From the Klinik für Herz- und Gefäßchirurgie

(Director: Professor Jochen Cremer)

at the University Medical Center Schleswig-Holstein, Campus Kiel

at Kiel University

Perioperative risk factors for mortality in patients with acute type A aortic dissection: A retrospective analysis of a center experience over 15 years

Dissertation

to acquire the doctoral degree (Dr. med)

at the Faculty of Medicine

at Kiel University

presented by

Mohamed Salem

from

Kairo, Ägypten

Kiel, 2019

1st Reviewer: Herr Professor Dr. med. Assad Haneya

2nd Reviewer: Herr Professor Dr. med. Thomas Herdegen

Date of oral examination: 22.12.2020

Approved for printing, Kiel,

Signed: Pr. Doz. Dr. Gunnar Elke

(Chairperson of the Examination Committee)

List of Contents

List of Figures

List of Tables

List of Abbreviation

Acute aortic dissection (AAD)

Acute aortic type A dissection (AAAD)

Cardiopulmonary bypass (CPB)

Computed tomography (CT)

Ejection fraction (EF)

Electrocardiogram (ECG)

Intensive care unit (ICU)

Magnetic resonance tomography (MRT)

Moderate hypothermic circulatory arrest (MHCA)

Transesophageal echocardiography (TEE)

Transthoracic echocardiography (TTE)

1. Introduction

1.1 Definition

Acute aortic dissection (AAD) is an acute fatal disease with sudden onset in which an intimal tear occurs with extensive hemorrhage formation between the innermost and outermost layers of the aortic wall (Figure 1). By divergence of the elastic fibers within the lamina media, a kind of canal called the false lumen originates next to the regular lumen of the aorta. This false lumen leads to narrowing of the true aortic lumen and can lead to occlusion of blood supply of different body organ when extended proximally or distally until it reaches the femoral arteries (Figure 2). That tear can also spread towards external lamina of the aortic wall weakening the aortic wall and can lead to aortic rupture within a short time. The presence of the false channel in the ascending aorta can result in regurgitation of the aortic valve as well as myocardial infarction. High grade of aortic valve regurgitation can lead to sudden symptoms of heart failure.

An acute aortic dissection usually causes severe sharp pain in the chest wall and usually extends to the upper back. The pain may develop towards the abdomen. In some cases, they might be no symptoms or flu-like symptoms. The prevalence of aortic dissection ranges from 0.2 to 0.8 per 100,000 per year or roughly 2,000 to 3,000 new cases per year (Halstead JC et al. 2007, Di Luozzo G et al. 2007).

Acute aortic type A dissection (AAAD) reaches its peak in the 5th to the 6th decade (Meszaros I et al. 2000, Hagan PG et al. 2000). The mortality rate of untreated AAAD increases by 1% to 2% every hour after its onset, and it reaches up to 50% in the first 48 hours. The disease mainly affects men more than women (88% vs. 12%) (Meharwal, Z. et al. 2006).

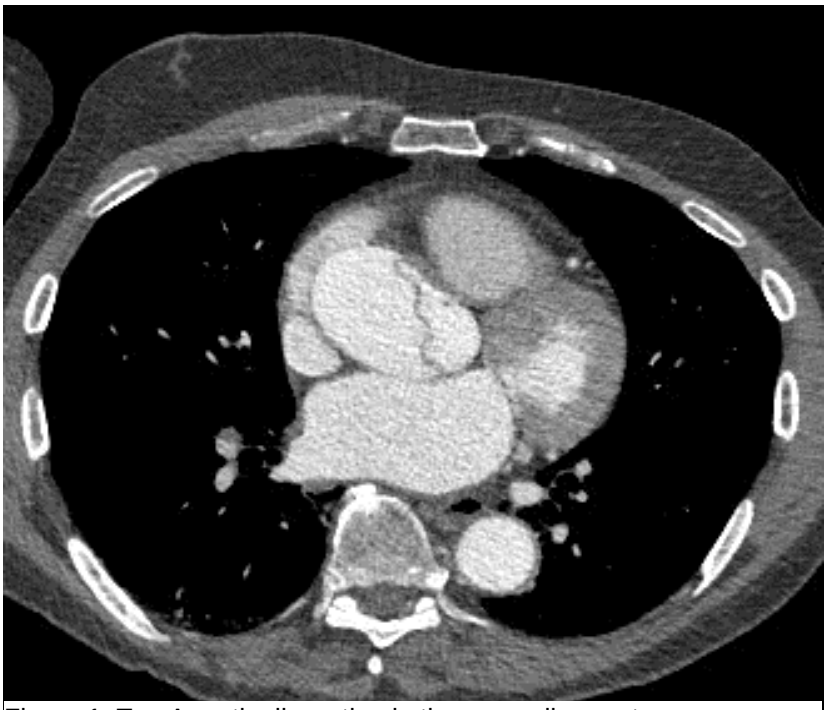

Figure 1. Typ A aortic dissection in the ascending aorta

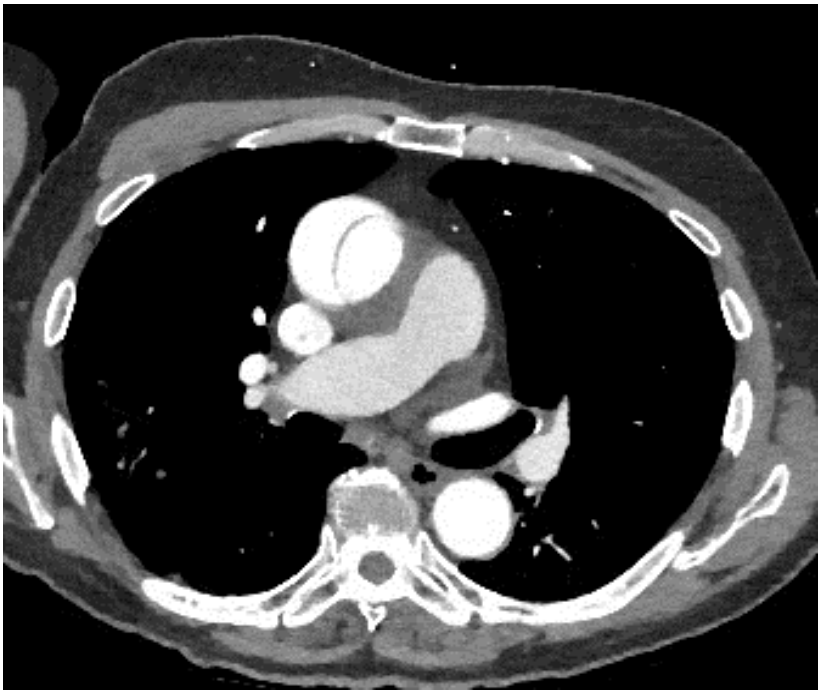

Figure 2. Diagram showing false and true lumen in patients with AAAD

1.2 Etiology

Aortic dissection is a result of an intimal tear that extends into the media of the aortic wall. Elastin, collagen, and smooth muscle breakdown in the lamina media are common cystic medial degeneration which predisposes to intimal disruption. Bleeding from the vasa vasorum also leads to AAAD. Inherited conditions with connective tissue disorders such as Marfan syndrome, Ehlers-Danlos-syndrome, osteogenesis imperfecta, and cystic median necrosis Erdheim-Gsell lead to a weakening of the media, thus predisposing to aortic dissection. Bicuspid aortic valve may be associated with a nonspecific connective tissue disorder and could be a predisposing factor for aortic dissection (Marta Moreno-Torres et al. 2018). Aortic atherosclerosis, inflammatory or traumatic conditions as well as infections, may also predispose to aneurysmal degeneration and dissection. Hypertension is also mentioned as an additional factor, especially when combined with hyperlipidemia and arteriosclerosis leading to a reduction of strength and elasticity of the aortic wall by an endoluminal atheromatous plaque (Prêtre and of Segesser 1997). Moreover, hypercholesterolemia and smoking are considered risk factors for AAAD. Other predisposing factors for aortic dissection represent congenital abnormalities such as aortic coarctation (in Turner syndrome), aortic valve stenosis, and aortic hypoplasia (Loren F. et al. 2010).

Moreover, high progesterone levels during pregnancy leading to softening of connective tissue. Endocrine disorders such as hyperparathyroidism and hypothyroidism are more common in patients suffering from aortic dissections (Robert S. et al. 2011).

Iatrogenic AAAD is a rare condition due to aortic manipulation associated with cardiac surgery or interventional procedures (Jonker FH. et al. 2010)

1.3 Pathophysiology

The initial event occurs through an intimal tear with subsequent degeneration of the medial layer of the aortic wall. The tears cause the blood to enter the aortic wall and create a second channel next to the actual true lumen extending distally or proximally and creating a false lumen. This false lumen usually forms between the middle and outer thirds of the aortic media. In the further course, a so-called "reentry" can arise, through which the bloodstream in the wrong lumen gets back connected to the true lumen. As the dissection extends, the blood flow through the false lumen can occlude the arterial branches of the aorta, including the coronary, brachiocephalic, renal, visceral, or iliac vessels till reaching the femoral arteries. The occlusion occurs when the line of dissection intersects the vessel origin with the progression of hematoma into the vessel wall. A dynamic occlusion of side branches could also occur when the true lumen collapses during diastole, and the intimal flap obstructs the outflow of the ostium of the branch vessel. Total flow occlusion can lead to end-organ ischemia (Hiratzka LF et al. 2010)

The intimal tears of dissection most commonly occur just within the first 2 centimeters above the aortic valve or opposite the departure of the brachiocephalic trunk in the aortic arch or distal to the exit of the subclavian artery (Nathan DP et al. 2011, Cachovan, M. et al.1999)

Extension of the dissection results from antegrade and retrograde blood flow. The retrograde blood flow in the ascending aorta can lead to aortic incompetence by separating the aortic valve from the aortic root. Rupture of the remaining thin media layers may end fatally when it occurs within the pericardium with mortality rate reaches up to 90 % (Hach-Wunderle et al. 2001).

