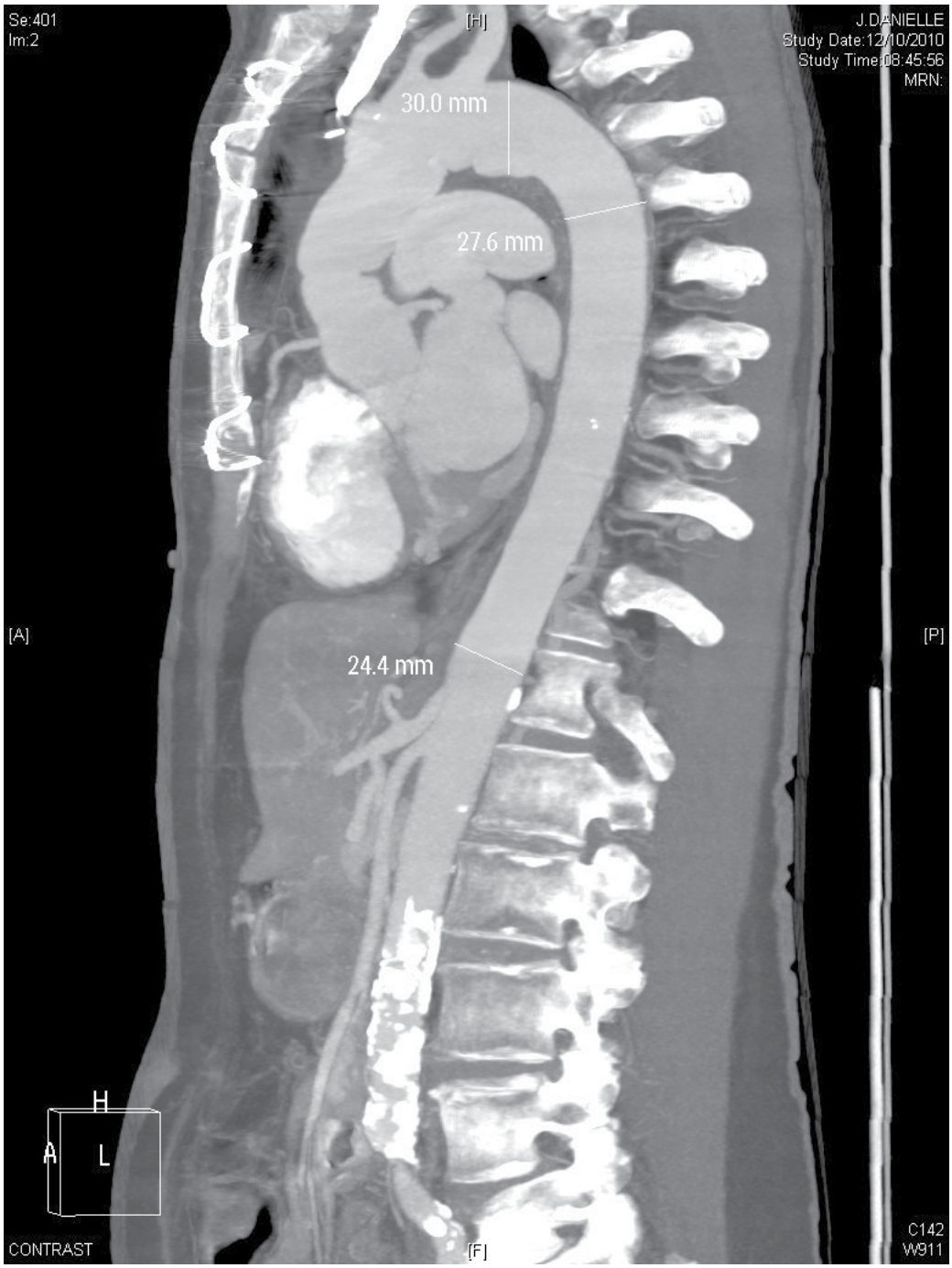
The surgical approach of type A aortic dissection remains questionable for many reasons. First, this pathology represents one of the major life-threatening emergency situations in cardiovascular diseases, due to the risk of aortic rupture into the pericardium, and to the consequences of malperfusion (cerebral, digestive, limbs) that can higher morbidity or mortality even if the surgical management of the ascending aorta itself is optimal [Nienaber et al, 2003a]. Second, type A aortic dissection presents the very bad habit of being a "mid-night pleasure"! Thus, a big majority of the surgeons tend to privilege a fast and easy technique. Third, the absence of dilatation of the aortic root is very often present, and in this case, total aortic root replacement (regardless to valve preservation or not) is difficult to justify because of a potentially higher surgical risk. Finally, and in many institutions, reimplantation techniques in scheduled patients are reserved for confirmed surgeons. Unfortunately, all of the surgeons who deal with type A aortic dissection in the middle of the night are not always used to this approach.



Time (months)	14	26	36	67
Patients at risk (n)	38	30	22	10

Fig. 1. Actuarial survival curve for patients with type A aortic dissection treated by reimplantation valve sparing technique according to David in association or not with arch replacement. Early mortality is included.

Supracommissural tube graft replacement in conjunction with reconstruction of the sinuses with glue is the easiest way to treat type A aortic dissection [Fann et al, 1991, Kouchoukos et al, 1991, Mazzucotelli et al, 1993]. This technique allows in almost 90% of the patients the restoring of the geometry of the aortic sinuses and subsequently the valve competence which is failing in many cases. If this surgical treatment brings entire satisfaction in immediate postoperative course, the long term outcome remains controversial. Supracommissural replacement has been proven by some authors inasmuch as the freedom for reoperation for aortic valve dysfunction was elevated after 10 years of follow-up (up to 91%) [Casselman et al, 2000, Driever et al, 2004]. Yet, others underscore that the progression of the disease, regardless to a pre-existing aortic aneurysm, could lead to aortic insufficiency by the absence of coaptation between the three leaflets. Simon *et al* found that 29% of the patients with supracommissural tube graft for type A aortic dissection developed a sinus of Valsalva aneurysm within 44±22 months after surgery [Simon et al, 1994]. Three reasons are often evoked as an explanation: first, the supracommissural replacement of the aorta leads to increased shear stress in the sinuses because of the absence of elasticity of the Dacron™, especially during diastole, thereby transferring the diastolic pressure to the only sinuses [Simon et al, 1999]. Second, a long aortic root remnant has by itself a dilatation risk due to cystic medial necrosis that is diffusely present in the aortic structure and which is the primary reason for aortic dissection [Marsalese et al, 1990]. Third, the use of gelatine-resorcinol-formaldehyde has been incriminated in a higher incidence of false aneurysms or re-dissections, particularly in the proximal part of the aorta [Kirsch et al, 2002]. For all these reasons, some authors have strongly recommended total aortic root replacement by a composite graft, subsequently to eliminate the entire diseased aortic root [Ergin et al, 1996, Hagl et al, 2003]. Yet, solving a problem was to create another one: biological tubes lead to valve failure, and mechanical ones to lifetime anticoagulation. Thus, the valve preserving techniques (remodelling/reimplantation) have gained more interest these past years in type A aortic dissection treatment along with their development in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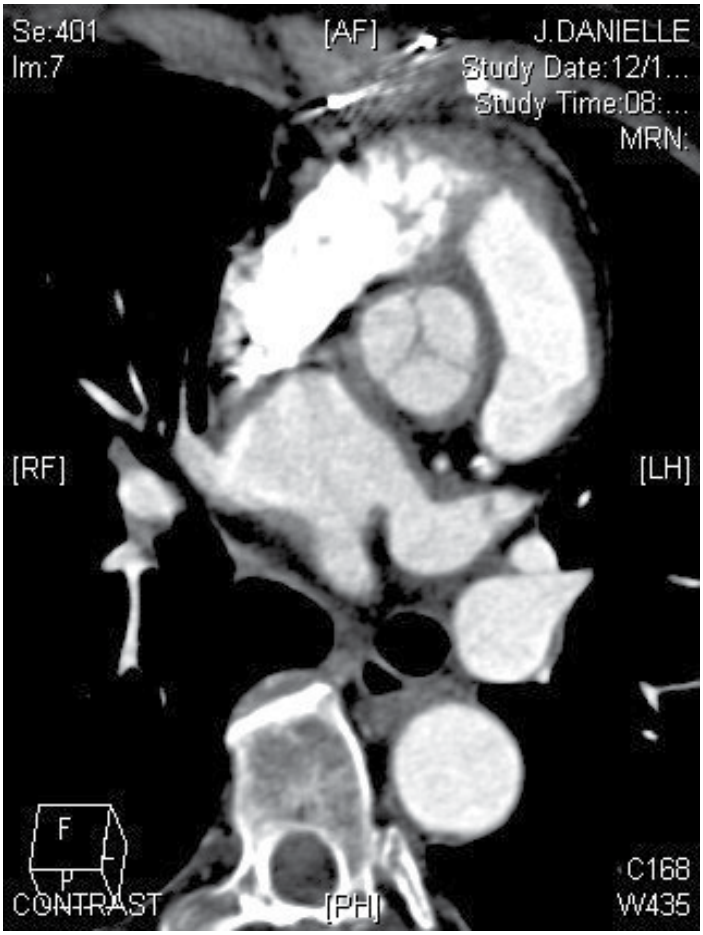