As an alternative theory for the pathogenesis of aortic dissection is the formation of intramural hematoma which may represent up to 30% of cases of acute aortic syndromes (Evangelista et al. 2003). It was firstly described by Krukenberg, where rupture of the vasovasorum into the aortic wall, resulting in hemorrhages formation into the media (Krukenberg et al. 1920). The knowledge behind the aortic intramural hematoma is still limited, as it was obtained from case reports and limited studies (Sawhney et al. 2001). An intramural hematoma is difficult to be differentiated from the classic aortic dissection. It is characterized initially by the absence of intimal tear, which in progress could be

transformed into a tear in the intima resulting in acute aortic dissection. Intramural hematoma may progress into the layers of the aortic wall, leading to rupture or pseudoaneurysm formation. Predisposing risk factors and presenting symptoms are similar to classic aortic dissection. However, males and females seem to be equally affected (Pawan D, Patel, et al. 2008).

1.4 Classification

According to the time of onset, one classification divided the aortic dissections into hyperacute (<24 hours duration), acute (2–7 days), subacute (8–30 days), and chronic (>30 days) (Lech. et al. 2017). Another classification defined the acute aortic dissection if the diagnosis is within the first 14 days after the occurrence of complaints, where chronic aortic dissection occurs if the diagnosis exceeds two weeks after onset of complaints (Pawan D. Patel et al. 2008). Hirst et al reported that about 74% of untreated patients with aortic dissection died during the first two weeks (Hirst et al. 1958)

Nowadays there is mainly two classifications of aortic dissection according to localization and extent:

- The DeBakey classification (DeBakey, McCollum et al. 1982)

- The Stanford classification (Daily et al. 1970).

The DeBakey classification contains 3 types of aortic dissection, in which the third type is subdivided into two subtypes:

- Type I: the dissection originates in the ascending aorta and propagates at least to the aortic arch and may involve the descending thoracic aorta till iliac vessels.
- Type II: the dissection originates and remains limited to the ascending aorta.
- Type III: The dissections involve only the descending aorta, where the ascending aorta is not affected.
    a. Typ III a: if the dissection is limited only to the thoracic aorta.
    b. Typ III b: If the dissection extends beyond the diaphragm.

Type I and II dissections are commonly referred to as proximal or ascending dissection while Type III dissections are known as descending or distal dissections.

The Stanford classification classifies the aortic dissection as follows:

- Type A: It includes any dissection involving the ascending aorta. The dissection originates in the ascending aorta, mostly within a few centimeters of the aortic valve and may spread to the aortic arch and into the descending aorta until it reaches the iliac and femoral vessels.

- Type B: The dissection originates distal to the origin of the left subclavian artery and only involves the descending aorta.

The Stanford classification system considered only the presence or absence of involvement of the ascending aorta. Moreover, it does not account for involvement limited only to the aortic arch. Thus a non-A/ non-B aortic dissection was introduced by Von Segesser et al. (1994), which refer only to the dissection involving the aortic arch.

Type I and Type II dissections of the DeBakey system correspond to Stanford Type A dissection, whereas Type III of DeBakey classification corresponds to Stanford Type B.

Penetrating atherosclerotic ulcer and intramural hematoma of the aorta led to a new classification scheme by the European Cardiology, which is composed of five classes as follows (Erbel et al. 2001):

- Class 1: classic aortic dissection with an intimal flap
- Class 2: intramural hematoma/hemorrhage
- Class 3: discrete dissection without hematoma
- Class 4: penetrating atherosclerotic ulcer
- Class 5: iatrogenic or traumatic dissection

1.5 Clinical symptoms and signs

Acute aortic dissection is known with a circadian rhythm demonstrated with peak incidence during the early morning hours, between 6:00 a.m. and noon (Hagan et al. 2000). A seasonal variation with the highest rate of aortic dissection observed during the winter was noted by Mehta et al. (2002). The International Registry of Acute Aortic Dissection (IRAD) findings demonstrated that patients typically present with severe sudden onset of chest pain. Approximately 95% of patients reported pain, with 85% of recalling an abrupt onset of the pain. The type of pain is usually sharp in 64% of patient and less frequently as a tearing, ripping, or stabbing pain in approximately 51 % of patient with maximal intensity at onset (Hagan et al. 2000; Svensson et al. 1992; Slater et al. 1976). Proximal dissection of ascending aorta is usually associated with chest pain while distal dissection is associated with back or intrascapular pain (Hagan et al. 2000). The pain can be differentiated by its maximal intensity at onset from the pain of myocardial infarction, which increases gradually with the progression of the infarct. Moreover, the pain travels accompanying the progression of the dissection membrane. A painless aortic dissection has been reported in some cases of chronic dissection with a duration of more than 14 days (Erbel, Alfonso et al. 2001).Severe aortic regurgitation could lead to symptoms of cardiac failure. Cardiac tamponade may lead to hypotension and syncope. Syncope could be also a result of prolonged severe pain or due to obstruction of cerebral vessels or activation of aortic baroreceptors (Erbel, Alfonso et al. 2001).

Propagation of the dissection membrane could result in symptoms and signs of ischemia in various organs such as myocardial infarction, stroke (20 %; Erbel, Alfonso et al. 2001)and kidney failure (Erbel, Alfonso et al. 2001), if the true lumen or the opening of aortic side branches was occluded by false lumen. Either pulse fluctuations or the complete absence of the pulse at the femoral arteries can be found according to the extent of dissection membrane (Goudot et al. 1999). Absence or lack of the classical symptoms and signs of aortic dissection in old patients should not reduce clinical suspicion. The elderly patient, more the 70 years old may have a clinical presentation with acute aortic type A dissection which may differ from that of younger patients (Mehta et al. 2002b). Acute aortic dissection in elderly patients may be atypical with no abrupt onset of chest or back pain. Moreover, the murmur of aortic insufficiency may be less common in older

Patients. Patients younger than 40 years old were less likely to have hypertension or atherosclerosis. Young patients have more frequently bicuspid aortic valve, Marfan syndrome or underwent more aortic valve replacement surgery (Januzzi et al. 2004).

Although high fever is uncommon in patients with aortic dissection, it can be caused by the release of pyrogenic substances from the torn aortic wall (Erbel, Alfonso et al. 2001). Low hemoglobin level is usually associated with bleeding and hematoma. High creatinine, lactate dehydrogenase level, acute phase proteins as well as Leukocytosis are usually found by AAAD (Anagnostopoulos et al. 1972, Erbel, Alfonso et al. 2001)

Presence of persistent abdominal pain with elevation of acute phase proteins and an increase of lactate dehydrogenase are common indicators of involvement of the coeliac and mesenteric artery (Slater et al. 1983, Fann et al. 1990, Erbel, Alfonso et al. 2001).

1.6 Diagnosis

1.6.1 Physical examination

Physical examination is important in the diagnosis of acute aortic dissection. It could help to recognize the origin and the extent of the dissection. Hypertension was presented in 49% of patients In the International Registry of Acute Aortic Dissection (Hagan et al. 2000). The presence of hypertension may refer to a distal involvement of the aorta. The International Registry of Acute Aortic Dissection indicated that hypertension might be present in 70% of patients with distal dissection and in 36% of proximal dissections. In contrast, hypotension is more frequently in proximal dissection than distal dissection (Hagan et al. 2000).

Absence or weakness of pulse in carotid, femoral, or brachial arteries, is present in approximately 30% to 50% of patients with aortic dissection and it could be associated with an increased mortality rate as well as neurological and renal complications (Bossone et al. 2002). The pulse deficit could be transient due to changing the position of the dissected membrane.

Neurological complications such as loss of consciousness and paresis occur in up to 40% of patients with proximal aortic dissection (Svensson et al. 1992, Fann et al. 1990). AAAD could be accompanied by rare signs and symptoms such as vocal cord paralysis due to compression of the left recurrent laryngeal nerve, haematemesis or hemoptysis due to haemorrhage into the bronchial tree or perforation into the oesophagus (Roth et al. 1978), compression of upper airway, Horner's syndrome due to compression of the superior cervical sympathetic ganglion, superior vena cava syndrome (Spritzer et al. 1973), or signs of mesenteric or renal ischemia (Hagan et al. 2000, Yamada et al. 1995, Spittell et al. 1993). Leriche's syndrome with loss of pulse in both legs could be a result of total obstruction of the iliac bifurcation. If only one of the subclavian artery is involved by the dissection, this could result in a difference in the systolic blood pressure between both arms. A diastolic murmur over the right sternal border due to severe aortic regurgitation may be present in about half of the patients with proximal aortic dissection (Slater et al. 1976, Hagan et al. 2000, Spittell et al. 1993). Cardiac Tamponade could result from rupture of the dissection into the pericardial sac. Presence of pleural effusions with

diminished breath sounds may be caused by rupture of the aorta into the pleural space, where the left side is more common than the right side.

Studies showed that up to 30% of patients with aortic dissection are initially diagnosed to have other conditions such as acute coronary syndromes or pulmonary embolism (Alfonso et al. 1997, Svensson et al. 1992, Spittell et al. 1993). Aortic dissection should be directly suspected in the differential diagnosis for any patient presenting with back pain accompanied with neurological symptoms, unexplained syncope or acute onset of congestive heart failure, and acute ischemia of extremities or viscera, even when the typical chest pain of aortic dissection is not present. An imaging procedure needs to be carried out as soon as possible to either exclude or to confirm the presence of dissection.

1.6.2 Diagnostics

An acute aortic dissection is a life-threatening situation in most cases. The aim of all diagnostic procedures in aortic dissection is the rapid and secure diagnosis to enable fast and effective therapy. In addition to the history elevation of symptoms, the physical examination is of high importance. The focus here is mainly on pulse status and neurological deficits. Various imaging modalities are available for the diagnosis of aortic dissection such as the transesophageal echocardiography, computed tomography (CT), coronary angiography and magnetic resonance imaging (MRI).

Mostly by suspicion of aortic dissection, computed tomography is usually performed. CT is helpful for more accurate surgical planning. The sensitivity of computed tomography is between 83 - 100% and the specificity between 87 - 100%. In addition to the non-invasiveness, the relatively short time is considered an advantage of computed tomography in the diagnosis of aortic dissection. As a disadvantage, the inability to show any existing aortic insufficiency as well as the use of contrast medium in patients with aortic dissection with reduced kidney function is considered to be critical (Cigarroa, Isselbacher et al. 1993).

Magnetic resonance imaging is another method for diagnosis of AAAD. It produces high contrast images without using nephrotoxic intravenous dye. It evaluates the entire aorta, the involvement of the branch vessel, and associated complications of aortic dissection. Magnetic resonance has the highest sensitivity and specificity for detecting all classes of aortic dissection with the exception of class III lesions (Erbelet al. 2001). The sensitivity of magnetic resonance imaging can reach up to between 100% (Pohost et al. 2000). Magnetic resonance image is particularly helpful in identifying aortic dissection in patients with preexisting aortic disease. It is contraindicated in patients with metallic hardware and maybe not available in emergent situations. In addition, intubated unstable patients who require intensive hemodynamic monitoring devices may not be ideal for MRI.

However, the transesophageal echocardiography (TEE) is the fastest method for the diagnosis. TEE has a sensibility of up to 99% and specificity up to 100 % (Cigarroa, Isselbacher et al. 1993). During transesophageal echocardiography, blood pressure must

be continuously monitored to prevent any increase in blood pressure and thus the risk of early aortic rupture. Compared to all other methods of investigation, the TEE still has a great advantage that it can be done very quickly to diagnose the AAAD (Nienaber, Spielmann et al. 1992). The TEE can be performed on the bed of the patient and the patient does not have to be driven to CT or MRI. It allows the diagnosis of the free-floating intimal lamella and duplication of the aortic wall echoes as a sign of dissection, as well as a possible existing aortic insufficiency and blood flow in the wrong lumen (Cigarroa, Isselbacher et al. 1993).

In addition to the TEE, there is a second possibility of ultrasound examination using transthoracic echocardiography (TTE). However, the use of TTE is limited because the TTE only has a sensitivity of 59 - 85% and has a specificity of 63 - 96%. In addition, their use is limited by the adipose patient and possibly existing emphysema, small intercostal spaces and also through mechanical ventilation (Cigarroa, Isselbacher et al. 1993). Moreover, dissections in the descending part of the aorta could not be recognized (Treasure and Raphael et al. 1991).

A chest x-ray is mostly the first diagnostic and may suggest dissection but lacks specificity for the diagnosis of aortic dissection. A chest x-ray will be abnormal in 60–90% of cases of aortic dissection, but a normal chest x-ray is not sufficient to rule out aortic dissection (Hagan et al. 2000). A previous study demonstrated that a chest x-ray has a sensitivity of 67% and a specificity of 70% for aortic dissection. The classic radiological sign characteristic of aortic dissection are mediastinal broadening, double contours of the aortic arch, pleural effusions, as well as size differences between ascending and descending aorta (von Kodolitsch et al. 2004).

To verify the diagnosis, the investigator should carry further investigation. The electrocardiogram (ECG) is used to exclude acute myocardial infarction. This misdiagnosis becomes common because the main symptoms of dissection and infarction are the same or at least strongly similar. Approximately 20% of patients with type A dissection have electrocardiogram evidence of myocardial ischemia or infarction (Erbel et al. 2001). However, the dissection often involves the coronary arteries or the dissection membrane at least partially relocates the ostium of the coronary artery. Thus both

diseases are often present together (Bachet, Goudot et al. 1999). However, one-third of all patients with coronary involvement have a normal ECG (Erbel, Alfonso et al. 2001).

Aortography is another tool in the diagnosis of aortic dissection. Various direct and indirect signs of dissection can be recognized angiographically. Direct signs are the identification of the double lumen and the intima lamellae. All indirect signs could indicate a dissection but are not proof of it. These indirect signs include the compression of the true lumen of the aorta due to the false lumen, the thickening of the aortic wall, abnormalities in the area of the aortic arch branches and the proof of aortic insufficiency (Anagnostopoulos, Prabhakar et al. 1972; Cigarroa, Isselbacher et al. 1993). Advantages of aortography are the assessment of outgoing branches, the coronary arteries, aortic insufficiency, and thrombosis of the false lumen. Certainly, a disadvantage is that this method is an invasive procedure. Due to the use of contrast medium, the procedure is difficult in patients with hemorrhagic shock or renal failure (Anagnostopoulos et al. 1972; Treasure et al. 1991; Cigarroa, Isselbacher et al. 1993)

1.7 Therapy

Nowadays, it is widely accepted that acute type A dissection should be surgically treated. Surgical treatment of aortic dissection have several goals; to stabilize the dissection membrane and prevent the progression or rupture of the aorta, to eliminate the compression of the aorta and its outgoing branches as well as treatment of a possibly existing condition such as aortic valve insufficiency. Surgery should be done on an emergency basis to avoid the aortic rupture in the Pericardium.

Drug therapy for AAAD in a follow-up study from Dalen et al showed a low survival rate (22%) when compared with survival rate after surgical repair (64%). (Dalen, Alpert et al. 1974).

Surgical therapy of AAAD is carried out using various techniques after the excision of the dissected intimal tear to close the entrance of the false lumen. A Dacron graft is usually used to replace the ascending aorta. The aortic valve is replaced if it is presented with dysfunction. Several surgical techniques are used to repair AAAD including Bentall, valve-sparing operations and Elephant Trunk procedures.

Bentall technique is the most commonly used technique for treating AAAD involving the aortic valve and its root (Hagl et al. 2003). It was first described by Bentall and De Bono (Bentall, H. et al. 1968).

Valve-sparing operations such as David and Yacoub procedures offering the possibility of preserving or reconstructing the native (natural) aortic valve. The openings of the coronary arteries are cut together with a patch from the aorta and later integrated into the new prosthesis (Yacoub et al. 1998; David and Feindel, 1992).

The Elephant trunk technique was first described by Borst and colleagues in 1983 (Borst et al. 1999). It is used in AAAD with extensive aortic damage requiring two-stage repairs of ascending aorta and/or arch as well as the descending aorta in which the graft is introduced in the lumen of the descending aorta to close the false lumen and preventing the blood flow in the false lumen through the entry site.

1.8 The aim of the study

The aim of the study was to analyze the pre-, intra- and postoperative variables that influence the postoperative outcomes and survival rates after surgical repair of AAAD. The evaluation included all data of patients who underwent surgery for AAAD in moderate hypothermic circulatory arrest (MHCA) between 2001 and 2016 in the university hospital of Schleswig-Holstein, Campus Kiel. Therefore, we compared between 2 groups of patients; those who survived 30 days postoperative (30-d survivors) and those who didn't survive 30 days postoperatively (30-d deceased).

The preoperative analysis included relevant factors such as age, gender, EuroSCORE, and the clinical picture at the hospital admission. Intraoperative factors were initially the performed surgical technique, the duration of surgery, circulatory arrest times, bypass times on the heart-lung machine, and transfusion of blood products. Postoperative evaluation included parameters like the amount of blood loss, exposure to redo operation, duration of ventilation, renal function and onset of dialysis, infection, and onset of neurological complications. The collected data were statistically analyzed and compared with the findings and results obtained in the literature.