(b)

Fig. 2a. and 2b. CT-scan showing transverse (a) and sagittal (b) views of the aorta and aortic leaflets. The sinuses' diameter is 20 to 25% larger than the annulus diameter. The three leaflets are well identified and coaptation can be assessed

elective cases, such as aortic root aneurysms. Kallenbach *et al* have reported that the aortic valve preservation techniques can be performed with favourable functional results regardless to the underlying aortic lesion (type A aortic dissection or aneurysm) [Kallenbach et al, 2004]. Yet, Leyh *et al*, from the same team, noted a higher failure rate in aortic root remodelling, in patients with type A aortic dissection, comparatively to a reimplantation technique [Leyh et al, 2002]. These results can be easily understandable: the remodelling is based upon the suture of a Dacron™ tube, which is previously three folded, directly to the 3 to 4mm remnants of the sinuses of Valsalva. This suture is made on a diseased tissue, without any protection against further dilatation of the aortic annulus.

Our prospective series was carried on to find out whether a near systematic performance of a reimplantation technique is accompanied with a higher mortality or morbidity risk. Post operative death proportion in our series is comparable to what we can find all along the literature. Yet, many points are remarkable in this series. In opposition to what previously

described in the literature, preoperative malperfusion, shock or age of the patients were not found to be risk factors of perioperative mortality. Arch replacement, as well as direct aortic cannulation, didn't emphasize the postoperative risk of stroke.

Different points are to be discussed in our global strategy. First, we did direct aortic cannulation into the dissected aorta for 38 patients. This technique was first described by Lijoi *et al*, who performed two cases of aortic replacement in type A aortic dissection, with direct aortic cannulation and deep hypothermia [Lijoi et al, 1998]. Minatoya *et al* reported a series of 14 patients with direct aortic cannulation, without rupture or peroperative malperfusion [Minatoya et al, 2003]. The difference with the Lijoi description is that the arch replacement is performed under mild (28°C) hypothermia and antegrade cerebral perfusion, like reported in our series. Beside the aortic rupture risk, the elective perfusion of the false lumen is the other pitfall of this technique. This problem can only be tracked down at cross clamping, when the proximal intimal aortic tear is excluded and doesn't anymore constitute an entry site for the perfusion of the true lumen. This complication can be suspected easily while the right radial pressure drops (along with a preservation of the pressure in the femoral artery), witnessing of a malperfusion of the arterial brachiocephalic trunk. Minatoya *et al* have also reported this complication. We propose a simple fenestration of the intima in the arch, that is to recreate a downstream re-entry site and to perfuse adequately the true lumen. The second point of our technique is the arch replacement under mild hypothermia with selective antegrade cerebral perfusion. Minatoya *et al* have recently reported the absence of difference upon neurological outcome with antegrade cerebral perfusion, comparatively between three groups with a body temperature of 20, 24 and 28°C [Minatoya et al, 2005]. Karck *et al* performed prolonged circulatory arrest times (up to 62±14min) in combined aortic arch and descending aortic replacement, using a 28°C antegrade cerebral perfusion, without major cerebral complications [Karck et al, 2005]. This technique brings the advantage of shortening the CPB time, reducing the platelets dysfunction and subsequently the postoperative bleeding. Regarding the postoperative neurological events, direct aortic canulation and arch replacement were not found to be risk factors when considered alone. The third point of our approach is the use of a Gelweave Valsalva™ prosthesis for the root replacement. This tube was designed to reproduce the anatomic and physiologic features of the normal aortic root. The root of the tube, shaped as a skirt, has vertical crimps, allowing it to expand transversally along with the cardiac systole and diastole, contrarily to the body of the tube, which has horizontal crimps. In a normal aortic root, the sinuses of Valsalva create eddy currents, first described by DaVinci, with a major importance in the aortic leaflets motion: on valve opening, they prevent the cusps' edges from impacting the aortic wall, and they participate to the initiation of the aortic valve closure [Hopkins et al, 2003, Kunzelman et al, 1994, Leyh et al, 2003]. One of the suggested reasons for mid term failure of the reimplantation technique is the use of a straight Dacron™ tube without any stretching structure allowing the transversal expansion during systole. The consequence is repetitive impaction of the cusps' free edges on the tube's walls, leading to a progressive fibrotic retraction of the cusps with subsequent coaptation default. We believe that the Valsalva shaped tube prevents from this evolution by recreating the anatomy and the haemodynamic of a normal aortic root. Along with the progression of the series, we noticed during echographic control that the Valsalva segment was far from the free edge of the cusps during systole.

Follow up was done for 34±25 months and was completed in all cases. We didn't observe any evolution towards aortic insufficiency in any patient, and previous aortic aneurysm didn't constitute a risk factor for aortic repair failure [Leyh et al, 2003]. None of the patients

had anticoagulant treatment. Mean aortic gradients and effective permeability index were acceptable, without difference between the postoperative period and follow-up. CT-scan reconstructions allowed a perfect visualization of the aortic root, showing the shape of the Valsalva skirt. In 9 patients, we noted a thrombosis of the false lumen. The persistence of perfusion in the other patients is probably related to the re-entry sites situated distally on the descending and abdominal segments. One patient presented an evolution to dilatation of the descending aorta, without reaching surgical criteria.

5. Conclusion

Based upon our experience in the management of type A aortic dissection, the reimplantation valve sparing technique could be performed systematically without emphasizing perioperative risk. Our results during follow-up, along with other results published by many authors, seem to be encouraging, and push up to keep on performing this technique routinely in type A aortic dissection. Preoperative malperfusion or shock shouldn't push the surgeon to counter indicate the patients to undergo surgery. We also think that the use of a Valsalva tube grandly contributes to these mid term good results.

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13

Prevention of Spinal Cord Injury After Thoracoabdominal Aortic Aneurysm Repair

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1. Introduction

Thoracoabdominal aortic aneurysm (TAAA) repair still remains a challenging operation since it necessitates extended exposure of the aorta and reimplantation of the vital aortic branches. Among possible postoperative complications, spinal cord injury (SCI) seems one of the most formidable morbidities. Even by experts who have championed in TAAA repair the incidence of SCI remained as high as 16% in the early 1990s (Svensson et al., 1993). Thanks to numerous experimental investigations and technical advances or modifications, it has improved up to 3.6%-4.6% in the worldwide largest centers with a contemporary strategy (i.e. aggressive use of distal aortic perfusion) (Safi et al., 2003, Coselli et al., 2007, Zoli et al., 2010). However, this incidence of SCI should vary according to the extent of aortic involvement. In 1986, Crawford and his colleagues proposed classification of TAAA into four groups according to the extent of aortic involvement and clearly showed that this classification could predict late death and neurological deficit (Crawford et al., 1986). Their classification is as following; group I involves most of the descending thoracic and upper abdominal aorta. Group II involves most of the descending thoracic aorta and most or all of the abdominal aorta. Group III involves the distal descending thoracic aorta and varying segments of abdominal aorta. Group IV involves most or all of the abdominal aorta including the segment from which the visceral vessels arise. Later, Safi and his co-workers advocated additional group V that involves below the sixth intercostal space to just above the renal arteries (Safi et al., 1998, 1999, 2003) (Figure 1). As shown later in Table 3, this classification correlates well with postoperative SCI still in contemporary era, thus it has been used widely to date. In the most extended type of TAAA (type II), SCI still occurs in 4.2-15.8% despite with experienced hands in the last decade (Safi et al., 2003, Jacobs et al., 2006, Coselli et al., 2007, Conrad et al., 2007, Acher et al., 2008, Zoli et al., 2010). Thus spinal cord protection during TAAA repair has emerged as great clinical importance. The primary aim of this review is to provide a better appreciation and understanding of the mechanisms and pathophysiology of SCI after TAAA repair.