2. Method and Patients

2.1 Method

Data were supplied from the institution's database and from medical records. The study protocol was approved by the local Ethics Committee. The patient records were analyzed retrospectively. An evaluation sheet was created according to various established previous studies in our center on AAAD. The analysis sheet was divided into three main sections for preoperative, intraoperative and postoperative parameters with 30 days follow up.

a- The preoperative part of the sheet included personal information such as age, gender, body mass index, weight and height of the patient as well as some risk factors for cardiac diseases such as smoking history, hypercholesterolemia, diabetes mellitus, hypertension, positive family history, and renal insufficiency. Preoperative status included also the shock condition, neurological status, ECG changes and the ejection fraction as well as various laboratory parameters and preoperative medication. All related cardiac findings are documented. This included the degree of aortic insufficiency or stenosis, mitral regurgitation, the presence of a preoperative operation, aortic aneurysm and its size, or aortic valve abnormality

b- The intraoperative part included the surgical technique, the size of prostheses, duration, and extent of surgery, the duration of Heart-lung machine, cardiac arrest, and the used technique for arterial and venous cannulation. All additive cardiac procedures such as CABG or isolated aortic valve replacement as well as transfusion of blood products (such as fresh frozen plasma and red blood cells) were documented.

c- The postoperative part included the degree of patient condition stability after the end of surgery and admission at ICU, the amount of bleeding and exposure to redo surgery, the absolute duration of ventilation, neurological deficits, renal insufficiency, onset and duration of dialysis, sepsis and pulmonary infection, wound healing disorders, 7-days and 30-days mortality as well as causes of death.

2.2 Patient Population

A retrospective analysis included 344 consecutive patients who underwent surgical repair for AAAD in moderate hypothermic circulatory arrest (MHCA) (20-24 °C) between 2001 and 2016. Patients were divided into two groups: those who survived 30 days postoperative (30-d survivors group; 82 %) and those who didn't survive 30 days postoperatively (30-d deceased; 18 %).

2.3 Patient Management

Patients with acute type A aortic dissections were operated on an emergency basis and transported directly to the operating room. The diagnosis was confirmed preoperatively by a non-contrast computed tomography (CT-scan) to detect the exact location and extension of the dissection membrane. Patients with confirmed AAAD bypass the emergency department and intensive care unit. If possible, patients are investigated for neurological symptoms and signs and any findings are documented on the admission sheet for further use. Transesophageal echocardiography is performed intraoperatively under general anesthesia.

2.4 Surgical procedure

In our center, all patients underwent corrective surgery performed by senior surgeons. A standard median sternotomy followed by T-shaped pericardiotomy was performed under general anesthesia. The pericardium was attached to the outer thorax with sutures. Any existing hemopericardium was aspirated. The cardiopulmonary bypass (CPB) was performed with retrograde femoral artery cannulation or directly in the aorta. Since 2010, CPB was established using antegrade transatrial cannulation of the left ventricle (Schöneich et al. 2019) as an alternative for arterial cannulation under moderate hypothermic circulatory arrest (MHCA) with core temperature between 20-24 °C. Venous drainage is performed either through direct cannulation of the right atrium or through the femoral vein with a cannula that extends to the right atrium. The extent of femoral vein cannula was controlled with TEE. Before connecting to the extracorporeal circulation, the patient was heparinized. A standard retrograde injection of cold blood cardioplegic solution for myocardial protection was performed in all case. Antegrade cerebral perfusion with oxygenated cold blood (18°C) was introduced through a balloon catheter inserted in

arch vessels with flow pressure of 50-60 mmHg. The distal extent of aortic repair was depended on the extent of the dissected intimal tear. The aortic repair was limited to the ascending aorta just proximal to the innominate artery if the intimal tear does not extend or originated from the aortic arch, otherwise, the aortic repair extended to hemiarch or total arch replacement in cases where the intimal tear extended to the aortic arch, with re-implantation of head and neck arteries. In several cases, an elephant trunk was also introduced in the proximal descending aorta. Before performing the anastomosis, the intimal tears at the proximal and distal aortic stumps were repaired using Gelatin-resorcinol-formaldehyde biologic glue and the edges were compressed by flattened forceps circularly for 5 minutes. The stumps were then sharply circularly cut to achieve a clean edge. After insertion of the perfusion cannula directly into the graft, CPB restarted again slowly. The proximal aortic repair was performed either through isolated supra-coronary ascending aorta replacement or either through Bentall-Op, David-Op or with extra isolated aortic valve replacement with preservation of aortic root in case of associated isolated aortic valve disease. After the establishment of the proximal anastomosis, residual air was removed by restarting retrograde perfusion via the venous cannula. Continuous CO2 insufflation was used as a standard for the cardiac de-airing. Transoesophageal echocardiography was performed to control the presence of residual air in the left side of the heart. During the rewarming phase with warm blood, other procedures, if required (such as CABG), were performed. External pacemaker electrodes were sutured externally to the myocardium due to high risk of cardiac arrest and arrhythmia after hypothermic circulatory arrest. The wires were led to the outside and could be used to connect an external pacemaker if needed.

After careful control for bleeding in the operating area, drains were placed in the heart cavity and guided to the outside, and then the sternum was closed again with wire cerclages from cranial to caudal, followed by subcutaneous and intracutaneous skin suture. The patient was transferred to the intensive care unit for postoperative monitoring.

2.5 Statistical analysis

Statistical analysis was performed using the SPSS 18.0 software (SPSS, Chicago, IL, U.S.A.). Normality of continuous variables was assessed by Kolmogorow-Smirnow test. Values of continuous data are presented as mean ± standard deviation or as median with range or interquartile range when appropriate and compared by unpaired t-test, whereas not-normally distributed continuous were compared by Mann-Whitney U test. Categorical variables are displayed as frequency distributions (n) and simple percentages (%). Univariate comparison between the groups for categorical variables was made using the Chi2-test and the Fisher's exact test when appropriate. Statistical significance was considered when $p \leq 0.05$. Logistic regression analysis was used to determine the hazards ratio (HR) of risk factors upon the 30-days survival time. The task of logistic regression is to derive from a pool of predictor the variables that have significant influence within a multivariate model and to estimate their coefficients.

3. Results

The evaluation included 344 patients, two groups were compared; survival group (30-d survivors) included 282 patients (82%) and non-survivors group (30-d deceased) with 62 patients (18%) who died during the observation period. Female gender was represented by 93 patients (33.0%) of the survivor and 24 patients (38.7%) of nonsurvivors. Old patients with age more than or equal 75 years were 44 patient (15.6%) vs. 19 (30.6%). A different distribution between the two groups occurred with the attribute to shock state: Thus, only 19 patients (= 6.8%) in the survivors group were in a shock state, whereas in the deceased group there were 8 patients (=13.3%) (p = 0.111).

There were also differences between the two groups with regard to the available data for measured ejection fraction (EF); in the survivors group, the average EF was 65% (55;70), while in the deceased group it was 60% (34;66) (p=0.024).
There were no statistically significant differences in terms of aortic insufficiency grade; in the survivors group, 108 patients (= 43.9%) had aortic insufficiency vs. 13 patients (= 24.5%) in the deceased group.

The preoperative analysis reported the risk factors for AAAD as shown in table 1. Arterial hypertension was the most common risk factor for AAAD presented in 72.4% of the study population, followed by the presence of aortic valve insufficiency in 40.5%. Patients with an aortic aneurysm represent 31.5% of the study population. 24% of patients were current smokers and 18.9% had an old history of smoking. Average body mass index was 26.3 with 14.4% suffered from hyperlipoproteinemia and 6.1 % suffered from type 2 diabetes mellitus. 13.6 % of patients are admitted with chronic renal insufficiency, with 2.1% receiving renal replacement therapy. Patients who did not survive the 30-day mortality were significantly older (65.7±12.0 years vs. 62.0±12.5 years; p=0.034) with significantly higher Euro-SCORE II [15.4% (6.6;23.0) vs. 4.63%(2.78;9.88) p<0.001). Moreover, patients older than 75 years had a higher mortality rate reached up to 30.6%. The calcified ascending aorta was found significantly higher in nonsurvivors than survivors (6.5% vs. 1.4%, p=0.039). Coronary heart diseases were found in 18.3% of the study population, in which non-survivors suffered from a significantly higher percentage of coronary heart diseases when compared with survivors (35.8% vs. 14.9%, p<0.001). Non-survivors group

was more likely to suffer from preoperative cardiogenic shock than survivors (13.3% vs. 6.8%; p=0.111).

Table 1. Demographic and clinical characteristics of the study population

	Total	**30-d survivors**	**30-d deceased**	**P-value**
No. of surgical procedures	344 (100%)	282 (82 %)	62 (18 %)	
Age, years	62.7±12.4 63.1 (54.1;72.1)	62.0±12.5 62.6 (54.2;70.9)	65.7±12.0 68.9 (53.7;75.3)	**0.034**
Age ≥ 75 years	63 (18.3%)	44 (15.6%)	19 (30.6%)	0.006
Female	117 (34.0%)	93 (33.0%)	24 (38.7%)	0.388
EuroSCORE II (%)	5.49 (3.06;12.99)	4.63 (2.78;9.88)	15.4 (6.6;23.0)	**<0.001**
Body mass index, kg/m2	26.3 (24.0;28.6)	26.3 (24.1;28.6)	26.3 (23.8;28.6)	0.934
Arterial hypertension	244 (72.4%)	210 (75.0%)	34 (59.6%)	**0.018**
Pulmonary hypertension	3 (0.9%)	3 (1.1%)	0 (0.0%)	1.000
Type 2 diabetes mellitus	20 (6.1%)	14 (5.1%)	6 (10.9%)	0.118
Diabetic neuropathy	1 (0.3%)	0 (0.0%)	1 (1.9%)	0.164
Hyperlipoproteinaemia	47 (14.4%)	38 (13.9%)	9 (16.7%)	0.599
Chronic renal failure/insufficiency	45 (13.6%)	37 (13.5%)	8 (14.5%)	0.830
Renal replacement therapy	7 (2.1%)	6 (2.2%)	1 (1.8%)	1.000
COPD	20 (6.0%)	14 (5.0%)	6 (10.7%)	0.119
Smoking	69 (24.0%)	61 (25.3%)	8 (17.4%)	0.249
Previous smoking	54 (18.9%)	48 (20.0%)	6 (13.3%)	0.295
Coronary heart disease	60 (18.3%)	41 (14.9%)	19 (35.8%)	**<0.001**
Previous PCI	23 (6.9%)	14 (5.0%)	9 (16.4%)	**0.006**
Previous CABG	12 (3.6%)	6 (2.1%)	6 (10.9%)	**0.006**
Peripheral vascular disease	14 (4.2%)	9 (3.2%)	5 (9.3%)	0.059
LVEF (%)	61 (54;70)	65 (55;70)	60 (34;66)	**0.024**
Marfan syndrome	9 (2.7%)	6 (2.2%)	3 (5.0%)	0.202
Aortic aneurysm	108 (31.5%)	93 (33.1%)	15 (24.2%)	0.172
Diameter of aneurysm, mm	50 (45;60)	50 (45;60)	60 (45;70)	0.177
Calcific aortic disease	8 (2.3%)	4 (1.4%)	4 (6.5%)	**0.039**
Bicuspid aortic valve	9 (2.4%)	8 (2.6%)	1 (1.6%)	1.000
Aortic valve insufficiency	121 (40.5%)	108 (43.9%)	13 (24.5%)	
Neurological deficits	69 (20.5%)	53 (19.0%)	16 (27.6%)	0.140
CPR (48h)	30 (8.8%)	11 (3.9%)	19 (31.1%)	**<0.001**
Transfer from intensive care unit	41 (12.1%)	27 (9.7%)	14 (23.0%)	**0.004**
Intubated	37 (10.9%)	19 (6.8%)	18 (29.5%)	**<0.001**
Cardiogenic shock	27 (7.9%)	19 (6.8%)	8 (13.3%)	0.111

COPD: Chronic obstructive pulmonary disease, PCI: Percutaneous coronary intervention, CABG: Coronary artery bypass grafting, LVEF: The left ventricular ejection fraction, CPR: Cardiopulmonary resuscitation

Intraoperatively (table 2), the length of surgery was significantly shorter in survivors [275 min (227;331) vs. 319 min (239;410); p=0.004]. Survivors had significantly shorter cardiopulmonary bypass times [163min (134; 206) vs. 198 min (150;245); p=0.001]. However, the hypothermic circulatory arrest time was similar between both groups [33 min (25;45) 33 min (27;49); p=0.368]. Moreover, survivors received a significantly fewer number of transfused packed red blood cells than non-survivors [3 units (0;6) vs. 5 units (2;10); p= <0.001]. Non-survivors underwent total arch replacement more frequently than survivors (19.4% vs. 12.8%; p=0.175). The surgical procedure was extended to include coronary artery bypass surgery more frequently in non-survivors (25.0% vs. 6.4%; p<0.001)

The site of arterial cannulation was evenly distributed in both groups: the arterial limb of the heart and lung machine (HLM) was connected in the survivors group vs. the non-survivors group as follows: the femoral artery in 56 (21.3%) vs.13 (27.7%), the ascending aorta in 69 (26.2%) vs. 10 (21.3%), the aortic arch in 11 (4.2%) vs. 2 (4.3%), the subclavian artery in 1 (0.4%) vs. 0 (0.0%), the apex of heart in 4 (1.5%) vs. 1 (2.1%) and transatrial cannulation of the left ventricle via the pulmonary vein in 122 (46.4%) vs. 21 (44.7%).

Table 2. Intraoperative data.

	Total	**30-d survivors**	**30-d deceased**	**P-value**
Length of surgery, min	280 (227;346)	275 (227;331)	319 (239;410)	**0.004**
Cardiopulmonary bypass time, min	168 (136;214)	163 (134;206)	198 (150;245)	**0.001**
Cross-clamp time, min	91 (70;127)	89 (68;126)	101 (77;135)	0.114
Circulatory arrest, min	33 (26;46)	33 (25;45)	33 (27;49)	0.368
Number of packed red blood cells	3.5 (0;6)	3 (0;6)	5 (2;10)	**<0.001**
Number of platelet concentrate	2 (1;2)	2 (1;2)	2 (2;3)	**0.001**
Supracoronary aortic replacement	171 (49.7%)	138 (48.9%)	33 (53.2%)	0.541
Partial arch replacement	70 (20.3%)	62 (22.0%)	8 (12.9%)	0.108
Total arch replacement	48 (14.0%)	36 (12.8%)	12 (19.4%)	0.175
CABG	33 (9.7%)	18 (6.4%)	15 (25.0%)	**<0.001**
Aortic valve replacement	55 (16.0%)	44 (15.6%)	11 (18.0%)	0.639
Arterial cannulation				
-Femoral artery	69 (22.3%)	56 (21.3%)	13 (27.7%)	
-Ascending aorta	79 (25.5%)	69 (26.2%)	10 (21.3%)	
-Aortic arch	13 (4.2%)	11 (4.2%)	2 (4.3%)	
-Subclavian artery	1 (0.3%)	1 (0.4%)	0 (0.0%)	
-Apex	5 (1.6%)	4 (1.5%)	1 (2.1%)	
-Transatrial cannulation of left ventricle	143 (46.1%)	122 (46.4%)	21 (44.7%)	
Venous cannulation				
-Right atrium	298 (96.1%)	256 (97.0%)	42 (91.3%)	
-Bicaval	4 (1.3%)	4 (1.5%)	0 (0.0%)	
-Femoral vein	8 (2.6%)	4 (1.5%)	4 (8.7%)	

CABG: Coronary artery bypass grafting

Postoperatively, 15.6% patients of survivors were re-explorated due to bleeding and/or tamponade vs. 24.6% patients of non-survivors. There was also a significant difference in the incidence of neurological deficits and stroke; 12.1% of survivors suffer from paresis, paralysis, sensorimotor failure or cerebral infarctions vs. 27.9% patients in non-survivors (p=0.002). The incidence of AKI (55.9% vs. 15.2%; p<0.001) and sepsis (18.0% vs. 2.1%; p<0.001) were also significantly higher among non-survivors. The 30-day mortality rate

for all patients was 18%, in which 56.6% of causes of deaths were due to cardiac failure and 32.3% were due to multi-organ failure.

Table 3. Postoperative data and outcomes

	Total	**30-d survivors**	**30-d deceased**	**P-value**
AKI KDIGO	76 (22.4%)	42(15.0%)	34 (57.6%)	**<0.001**
New –onset of hemodialysis	76 (22.3%)	43 (15.2%)	33 (55.9%)	**<0.001**
48 h-drainage loss, ml	825 (488;1250)	750 (450;1200)	1010 (600;1775)	**0.040**
Number of packed red blood cells,	2 (0;7)	2 (0;6)	4 (0;12)	0.074
Number of fresh frozen plasma	0 (0;4)	0 (0;4)	4 (0;12)	**0.001**
Number of platelet concentrate	0 (0;1)	0 (0;1)	0.5 (0;3)	**0.001**
TIA/Stroke (CT-proofed)	51 (14.9%)	34 (12.1%)	17 (27.9%)	**0.002**
CPR	28 (8.2%)	17 (6.1%)	11 (18.0%)	**0.002**
Bacteriaemia/sepsis	17 (5.0%)	6 (2.1%)	11 (18.0%)	**<0.001**
Rethoracotomy	59 (17.2%)	44 (15.6%)	15 (24.6%)	0.092
30 d Hospital Mortality	62 (18%)	0 (0%)	62 (100%)	**<0.001**
Cardiac death	36 (56.3%)	0 (0.0%)	35 (56.5%)	

AKI: Acute kidney injury, KDIGO: kidney Disease: Improving Global Outcomes, TIA: Transient Ischemic Attack, CPR: Cardiopulmonary resuscitation

The multivariate logistic regression analysis confirmed that older age (>75years), previous cardiac surgery, preoperative CPR, intraoperative transfusion and postoperative AKI were statistically significant independent risk factors for 30-d-mortality ($p<0.05$). (Table 4)

Table 4. The multivariate logistic regression analysis for the 30-d-mortality in AAAD

	Odds ratio	**CI**	**P-value**
Age > 75 years	3.194	1.133-9.005	**0.028**
CPR	5.111	1.626-16069	**0.005**
Bypass time	1.010	1.004-1.015	**0.001**
AKI KDIGO	10.134	4.412-23.274	**<0.001**

AKI: Acute kidney injury, KDIGO: kidney Disease: Improving Global Outcomes, CPR: Cardiopulmonary resuscitation

4. Discussion

Acute aortic dissection is an event of sudden onset with an acutely life-threatening clinical picture in which the intimal tear with extensive hemorrhage occurs between the innermost and outermost layers of the aortic wall.