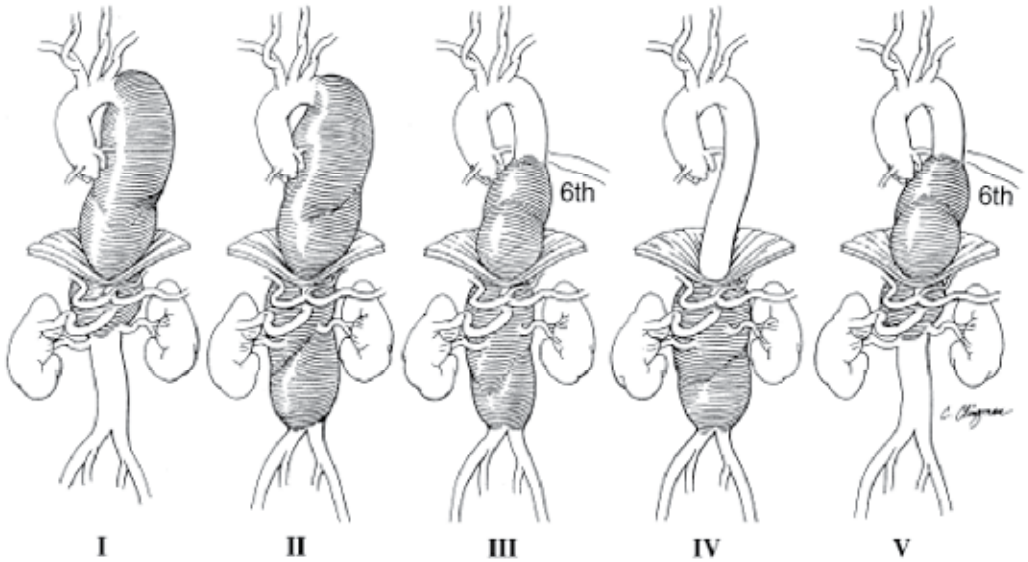

Fig. 1. Crawford/Safi's cllasification of the extent of aortic involvement (From; Safi, et al., 1999).

2. Mechanisms of spinal cord injury

Underlying mechanisms of SCI after TAAA repair are multifactorial, however, they can be primarily summarized into three key processes; 1) the duration and degree of ischemia, 2) failure to re-establish blood flow to the spinal cord after repair, and 3) a biochemically mediated reperfusion injury (Svensson 1997).

2.1 The duration and degree of ischemia

To reduce the duration and degree of spinal cord ischemia, either oxygen supply should be enhanced or oxygen demand attenuated. For these purposes, multi-segmental sequential clamping technique combined with mild hypothermic distal aortic perfusion has favorably been used in many institutions. When sequential clamping is not feasible, deep hypothermic circulatory arrest should be applied.

2.1.1 Distal aortic perfusion

Pioneers have used simple cross-clamping technique and reported acceptable outcomes (Crawford et al., 1986) (Schepens et al., 1994). Nowadays, majority of surgeons use distal aortic perfusion to reduce ischemia of the distal organs and cardiac afterload. Surprisingly, distal shunt was already used in a half century ago and has been applied with some modifications (Etheredge et al., 1955, Gott 1972, Cambria et al., 1998). Distal shunt has some advantages such as its simplicity and mild heparinization, but has also some disadvantages. Distal blood flow depends largely on proximal blood pressure and it is difficult to manage massive bleeding. On the other hand, left heart bypass using a centrifugal pump can provide flexible control of distal blood flow, thus it is currently used widely. Many experts have demonstrated that left heart bypass could significantly reduce the incidence of SCI

especially in extended TAAA (type II) repair (Safi et al., 1997) (Coselli et al., 1999, 2003). We have favorably used a partial cardiopulmonary bypass (CPB) through the femoral artery and vein. This alternative has some advantages in case with cardiopulmonary instability or massive bleeding. Some disadvantages such as acceleration of bleeding tendency has been resolved by reduction of heparin dosage using a fully heparin-coated closed-loop CPB system with a soft reservoir bag (Shiiya et al., 2005, 2006).

2.1.2 Multi-segmental sequential clamping

Blood flow of the anterior spinal artery is primarily supplied by some radicular arteries. The radicular artery has a rich collateral network between adjacent intercostal/lumbar arteries. Therefore it may be beneficial to maintain this collateral blood flow during reattachment of the intercostals/lumbar arteries. Especially in patients with degenerative aortic aneurysm, occlusion or stenosis of the intercostals/lumbar arteries may alter and complicate this collateral pathway, which may emphasize the importance to preserve it. In addition, during reattachment of the intercostals/lumbar arteries, back bleeding from adjacent one may accelerate steal phenomenon (Christiansson et al., 2001). The Mount Sinai group emphasized importance of avoiding steal phenomenon. They sacrificed all involved intercostals/lumbar arteries outside of the aorta to avoid steal phenomenon in 100 cases and experienced only 2% SCI (Etz et al., 2006). Their findings have a great implication for extensive deployment of endocasvular stentgraft.

On the other hand, the anterior spinal artery has a narrow critical zone at around T4 level, where the spinal cord is susceptible to ischemia (Dommisse 1974, Svensson et al., 1986). Thus an ascending blood flow through the anterior spinal cord artery alone is not enough to feed this area. These mechanisms may explain why distal aortic perfusion alone was not beneficial to prevent SCI in the early era (Crawford et al., 1988). Therefore segmental sequential clamping seems advantageous to preserve collateral blood flow to the spinal cord during reattachment of the critical intercostals/lumbar arteries (Kuniyoshi et al., 2003). Trend has become toward clamping shorter segments (multi-segmental sequential clamping). We experienced no postoperative SCI when less than two pairs of intercostals/lumbar arteries were involved between segmental clamping. We identified that multi-segmental sequential clamping in combination with distal aortic perfusion was the only significant predictor for SCI after type I and II TAAA repair in multivariate analysis (Shiiya et al., 2005). The fact that a previous abdominal aortic aneurysm repair is a significantly high risk for postoperative SCI may support this collateral network concept (Svensson 2005).

2.1.3 Hypothermia

It has been widely accepted that mild hypothermia is clinically effective to prevent SCI. A reduction in temperature of 3˚C provides a 2-fold increase of the tolerable ischemic interval in rabbit (Vacanti et al., 1984) and a 5˚C reduction does a 2.5-fold increase in pig (Strauch et al., 2004). Therefore almost all aortic surgeon currently use mild hypothermia (32-34˚C) using heat-exchanger or permissively in combination of distal aortic perfusion. Whenever the aorta cannot be safely clamped, use of deep hypothermic circulatory arrest should be warranted. Clinically, moderate to profound hypothermia was proved to prolong tolerable ischemic interval, which enables secure reconstruction of the aorta for aortic surgeons (Svensson et al., 2003) (Fig. 2).

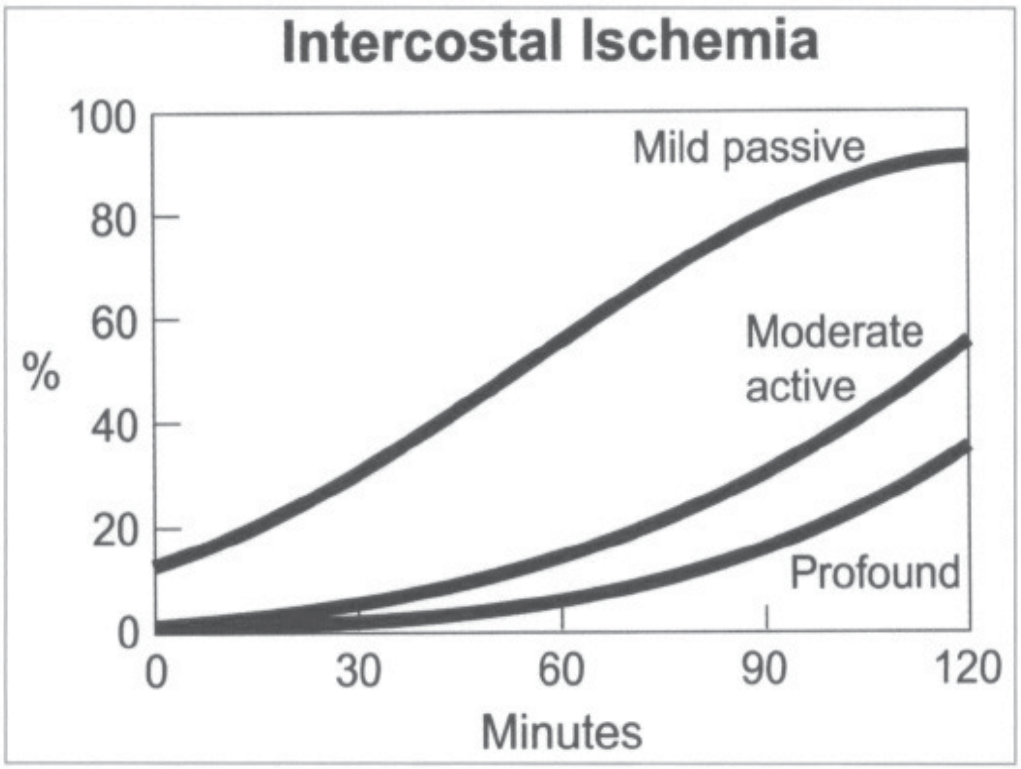

Fig. 2. Relationship between interval of spinal cord ischemia and risk of neurological deficit stratified by systemic temperature (Svensson 2005).