In recent decades, there was a huge improvement in the rapid diagnosis of AAAD, patient emergency transport, perioperative and operative management. Advanced cerebral protection (Ueda Y et al. 1990, Kazui T et al. 1992), and antegrade arterial perfusion is used nowadays to achieve organs perfusion (David TE et al. 2001). However, its hospital mortality rate is still high; it ranges between 20% and 30% (Ehrlich MP et al. 2001, Moon MR et al. 2001). In the present evaluation, 18% of patients with AAAD who underwent surgical repair of AAAD died. A nationwide inpatient survey in the USA with a cohort of 3,013 patients with thoracic or thoracoabdominal dissection that underwent aortic repair of dissection between 1995 and 2003 showed a similar hospital mortality rate of 26% to our study (Knipp BS et al. 2007).

In the current study, we analyzed the perioperative risk factors that lead to postoperative mortality after surgical repair of AAAD.

According to the current analysis, AAAD affects 66% of men and 34% of women. Meherwal et al. found also a higher incidence of AAAD in men (Meharwal et al. 2006). Arterial hypertension was the most common risk factor in those patients affected by AAAD, presented in 72.4% in patients, followed by the presence of aortic valve insufficiency in 40.5% of patients. The presence of aortic aneurysm was also a risk factor found in 31.5% of the study population. Either 24% of patients with AAAD were current smokers or 18.9% had an old history of smoking. Presence of chronic renal insufficiency was in 13.6 % of patients, with 2.1% receiving renal replacement therapy. Patients who did not survive had a higher Euro-SCORE II than survivors [15.4% (6.6; 23.0) vs. 4.63% (2.78; 9.88) $p<0.001$).

Our large analysis showed that mortality within 30 days postoperative was higher in patients older than 75 years (30.6%). Moreover, non-survivors were significantly older than survivors (65.7±12.0 years vs. 62.0±12.5 years; $p=0.034$). Previous studies showed that increased age is associated with increased short- and long-term mortality rates after

surgical repair of AAAD (Mehta RH et al. 2002, Tan ME et al. 2005). Trimarchi et al. confirmed that increased age (70 years or more) is an independent predictor of in-hospital mortality [(38.2% (> 70 y) vs 26.0% (<70); p<.0001, odds ratio 1.73)] (Trimarchi S. et al. 2010).

Calcified ascending aorta or aortic arch may predispose to AAAD. Formation of an aortic hematoma within the aortic media may also occur with penetrating ulceration of atherosclerotic aortic plaques, leading to weakening of the aortic wall and thus results in AAAD. The development of aortic imaging techniques played a major rule to understand the origin of the penetrating aortic ulcer of the calcified aorta (Demers et al. 2004). Penetrating aortic ulcers are associated with extensive atherosclerotic disease (Pawan D. et al. 2008). About 40% to 50% of penetrating atherosclerotic ulcers show signs of extension and progression to aortic rupture or less commonly classical aortic dissection. Moreover, they are usually located in the descending thoracic aorta (Ganaha et al. 2002). O'Gara stated that although the progression of penetrating ulceration of atherosclerotic aortic plaques may result in aortic dissection, it rarely involves the side branch vessels (O'Gara et al. 1995). The calcified ascending aorta is considered not an only a risk factor that predisposes to AAAD, but it could be a possible risk factor for postoperative mortality. In our current study, we found that patients with 30days mortality suffered from more significant calcified ascending aorta than survivors (6.5% vs. 1.4%, p=0.039).

Presence of preoperative cardiac shock condition is considered a risk factor for postoperative mortality. Nonsurvivors group was more likely to suffer from preoperative cardiac shock than survivors (13.3% vs. 6.8%; p=0.111). This feature was also identified by Trimarchi et al. as a risk factor for postoperative mortality (Trimarchi, Nienaber et al. 2005).

Myocardial ischemia is considered one of the most frequent complications after AAAD due to obstruction of coronary blood flow resulting in coronary malperfusion. Usually, the right coronary artery is involved leading to acute inferior myocardial infarction (Rampoldi V et al. 2007, Kawahito K et al. 2003). Those studies went in line with our study, stated that coronary malperfusion is considered a risk factor associated with higher mortality rates. Our study showed that patients with coronary artery disease who underwent CABG

due to myocardial ischemia or infarct associated with surgical repair of AAAD suffer from high mortality rate than those without CABG (25.0% in non-survivors vs. 6.4% in survivors; p<0.001). Acute myocardial infarction could also delay the diagnosis of AAAD due to the similarity in symptoms as well as increase the risk of bleeding due to its treatment with antiplatelet and anticoagulant drugs.

The intraoperative analysis showed that the extension of surgical repair of AAAD distally involving total arch replacement (22.0% in non-survivors vs. 12.9% in survivors) increased the mortality rate in comparison with those patients who underwent only replacement of ascending aorta or even receive a slightly extended surgical repair including partial replacement of aortic arch. Lansmann et al. stated that the extension of intimal teal either in aortic arch or more distally increased the in-hospital mortality rate (Lansmann et al. 1999). Extension of surgical repair led to a longer duration of the operation. The evaluation confirmed that the non-survivor group had a significantly longer duration of surgery than the survivor group (319 minutes vs. 275 minutes; p=0.004). Furthermore, the need for a prolonged cardiopulmonary bypass time intraoperatively worsened the postoperative outcome. Non-survivors had significantly longer cardiopulmonary bypass times when compared to the survivor group [198 min (150; 245) vs. 163 min (134; 206); p=0.001]. Those finding was confirmed by Sun et al. (Sun, Liu et al. 2006).

Cerebral tissue protection was a major concern in our surgical repair of AAAD due to the high susceptibility of nerve tissue to ischemic adverse effects. Neurologic manifestations included transient ischemic attack, spinal cord ischemia or hypoxic encephalopathy. These manifestations could be attributed to the malperfusion of brain and nervous tissue supporting blood vessels. Syncope is considered one of the common manifestations in aortic dissection either due to acute hypotension caused by cardiac tamponade following aortic rupture or due to cerebral vessel obstruction by the dissected membrane or following activation of cerebral baroreceptors. Thus, AAAD should be considered in the differential diagnosis in cases of unexplained syncope (Trimarchi, Nienaber et al. 2005). To avoid or minimize the brain tissue damage and postoperative neurological adverse outcome, we used MHCA in our surgical repair. According to various studies, systemic hypothermia reduces the metabolic tissue rate and consequently protects the brain during

cardiac and aortic surgeries. Hypothermia was categorized by Yan et al. into four groups according to physiological findings, mild (34–28°C), moderate (28–20°C), deep (20–14°C) and profound (<14°C) (Yan TD et al. 2012). Ehrlich et al. stated that cerebral metabolic activity and its oxygen consumption can be reduced to 50% of baseline values at 28°C, 19% at 18°C and down to 11% at 8°C (ultra-profound hypothermia). This study demonstrated that cooling to temperatures below 18 degrees °C in pigs can achieve greater metabolic suppression although it may be associated with loss of cerebral autoregulation (Ehrlich MP et al. 2002). Several studies suggested that prolonged deep HCA more than 20 minutes reduce the postoperative cognitive function of life in patients undergoing thoracic aortic surgery and was associated with poorer neurological outcomes, necessitating the usage of antegrade (ACP) and retrograde cerebral perfusion (RCP) (Immer FF et al. 2004). However, ACP is not always easy to apply and cannot be used in patients with an extended dissected aortic membrane in brachiocephalic or carotid arteries. RCP leads to inadequate neuroprotection due to the inability of precise estimation of perfusion volume (Perreas K et al. 2016).

We agreed with those experiences that recommend the isolated application of MHCA, due to its simplicity and ease of application especially if the time of circulatory arrest is not expected to be longer than the average (14-40 min) (Uysal S et al. 2012). In spite of those used protective techniques, 27.9 % of non-survivors groups suffered from neurological adverse effect in comparison to 12.1% in survivors groups (p=0.002). The occurrence of those postoperative neurological deficits was considered a negative predictor of the outcome of the AAAD.

Blood loss has already been identified as a risk factor for poor postoperative outcome (Kawahito, Adachi et al. 2001). It is known that the more extensive surgery is bounded with a higher risk of bleeding. Thus, the more extensive surgical repair of AAAD could be a risk for postoperative mortality. In our analysis, the amount of bleeding in the first 48 hours postoperative was significantly higher in nonsurvivors group (1010ml vs. 750ml; p=0.040). This could be also attributed to the fact that non-survivors receive more extensive surgical repair than the survivors.

As it is expected, Goossens et al. confirmed that morbidity and lethality of aortic dissection increase proportionally with rethoracotomy (Goossens et al. 1998). In our analysis the

non-survivor group suffered from more re-exploration due to bleeding and/or tamponade than the other group (24.6% vs.15.6%).