Kouchoukos and his colleagues have aggressively performed TAAA repair under profound hypothermia and reported its substantial protective effect against SCI (2.9% paraplegia) (Kouchoukos et al., 2003). Using deep hypothermic circulatory arrest Coselli and his co-workers could reduce the incidence of SCI up to 1%, however on the other hand, it increased morbidity and mortality rate (Coselli et al., 2008). Therefore this alternative is currently limited to selected cases (large or extensive aneurysm, friable aortic tissue, high risk of embolization, complex repair, redo cases), principally due to risk of coagulopathy, pulmonary dysfunction, and massive fluid sift. Accordingly some experts have proposed regional epidural or intrathecal cooling (Black et al., 2003, Shimizu et al., 2010). Although conceptually promising, this alternative currently lacks the support of prospective randomized data in larger cohort.

2.2 Failure to re-establish blood flow to the spinal cord after repair

2.2.1 Preoperative identification of critical intercostals artery

There are some surgeons who will blindly re-attach every intercostal/lumbar arteries to secure spinal cord protection (so-called onlay patch methods) (DeAnda et al., 2005). However, this technique seems unrealistic because longer ischemic time is definitively associated with higher risk of SCI (Safi et al., 1998). In addition, considerable extent of aneurismal aortic wall remains to exist. To re-establish blood flow to the spinal cord,

therefore, it is crucial to identify critical intercostals artery to the spinal cord. This is normally the largest radiculomedullary artery; so-called "the Adamkiewicz artery". Preoperatively, it used to be identified by angiography, however, it appears rather invasive and difficult in case with large, thrombosed, or kinky aorta (Kiefer et al., 2002). Since we have visualized Adamkiewicz artery using multi-detector row computed tomography in 2003 (Maruyama et al., 2003), numerous reports have demonstrated that it is feasible in over 80% of cases by both computed tomography and magnetic resonance angiography (Yoshioka et al., 2006, Uotani et al., 2008) (Fig 3) (Table 1).

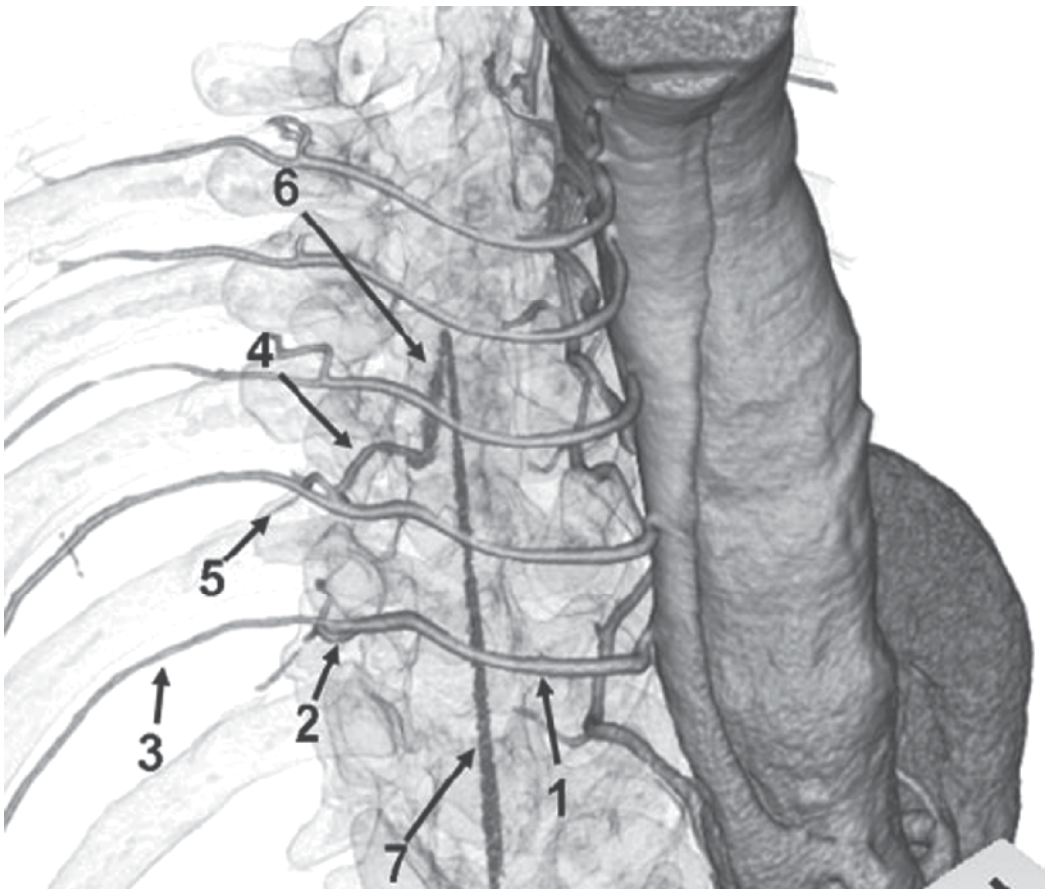

Fig. 3. Identification of the Adamkiewicz artery by 3D volume-rendered computer tomography. 1: Intercostal and lumbar arteries with their posterior (2) and anterior (3) branches, 4: Radiculomedullary artery and muscular branch (5), 6: the Adamkiewicz artery, 7: the anterior spinal artery. (Uotani et al., 2008)

The majority of the Adamkiewicz artery proved to originate from T8-L1 level with left dominancy, which was consistent with angiographic findings and cadaver study (Koshino et al., 1999, Kiefer et al., 2002) (Table 2, Fig 4-5).

MRA		
Nijenhuis RJ.	J Vasc Surg. 2007;45:677.	97%
Yoshioka K.	Radiographics. 2006;26:S63-73.	93%
Mell MW.	J Surg Res. 2008 Jun 20.	85%
Hyodoh H.	J Magn Reson Imaging. 2007;26:359.	82.4%
Ogino H.	Ann Thorac Surg. 2006;82:592.	70.7%
CT		
Nojiri J.	Eur J Cardiothorac Surg. 2007;31:249.	100% (I.A.)
Boll DT.	Am J Roentgenol. 2006;187:1054.	100%
Ou P.	Am J Neuroradiol. 2007;28:216.	95%*
Uotani K.	Am J Neuroradiol. 2008;29:314.	94% (I.A.) 60% (I.V.)
Yoshioka K.	Radiographics. 2006;26:S63-73.	83%
Utsunomiya D.	Eur Radiol. 2008;18:2684.	80%
Takase K.	J Comput Assist Tomogr. 2006;30:716.	80%
Nijenhuis RJ.	J Vasc Surg. 2007;45:677.	71%
Kudo K.	Am J Neuroradiol. 2003;24:13.	68%
Von Tengg-Kobligk H.	J Endovasc Ther. 2007;14:639.	59%
Angiography		
Kieffer E.	J Vasc Surg 2002;35:262.	86%
Heinemann MK.	Ann Thorac Surg. 1998;65:346.	65%
Williams GM.	J Vasc Surg. 2004;39:314.	43%

Table 1. Preoperative identification rate of the Adamkiewicz artery using different modalities. *child cases (7.5 +/- 5 years old), I.A. or I.V.: intra arterial or venous injection of contrast materials, respectively.

	Rt	Lt	Total
Th7	-	1	1
Th8	2	3	5
Th9	1	4	5
Th10	1	6	7
Th11	2	1	3
TH12	3	4	7
L1	-	4	4
L2	-	2	2
L3	-	1	1
L4~	1	-	1
	10 (27%)	27 (73%)	37

Table 2. Our experience to detect the Adamkiewicz artery in 48 cases using a computer tomography between 2001 and 2004. Detection rate was 77% and 86% of the Adamkiewicz artery originated from T8-L1

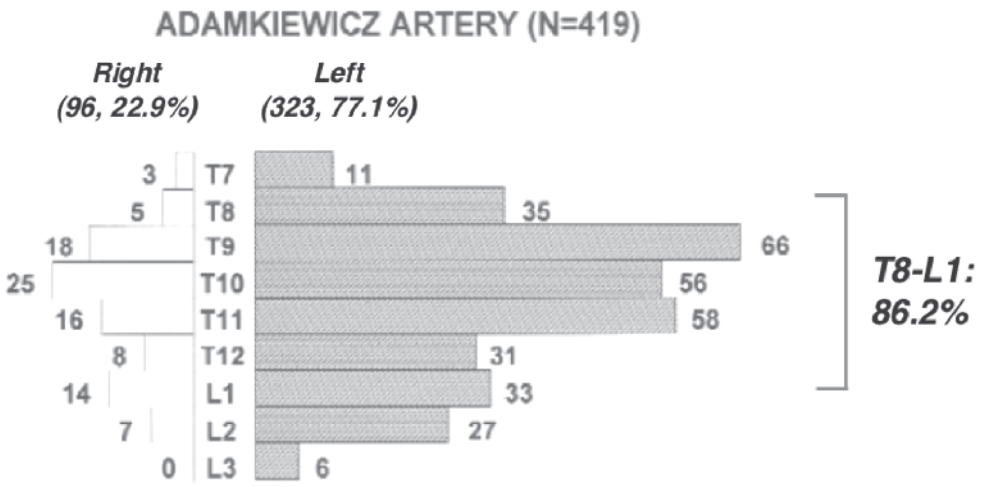

Fig. 4. Identification of the origin of the Adamkiewicz artery using an angiography (Kiefer et al., 2002 with modification)

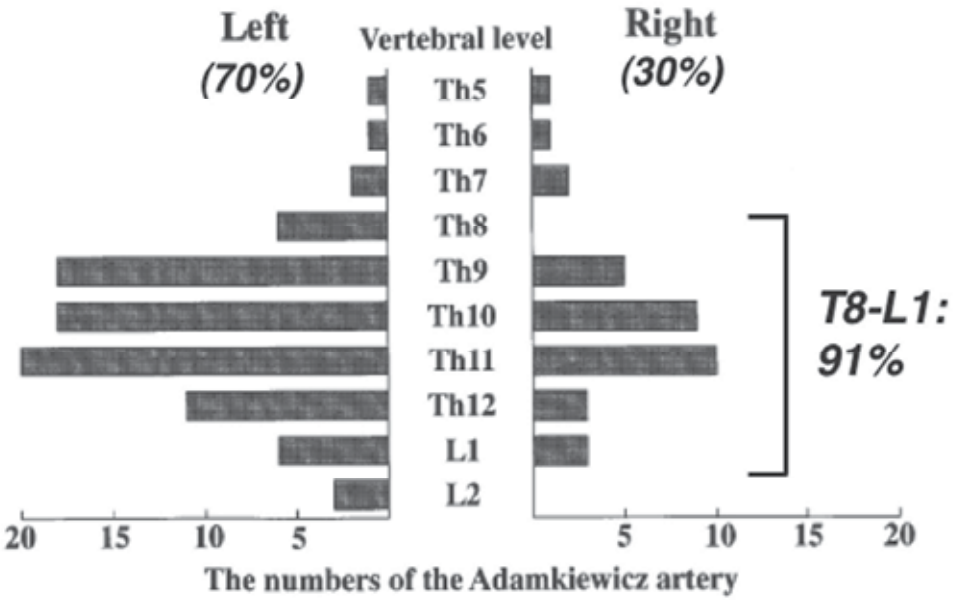

Fig. 5. Identification of the origin of the Adamkiewicz artery from 90 cadavers. (Koshino et al., 1999 with modification)

2.2.2 Intraoperative identification of critical intercostals artery

To identify the Adamkiewicz artery intraoperatively, traditionally we used to apply evoked spinal cord potential, which required two electrodes placed in the epidural space and

published its usefulness to prevent SCI (Matsui et al., 1994, Shiiya et al., 1995). However, this method is more or less invasive and technical demanding, and although rare, complications related to epidural catheter are catastrophic. Therefore majority of surgeon are currently using motor evoked potentials (Jakobs et al., 2006). Nonetheless, these electrophysiological examinations have some disadvantages such as time delay or effect of electric noise, anesthetic agents, peripheral ischemia, and hypothermia. Therefore we have tried to measure immediate information of spinal cord oxygenation noninvasively using transcutaneous or transesophageal near-infrared spectrophotometry (Kunihara et al., 1998, Kunihara et al., 2004). Further studies and technical advance will be essential toward its clinical use.

2.3 A biochemically mediated reperfusion injury

2.3.1 Clinical siginificance of cerebrospinal fluid drainage

Cerebrospinal fluid (CSF) drainage (CSFD) may be one of the most promising procedures to prevent SCI. Its usefulness has already advocated in 1960 (Miyamoto et al., 1960). Acher and associates have reported that combined use of CSFD and naloxone hydrochloride (naloxone), an opioid receptor antagonist, reduces the risk of SCI in patients undergoing TAAA repair in 1994 (Acher et al., 1994). In 2002, CSFD itself proved to be beneficial to reduce the risk of SCI after TAAA repair in prospective randomized clinical trial (Coselli et al., 2002). Meta-analysis of three randomized controlled trials and five cohort studies revealed beneficial effect of CSFD on paraplegia (Fig 6) (Cinà et al., 2004). Although rare (0.2%), CSFD-associated complications are catastrophic (subdural hematoma, intracranial bleeding, meningitis), so that CSFD should currently be reserved for extended aneurysm (type I and II) or patient at high risk (Cinà et al., 2004, Wynn et al., 2009).

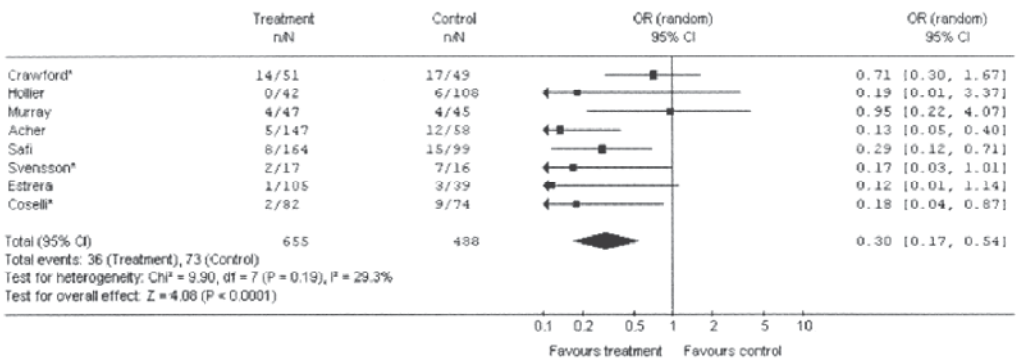

Fig. 6. Meta-analysis showing beneficial effect of cerebrospinal fluid drainage on paraplegia (Cinà et al., 2004).

2.3.2 Clinical siginificance of cerebrospinal fluid drainage

However, underlying mechanisms of CSFD to reduce SCI seems still unclear and it has not been investigated whether naloxone can alone attenuate the risk of SCI clinically like CSFD. Experimental studies have revealed that CSF pressure rises during aortic clamping, leading to decrease of spinal cord perfusion pressure (mean distal aortic pressure – CSF pressure) (Kaplan et al., 1995) (Fig. 7).