Renal failure is caused either due to hypotension or due to vascular compression by the false lumen of the dissected membrane. Anuria and renal failure are not a very common presentation until both renal arteries are occluded by the false lumen of the dissection (Brooke et al. 2012). In another retrospective study of all the cases presented to a center at Greece, renal failure or anuria was not the main common feature (Asouhidou I et al. 2009). However, preoperative renal failure in patients with AAAD was noted to be an independent predictor of mortality (Di Eusanio M et al. 2013). In our evaluation, renal failure was considered also as one of the predictors of adverse postoperative prognosis and mortality. Non-survivors suffered from renal failure approximately 3 times more than survivors. Also present of postoperative sepsis plays a major role in postoperative mortality. Patients in non-survivors group suffered significantly from sepsis nine times more than survivors (18.0% vs. 2.1%, $p<0.001$).

Various studies showed that old age, preoperative shock, the extent of aortic repair, length of operation, organ malperfusion as well as associated CABG are considered risk factors for hospital mortality among patients undergoing emergency surgical repair of AAAD (Crawford ES et al. 1992, Fann JI et al. 1995, Pansini S et al. 1998, Ehrlich M et al. 1998, Sabik JF et al. 2000, Neri E et al. 2001). We analyzed in our study the risk factors that lead to AAAD. Among those factors was the presence of arterial hypertension, aortic valve insufficiency, and aortic aneurysm, history of smoking, high body mass index as well as type 2 diabetes mellitus and chronic renal insufficiency. The multivariate logistic regression confirmed that older age, previous cardiac surgery, preoperative CPR, as well as intraoperative transfusion and postoperative AKI were statistically significant independent risk factors for death ($p<0.05$).

In spite of the high mortality rate after AAAD, especially in the elderly patient, surgical repair of AAAD still the treatment of choice. Although the mortality rate was higher in the elderly group, a study from the German Registry for Acute Aortic Dissection Type A on more than 2000 patients confirmed that age had no effect on postoperative stroke and

AKI rate (Rylski B et al. 2014). Piccardo et al. found that the less aggressive surgical approach is a key factor in reducing operative time and mortality (Piccardo A et al. 2013). We recommend, if possible, a less aggressively surgical repair in old patients, which considered safer and shorter in time than those operations where the surgical repair extends distally toward totally arch replacement.

5. Summary

Acute type A aortic dissection (AAAD) is associated with high mortality rate and frequent postoperative complications. This study was designed to evaluate perioperative risk factors for mortality in patients with AAAD.

Patients and methods

A retrospective analysis included 344 consecutive patients who underwent surgery for AAAD in moderate hypothermic circulatory arrest (20-24 C°) between 2001 and 2016.

Results

The 30-day mortality rate for all patients was 18%. Non-survivors were significantly older (65.7±12.0years vs.62.0±12.5 years; p=0.034) with significantly higher Euro-score II [15.4% (6.6;23.0) vs. 4.63% (2.78;9.88) p<0.001). Univariante analysis revealed several preoperative factors that were found to be statistically significant predictors for 30-day mortality: older age (>75years), coronary heart disease, previous cardiac surgery and preoperative cardiopulmonary resuscitation (CPR) (p<0.05). Intraoperatively, survivors had statistically shorter cardiopulmonary bypass times [163 min (134;206) vs. 198 min (150;245); p=0.001]. However, the hypothermic circulatory arrest time was similar between the groups. Postoperatively, the incidence of AKI (55.9% vs. 15.2%; p<0.001), stroke (27.9% vs. 12.1%; p=0.002) and sepsis (18.0% vs. 2.1%; p<0.001) were significantly higher among non-survivors. The multiple logistic regression confirmed that older age, previous cardiac surgery, preoperative CPR, intraoperative transfusion and postoperative AKI were statistically significant independent risk factors for death (p<0.05).

Conclusion

The current study suggested that AAAD remains associated with a high mortality rate. The reason for mortality and complications in patients undergoing surgical repair of AAAD was multifactorial, especially older age, previous cardiac surgery, preoperative CPR, transfusion, as well as postoperative AKI were considered risk factors for mortality.

References

Alfonso F, Almeria C, Fernandez-Ortiz A et al (1997). Aortic dissection occurring during coronary angioplasty: angiographic and transesophageal echocardiographic findings. Cathet Cardiovasc Diagn; 42: 412–5.

Anagnostopoulos, CE, M. J. S. Prabhakar et al. (1972). "Aortic dissection and aortic aneurysms." The American Journal of Cardiology 30: 263 - 273.

Asouhidou I, Asteri T, “Acute aortic dissection: be aware of misdiagnosis.” BMC research notes vol. 2 25. 20 Feb. 2009, doi:10.1186/1756-0500-2-25.

Bachet J, Goudot B, et al. (1988). "Replacement of the transverse aortic arch duringemergency operations for acute type A aortic dissection." The Journal of Thoracic andCardiovascular Surgery 96: 878 - 886.

Bachet J, Goudot B, et al. (1998). "Surgical treatment of the ascending aorta (20 years experience)." Chirurgie123(3): 229-237.

Bachet, J, Goudot B, et al. (1999). "Surgery for acute type a aortic dissection: The hospitalFoch experience (1977 - 1998)." The annals of thoracic surgery 67: 2006 - 2009.

Bentall H, De Bono A. (1968) A technique for complete replacement of the ascending aorta. Thorax 23(4): 338–339.

Borst HG. (1999) The elephant trunk operationin complex aortic disease. Curr Opin Cardiol 14(5): 427–431.

Bossone E, Rampoldi V, Nienaber, C.A, Trimarchi S, Ballotta A, Cooper J.V. et al. (2002). Usefulness of pulse deficit to predict in-hospital complications and mortality in patients with acutetype A aortic dissection. Am J Cardiol89 (7): 851–855.

Brooke V, Goswami S, Mohanty A, Kasi PM. Aortic dissection and renal failure in a patient with severe hypothyroidism. Case Rep Med. 2012;2012:842562.

Buja LM, Ali N, Fletcher RD, Roberts WC. Stenosis of theright pulmonary artery: a complication of acute dissectinganeurysm of the ascending aorta. Am Heart J 1972; 83: 89–92.

Cigarroa JE, Isselbacher EM, et al. (1993). "Diagnostic imaging in the evaluation ofsuspected aortic dissection: Old standards and new directions." New England Journalof Medicine 328: 35 - 44.

Crawford ES, Kirklin JW, Naftel DC, Svensson LG, CoselliJS, Safi HJ. Surgery for acute dissection of ascending aorta: should the arch be included? J Thorac Cardiovasc Surg 1992;104:46–59.

Daily PO, Trueblood HW, Stinson EB, Wuerflein RD and Shumway NE (1970) Management of acute aortic dissections. Ann Thorac Surg 10(3): 237–247.

Dalen JE,. Alpert JS, et al. (1974). "Dissection of the thoracic aorta: Medical or surgicaltherapy?" American Journal of Cardiology 34: 803 - 808.

David TE, Armstrong S, Ivanov J, Barnard S. Surgery for acute type A aortic dissection. Ann ThoracSurg 1999;67:1999–2001.

David TE, Feindel CM. (1992) An aortic valve-sparing operation for patients with aortic incompetence and aneurysm of the ascending aorta. J Thorac Cardiovasc Surg 103(4): 617–621.

Demers P, Miller DC, Mitchell RS, Kee ST, Chagonjian L. and Dake MD. (2004) Stent-graft repair of penetrating atherosclerotic ulcers in the descending thoracic aorta: mid-term results. Ann Thorac Surg 77(1): 81–86.

Di Eusanio M, Trimarchi S, Patel HJ, et al. (2013) Clinical presentation, management, and short-term outcome of patients with type A acute dissection complicated by mesenteric malperfusion: observations from the International Registry of Acute Aortic Dissection. J Thorac Cardiovasc Surg.Feb;145(2):385-390.e1. doi: 10.1016/ j.jtcvs. 2012.01.042.

Di Luozzo G, Tannous HJ, Ellozy SH et al. (2007). Delayed repair of acute type A aortic dissection in a patient with gastrointestinal bleeding and pulse deficit. Ann Thorac Surg. 2007 Dec;84(6):2097-9.

Ehrlich M, Fang WC, Grabenwoger M, Cartes-Zumelzu F, Wolner E, Havel M. Perioerative risk factors for mortality in patients with acute type A aortic dissection. Circulation1998;98:II-294–8.

Ehrlich MP, Ergin MA, McCullough JN, Lansman SL, Galla JD, Bodian CA, et al. Results of immediate surgical treatment of all acute type A dissections. Circulation.2000;102(19 Suppl. 3):III248-52.

Ehrlich MP, McCullough JN, Zhang N, Weisz DJ, Juvonen T, Bodian CA et al. Effect of hypothermia on cerebral blood flow and metabolism in the pig. Ann ThoracSurg 2002;73:191–7.

Erbel R, Alfonso F, Boileau C, Dirsch O, Eber B, Haverich A. et al. (2001) Diagnosis and management of aortic dissection. Eur Heart J 22(18): 1642–1681.

Evangelista A, Dominguez R, Sebastia C, Salas A, Permanyer-Miralda G, Avegliano G. et al. (2003) Long-term follow-up of aortic intramural hematoma: predictors of outcome. Circulation 108(5): 583–589.

Fann JI, Sarris GE, Mitchell RS et al. Treatment of patients with aortic dissection presenting with peripheral vascular complications. Ann Surg 1990; 212: 705–13.