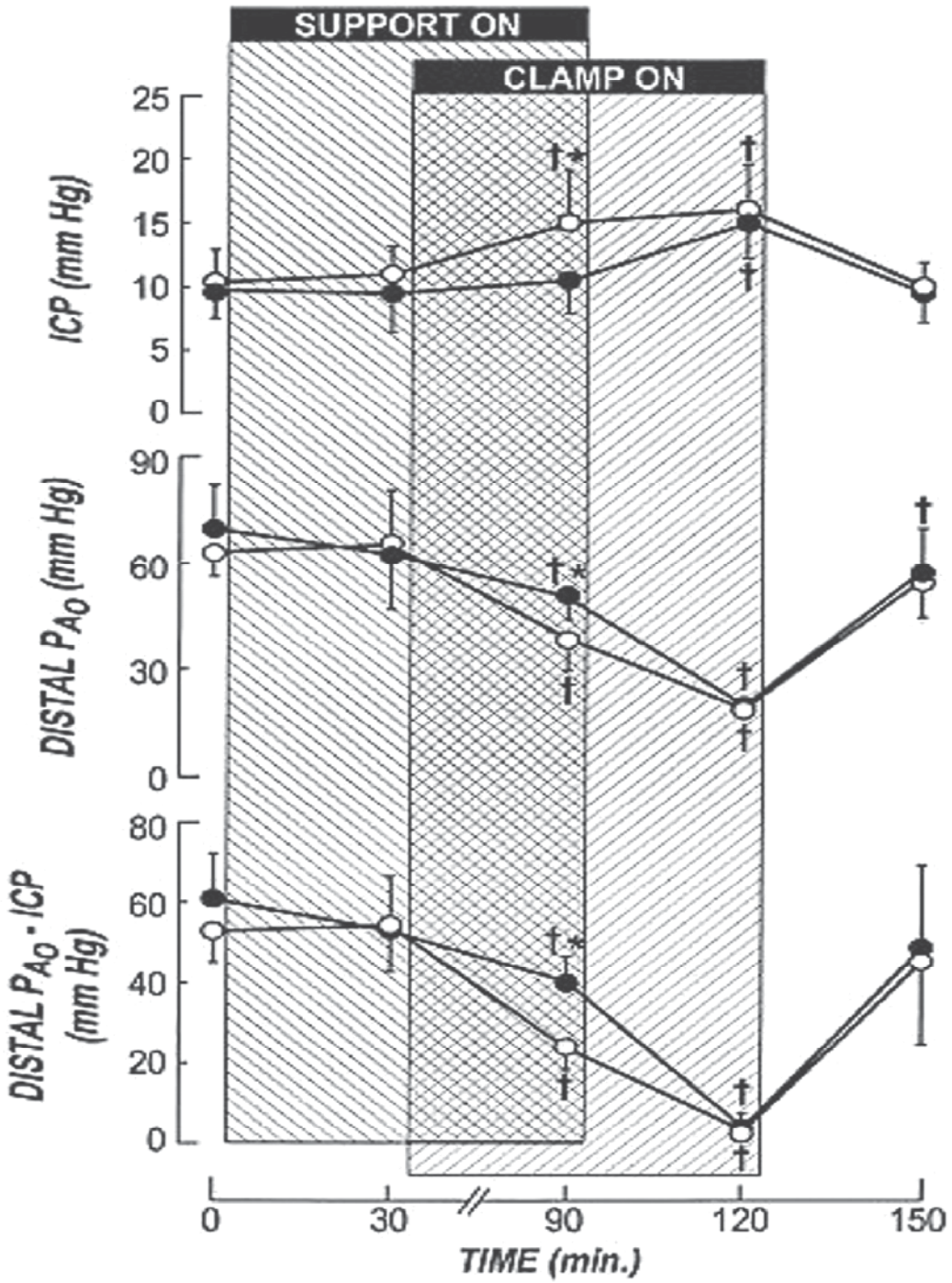

Fig. 7. Relationship between intracranial pressure (ICP), mean distal aortic pressure (DISTAL P_{Ao}), and spinal cord perfusion gradient (DISTAL P_{Ao} - ICP) during aortic clamping (Kaplan et al., 1995).

It has been believed that CSFD may restore spinal cord blood flow by decompressing spinal compartment syndrome caused by spinal cord edema in relation to ischemia-reperfusion injury (Safi et al., 1997) (Fig. 8). This speculation is supported by the clinical consequence that delayed-onset paraplegia could be successfully reversed by reducing CSF pressure (Cheung et al., 2002).

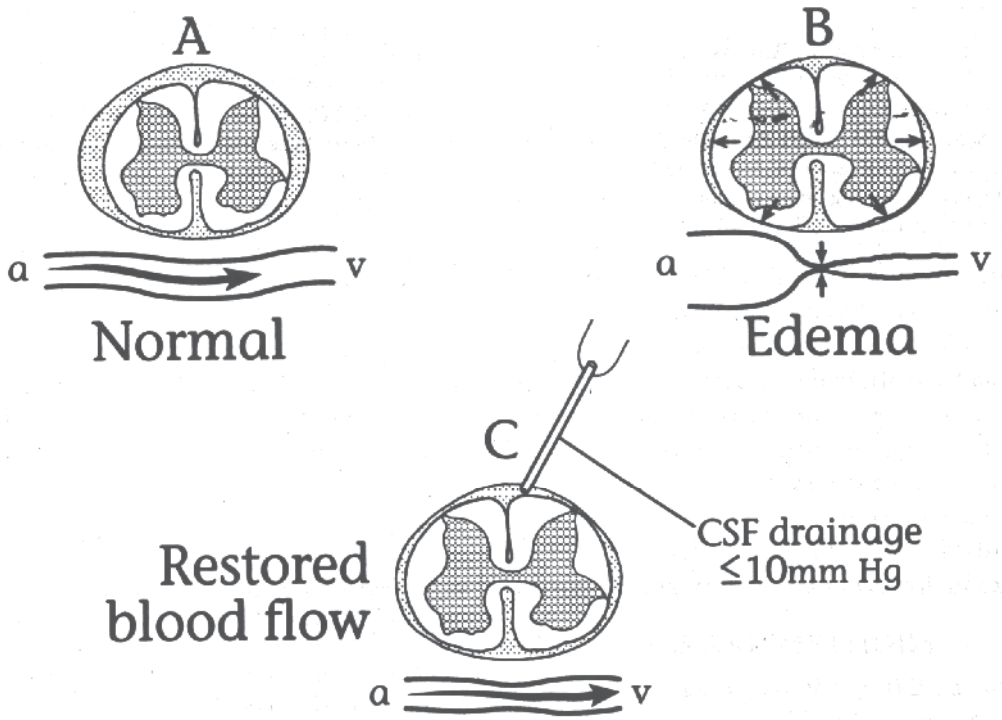

Fig. 8. Speculated mechanism of beneficial effect of cerebrospinal fluid drainage on spinal cord injury (Safi et al., 1997).

2.3.3 Role of cerebrospinal fluid drainage in ischemia-reperfusion injury

On the other hand, it has been well known that ischemia-reperfusion injury mediates some negative neurotrophic substances. Indeed, we showed that pro- and anti-inflammatory cytokines were generated in the rabbit spinal cord after ischemic SCI and they were clearly reversed by 21-aminosteroids (lazaroids) (Kunihara et al., 2000). Thus we have speculated that another key role of CSFD might be removal of negative neurotrophic substances. Actually, we revealed pro-inflammatory cytokines and S-100β protein were predominantly generated in CSF than in serum after TAAA repair and their levels were more pronounced and prolonged in patients with SCI (Kunihara et al., 2001, Kuniharat et al., 2001) (Fig. 9, 10). Moreover, CSF levels of excitatory amino acids in patients with postoperative SCI was significantly higher that those in patients without SCI. These elevated CSF levels of excitatory amino acids could be significantly antagonized by intraoperative continuous intravenous administration of naloxone (Kunihara et al., 2004) (Fig. 11).

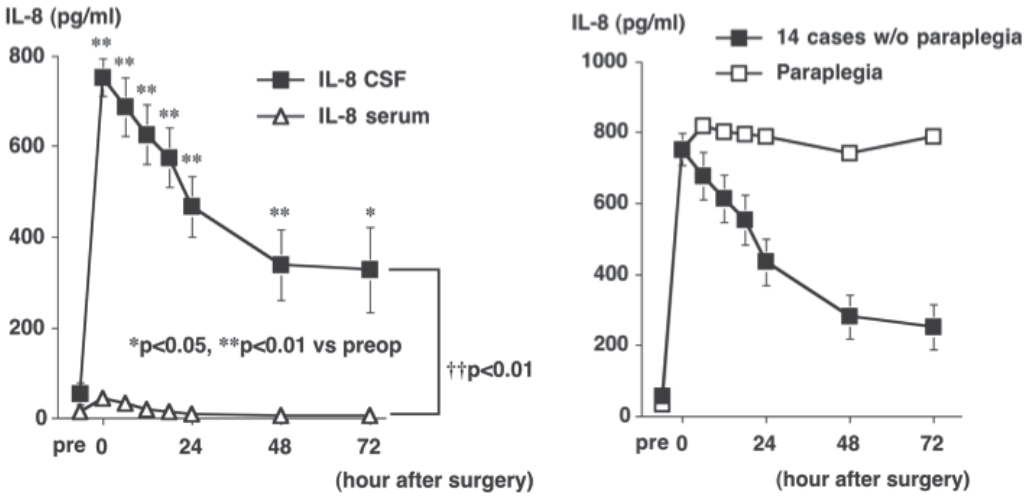

Fig. 9. Changes in serum and cerebrospinal fluid (CSF) interleukin-8 (IL-8) levels in overall patients (left). Changes in CSF IL-8 levels in patients with or without (w/o) paraplegia (right). (Kunihara et al., 2001)

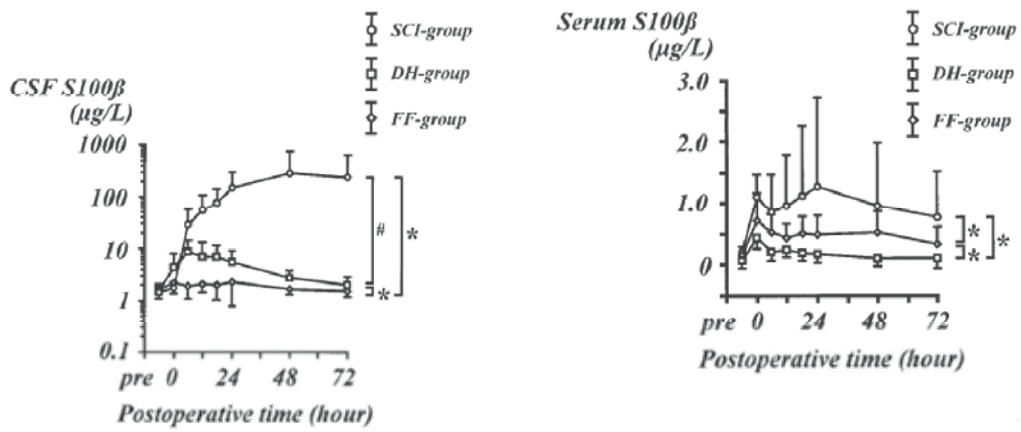

Fig. 10. Postoperative time course of S-100β protenin levels in the serum and CSF (Kunihara et al., 2001).

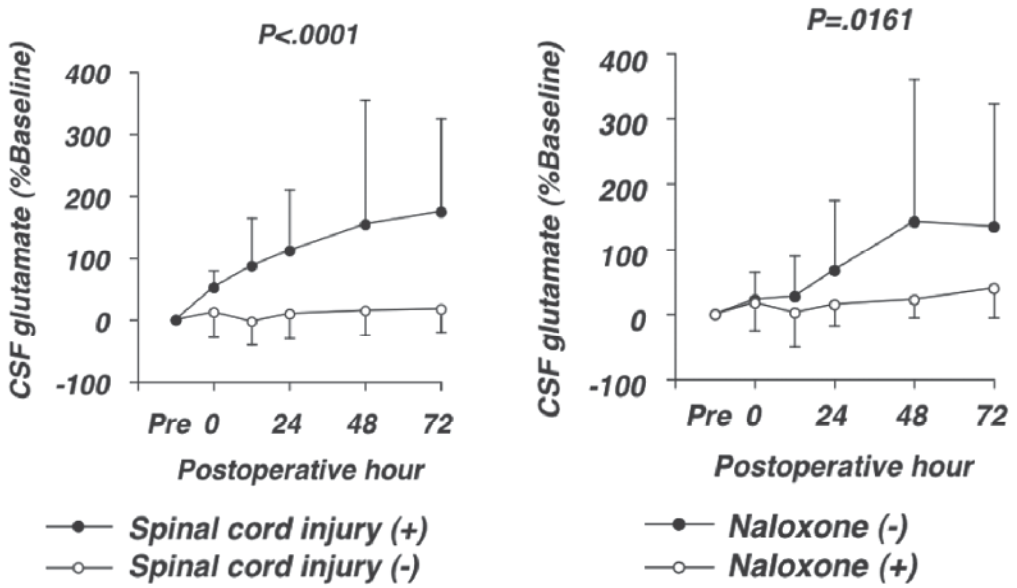

Fig. 11. Postoperative time course of CSF glutamete levels (Kunihara et al., 2004).

2.3.4 Pharmacological intervention

2.3.4.1 Naloxone hydrochloride

Numerous pharmacological interventions have been tried to attenuate postoperative SCI, however, no compound has become popular for a wide standardized clinical use. Above all, naloxone, the opiate antagonist, has gained increased attention since a report by Acher and associates was published in 1994, as described before (Acher et al., 1994). In general, excessive synaptic accumulation of excitatory amino acids during ischemia is associated with neuronal cell damage, which is mediated through overactivation of their receptors (i.e. N-methyl-D-aspartate receptor) followed by excessive influx of calcium. It has been shown that high concentration of naloxone attenuates N-methyl-D-aspartate-mediated neurotoxicity in an animal model (Kim et al., 1987). Clinically, Acher and his colleagues disclosed that the addition of naloxone resulted in a 30% reduction in the SCI rate (Acher et al., 2010). The important findings of our study that CSF excitatory amino acids were significantly suppressed by naloxone up to 72 hours after TAAA repair may have great implication because neurotoxicity mediated by excitatory amino acids is supposed to be a late-onset process (Nakamura et al., 1994) (Fig. 11). Therefore Acher and his colleagues recommended intravenous continuous administration of naloxone up to 48 hours postoperatively (Acher et al., 2010). We have experienced no side effect of naloxone at a rate of 1μg/kg/h even at postoperative period.

2.3.4.2 Other glutamate inhibitors

With the same mechanism, beneficial effects of other glutamate antagonists have been reported. Rokkas and his colleagues reported that Dextrorphan, a noncompetitive N-methyl-D-aspartate receptorantagonist, inhibited the release of excitatory amino acids in the spinal cord during ischemia (Rokkas et al., 1994). However, this agent is no longer used

clinically because of an unfavorable tolerance profile (Albers et al., 1995, Rokkas & Kouchoukos, 2001). Instead, other antiglutamate compounds such as Riluzole (Lang-Lazdunski et al., 2000), Memantine (Ehrlich et al., 1999), MK-801 (Cho et al., 2005) or Magnesium sulfate (Lang-Lazdunski et al., 2000) have been evaluated to have a neuroprotective effect after ischemia reperfusion of the spinal cord, although further evaluation should be necessary for their wide clinical use.

2.3.4.3 Steroid

In the early 1980's, beneficial effects of intravenous methylprednisolone (30 mg/kg) on experimental SCI have been confirmed (Hall & Braughler, 1982, Braughler & Hall, 1983, Laschinger et al., 1984). It has been believed that steroid act as cellular and lysosomal membrane stabilizers. Since the Second National Acute Spinal Cord Injury Study reported in 1990 that methylprednisolone improved neurologic recovery after acute SCI when it was given in the first eight hours, methylprednisolone has become a clinical mainstay in the treatment of acute SCI (Bracken et al. 1990). In the field of aortic surgery, methylprednisolone has been given in many institutions with various dosages (7 mg/kg: kouchoukus et al., 2003, 30 mg/kg: Hollier et al., 1992, Acher C. 2010) although its effect is still controversial. We have routinely administered 1g methylprednisolone intravenously prior to aortic cross-clamping and another 1g into CPB circuit (Kunihara et al., 2004). A drawback of steroid use such as postoperative hyperglycemia, disadvantageous to spinal cord protection, should be aggressively normalized. Recently, a new series of 21-aminosteroids (i.e. Lazaroids) have emerged as remarkable protective compounds against various ischemia-reperfusion injury model through the inhibition of irondependent lipid peroxidation (Sasaki et al., 1996, Holzgrefe et al., 1990, Johnson & Lefer, 1990). As was written above, these agents have also been shown beneficial effects of attenuating postischemic SCI (Fowl et al., 1990, Kunihara et al., 2000). Further examination will be required for clinical application.

2.3.4.4 Vasodilators

The other beneficial mechanisms against postischemic SCI include enhancing collateral blood flow to the jeopardized spinal cord. Systemic administration of vasodilators (i.e. nitroprusside) has been believed to decrease spinal cord perfusion pressure by reducing distal aortic pressure and increasing cerebrospinal fluid pressure, thus it should be avoided or combination with CSFD is recommended (Shine & Nugent, 1990, Marini et al., 1997). On the other hand, local use (i.e. intrathecal) of vasodilators can avoid reducing distal aortic pressure, thus may be beneficial for spinal cord protection. Svensson and his colleagues administered papaverine intrathecally and showed significant increase in spinal cord blood flow (Svensson 2005) and significant reduction of SCI clinically (Svensson et al., 1998) (Figure 12).

Prostaglandin E1 (PGE1) has also emerged as one of the promising compounds to enhance collateral blood flow to the spinal cord (Grabitz et al., 1993), however, it has also a dilemma to reduce distal aortic pressure. To avoid PGE1-induced hypotension in clinical use, Alprostadil, PGE1 incorporated in lipid microspheres to minimize metabolization and inactivation in the lung (Yone et al., 1999), has been examined to have the beneficial effect on ischemic SCI. In an experimental spinal cord ischemia model, we detected beneficial pharmacological effect of intravenous Alprostadil on the spinal cord oxygenation using

near-infrared spectrophotometry, which was not detected by spinal cord evoked potentials (Figure 13) (Kunihara et al., 2008). Thus Alprostadil can be given systemically, which may facilitate intraoperative management.

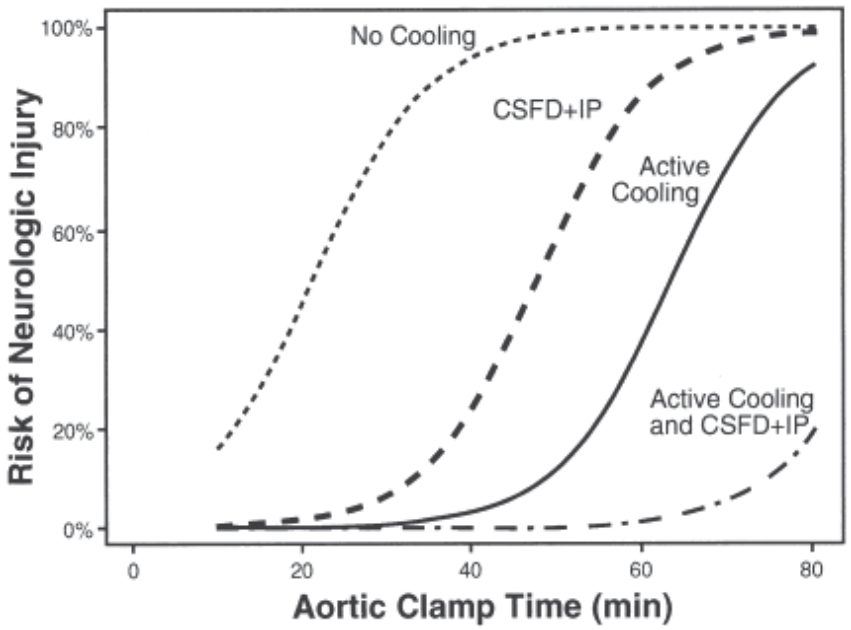

Fig. 12. Risk of spinal cord injury according to aortic cross-clamp time with no cooling or papaverine. cerebrospinal fluid drainage with intrathecal papaverine (CSFD+IP), active cooling with the combination. (Svensson et al., 1998)

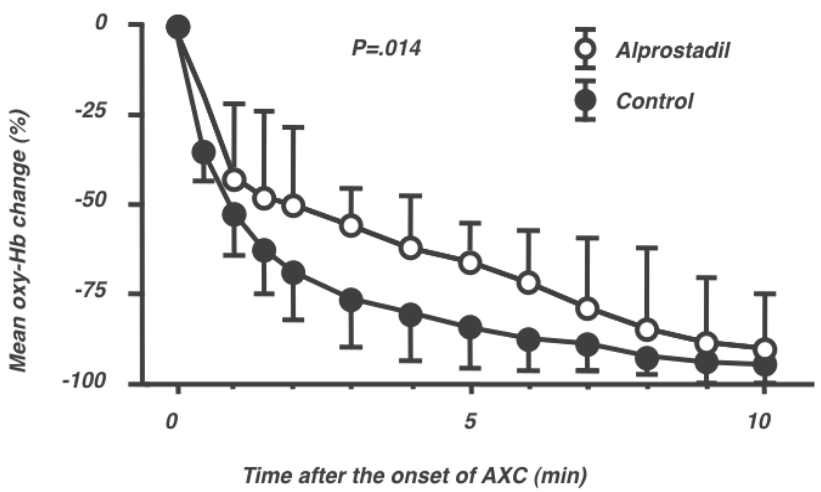

Fig. 13. Time course of mean %change of oxygenated hemoglobin (oxy-Hb) in the spinal cord measured by near-infrared spectrophotometry. AXC: aortic cross-clamping. (Kunihara et al., 2008)

2.3.4.5 Other drugs

Other numerous promising pharmacological interventions such as superoxide dismutase (Agee et al., 1991), allopurinol (Qayumi et al., 1994), calcium-channel blockers (Schittek et al., 1992), Adenosine (Seibel t al., 1993) or Adenosine A2A agonist (ATL-146e) (Reece et al., 2004) have been tested. We have seriously published beneficial effects of nicorandil (an adenosine triphosphate-sensitive potassium channel opener) (Wakamatsu et al., 2001), immunophilin ligands FK506 or cyclosporine A (Tachibana et al., 2005) on transient spinal cord ischemia in rabbits. However, their protective effects on SCI seem still controversial and may require further evaluations.

3. Clinical results

With a better appreciation and understanding of the mechanisms and pathophysiology of SCI and with many clinical evidences the neurological outcomes after TAAA repair have dramatically improved. Table 3 illustrated postoperative SCI stratified by the extent of aortic involvement reported from institutions with large case volume.

Author	Year	Cases	Crawford/Safi's classification					Total	DAP
			I	II	III	IV	V		
Svensson	1993	1509	15%	31%	7%	4%		16%	17%
Safi	2003	1004	0.5%	10.7%	6.0%	0.7%	2.0%	3.6%	73.8%
Jacobs	2006	112	0%	4.2%					100%
Coselli	2007	2286	3.3%	6.3%	2.6%	1.4%		3.8%	39.8%
Conrad/Cambria*	2007	455	9.1%	14.5%	11.6%	2.9%		9.5%	8%
Acher	2008	516	6.9%	15.8%	3.8%	0%		6.8%	no
Zoli/Griepp	2010	305	2.5%	11.5%	3.9%	2.2%		4.6%	95%

Table 3. Spinal cord injury after thoracoabdominal aortic aneurysm repair stratified by the extent of aortic involvement reported from institutions with large case volume. DAP: distal aortic perfusion. Conrad/Cambria*: only major paraplegia is demonstrated.

In spite of a contemporary and multidisciplinary approach with large experience, type II TAAA is still associated with high incidence of SCI as shown in table 3. Using a multivariate analysis, many authors have also emphasized that type II TAAA emerges as an independent predictor for postoperative SCI (Safi et al., 2005, Conrad et al., 2007, Schepens et al., 2009, Acher et al., 2010). Other preoperative independent predictors for postoperative SCI have been reported such as an emergent setting (Conrad et al., 2007, Acher 2010), aortic dissection (Schepens et al., 2009, Acher 2010), age >75 years old (Schepens et al., 2009), and renal dysfunction (Safi et al., 2005, 2008).

4. Conclusions

The underlying mechanisms and pathophysiology of SCI after TAAA repair may be multifactorial. We have thus reviewed the latest information with regard to this issue in this

manuscript briefly. From these considerable experimental and clinical evidences, we have evolved our strategy for TAAA repair over time as shown in Table 4 (Shiiya et al., 2005). We believe this may be the best and reasonable approach to prevent SCI after TAAA repair at the present moment. Nonetheless, Jacobs and his colleagues described; "despite all available measures, complete prevention of paraplegia in type II aneurysms seems to be unrealistic" (Jacobs et al. 2006). Our multidisciplinary effort to prevent SCI after extensive TAAA repair may be never ending

Mild hypothermic distal aortic perfusion or deep hypothermic circulatory arrest
Multi-segmental sequential clamping
Preoperative identification of the Adamkiewicz artery and reimplantation of responsible intercostal arteries
Without information, reconstruction of the intercostal arteries at Th8-L1 left
Avoidance of steal phenomenon during reconstruction of the intercostal arteries
Electrophysiological monitoring of the spinal cord function
Cerebrospinal fluid drainage
Intravenous administration of naloxone and methylprednisolone.

Table 4. Our strategy to prevent spinal cord injury.

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This book considers diagnosis and treatment of abdominal and thoracic aortic aneurysms. It addresses vascular and cardiothoracic surgeons and interventional radiologists, but also anyone engaged in vascular medicine. The book focuses amongst other things on operations in the ascending aorta and the aortic arch. Surgical procedures in this area have received increasing attention in the last few years and have been subjected to several modifications. Especially the development of interventional radiological endovascular techniques that reduce the invasive nature of surgery as well as complication rates led to rapid advancements. Thoracoabdominal aortic aneurysm (TAAA) repair still remains a challenging operation since it necessitates extended exposure of the aorta and reimplantation of the vital aortic branches. Among possible postoperative complications, spinal cord injury (SCI) seems one of the most formidable morbidities. Strategies for TAAA repair and the best and most reasonable approach to prevent SCI after TAAA repair are presented.

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