Fann JI, Smith JA, Miller DC, et al. Surgical management of aortic dissection during a 30-year period. Circulation 1995;92 (Suppl II):II-113–21.

Ganaha F, Miller DC, Sugimoto K, Do YS, Minamiguchi H, Saito H. et al. (2002) Prognosis of aortic intramural hematoma with and without penetrating atherosclerotic ulcer: a clinical and radiological analysis. Circulation 106(3): 342–348.

Goossens D, M. Schepens, et al. (1998). "Predictors of hospital mortality in type A aorticdissections: a retrospective analysis of 148 consecutive surgical patients." The journalof thoracic and cardiovascular surgery 6(1): 76-80.

Griepp RB, Stinson EB, Hollingsworth JF, Buehler D. Prosthetic replacement of the aortic arch. J Thorac. Cardiovasc. Surg 1975;70:1051–63.

Hach-Wunderle, V. (2001). Arterielle Gefäßkrankheiten. Basislehrbuch Innere Medizin. J. Braun and H. Renz-Polster. München - Jena, Urban & Fischer Verlag: 212 - 215.

Hagan PG, Nienaber CA, Isselbacher EM, et al. The International Registry of Acute Aortic Dissection(IRAD): new insights into an old disease. Jama 2000;283:897-903.

Hagl C, Strauch JT, Spielvogel D, Galla JD, Lansman SL, Squitieri R. et al. (2003) Is the Bentall procedure for ascending aorta or aortic valve replacement the best approach for long-term event-free survival? Ann ThoracSurg 76(3): 698–703.

Halstead JC, Meier M, Etz C et al. (2007), the fate of the distal aorta after repair of a type A aortic dissection. J Thorac Cardiovasc Surg. 2007 Jan;133(1):127-35.

Hiratzka LF, Bakris GL, Beckman JA, et al. 2010 ACCF/ AHA/ AATS/ ACR/ ASA/ SCA/ SCAI/ SIR/ STS/ SVM guidelines for the diagnosis and management of patients with thoracic aortic disease. Circulation. 2010;121:e266-e369

Hirst Jr AE, Johns Jr VJ., and Kime Jr SW. (1958) Dissecting aneurysm of the aorta: a review of 505 cases. Medicine (Baltimore) 37(3): 217–279.

Immer FF, Lippeck C, Barmettler H, et al. (2004). Improvement of quality of life after surgery on the thoracic aorta: effect of antegrade cerebral perfusion and short duration of deep hypothermic circulatory arrest. Circulation; 110:II250-5.

Januzzi JL, Isselbacher EM, Fattori R, Cooper JV, Smith DE, Fang J. et al. (2004) Characterizing the young patient with aortic dissection: results from the International Registry of Aortic Dissection (IRAD). J Am CollCardiol 43(4): 665–669.

Jonker FH, Schlosser FJ, Indes JE, et al. Management of type A aortic dissections: a meta-analysis of the literature. Ann Thorac Surg. 2010;89:2061-2066.

Kawahito K, Adachi H, Murata S, Yamaguchi A andIno T. Coronary malperfusion due to type a aorticdissection:mechanism and surgical management. Ann Thorac Surg 2003; 76: 1471–1476.

Kawahito K, H. Adachi, et al. (2001). "Preoperative risk factors for hospital mortality inacute type A aortic dissection." The annals of thoracic surgery 71: 1239 - 1243.

Kazui T, Inoue N, Yamada O, Komatsu S. Selective cerebral perfusion during operation for aneurysms of the aortic arch: a reassessment. Ann ThoracSurg 1992;53:109–14.

Knipp BS, Deeb M, prager RL, Williams CY, Upchurch GR and Patel HJ. A contemporary analysis of outcomes for operative repair of type a aortic dissection in the united states. Surgery 2007; 142: 524–528.

Krukenberg, E. (1920) Beitrage zur Frage des Aneurysma dissecans. Beitr. Pathol. Anat. Allg. Pathol 67:339–351.

Lansman SL, McCullough JN, Nguyen KH, Spielvogel D, Klein JJ, Galla JD, et al. Subtypesofacuteaorticdissection. Ann ThoracSurg1999; 67: 1975–1978.

Lech C, Swaminathan A. (November 2017). "Abdominal Aortic Emergencies". Emergency Medicine Clinics of North America. 35 (4): 847–67. doi:10.1016/j.emc. 2017.07.003. PMID 28987432.

Loren F. Hiratzka, George L. Bakris, Joshua A. et al ; 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the Diagnosis and Management of Patients With Thoracic Aortic Disease American College of Cardiology Foundation, American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, Society for Vascular Medicine, North American Society for Cardiovascular Imaging, Journal of the American College of Cardiology Apr 2010, 55 (14) e27-e129; DOI: 10.1016/j.jacc.2010.02.015

Marta Moreno-Torres, Jesper F. Havelund and Nils J. Faergeman, LC-MS Analyses of Lipid Species in Skeletal Muscle Cells and Tissue, Myogenesis, 10.1007/978-1-4939-8897-6_12, (213-228), (2018).

Meharwal Z, S. Khanna, et al. (2006). "Ascending aortic aneurysm resection: 15 years´experience." Asian Cardiovascular Thoracic Annals 14(4): 300-305.

Mehta RH, O'Gara PT, Bossone E, Nienaber CA, Myrmel T, Cooper JV, et al. Acute type A aortic dissection in the elderly: clinical characteristics, management, and outcomes in the current era. J Am CollCardiol. 2002;40:685-92.

Mehta RH, O'Gara PT, Bossone E., Nienaber CA, Myrmel T, Cooper JV. et al. (2002b) Acute type A aortic dissection in the elderly: clinical characteristics, management, and outcomes in the current era. J Am CollCardiol 40(4): 685–692.

Meszaros I, Morocz J, Szlavi J, et al. Epidemiology and clinicopathology of aortic dissection. Chest2000;117:1271-1278.

Moon MR, Sundt TM III, Pasque MK, et al. Does the extent of proximal or distal resection influence outcome for type Adissections? Ann ThoracSurg 2001;71:124450.

Nathan DP, Xu C, Gorman JH 3rd, et al. Pathogenesis of acute aortic dissection: a finite element stress analysis. Ann Thorac Surg. 2011;91:458-463.

Neri E, Toscano T, Massetti M, et al. Operation for acute typeA aortic dissection in octogenarians; is it justified? J Thorac Cardiovasc Surg 2001;121:259–67.

Nienaber, C. A., R. P. Spielmann, et al. (1992). "Diagnosis of thoracic aortic dissection: Magnetic resonance imaging versus transesophageal echocardiography." Circulation 85: 434 - 447.

Nienaber C, R. Fattori, et al. (2004). "Gender-related differences in acute aortic dissection." Circulation 109(24): 3014-3021.

O'Gara, P.T. and DeSanctis, R.W. (1995) Acute aortic dissection and its variants. Toward a common diagnostic and therapeutic approach. Circulation 92(6): 1376–1378.

Pansini S, Gagliardotto PV, Pompei E, et al. Early and late risk factors in surgical treatment of acute type A aortic dissection. Ann ThoracSurg 1998; 66:779–84.

Pawan D. Patel and Rohit R. Arora. (2008) Pathophysiology, diagnosis, and management of aortic dissection Therapeutic Advances in Cardiovascular Disease .2(6) 439–468 DOI: 10.1177/ 1753944708090830

Perreas K, Samanidis G, Thanopoulos A, et al. Antegrade or retrograde cerebral perfusion in ascending aortaandhemiarch surgery? A propensity-matched analysis. Ann Thorac Surg. 2016;101:146–52.

Piccardo A, Le Guyader A, Regesta T, et al. Octogenarians with uncomplicated acute type a aortic dissection benefit from emergency operation. Ann Thorac. Surg 2013;96:851-6.
Pohost GM, Hung L. and Doyle, M.(2003) Clinical use of cardiovascular magnetic resonance. Circulation 108(6): 647–653.

Prêtre R. and L. K. von Segesser (1997). "Aortic dissection."The Lancet 349: 1461 - 1464.

Rampoldi V, Trimarchi S, Eagle KA, Nienaber CA, OhJK, Bossone E, et al. Simple risk models to predict surgicalmortality in acute type A aortic dissection: theInternational Registry of Acute Aortic Dissection score. AnnThorac Surg 2007; 83: 55–61.

Robert S. Bonser, Aaron M. Ranasinghe, Mahmoud Loubani et al. Evidence, Lack of Evidence, Controversy, and Debate in the Provision and Performance of the Surgery of Acute Type A Aortic DissectionJournal of the American College of Cardiology Dec 2011, 58 (24) 2455-2474; DOI: 10.1016/j.jacc.2011.06.067

Roth JA, Parekh MA. Dissecting aneurysms perforating theesophagus. N Engl J Med 1978; 299: 776. Spitzer S, Blanco G, Adam A, Spyrou PG, Mason D. Superior vena cava obstruction and dissecting aortic aneurysm. JAMA 1975; 233: 164–5.

Rylski B, Hoffmann I, Beyersdorf F, et al. Acute aortic dissection type A: age-related management and outcomes reported in the German Registry for Acute Aortic Dissection Type A (GERAADA) of over 2000 patients. Ann Surg 2014;259:598-604.

Sabik JF, Lytle BW, Blackstone EH, McCarthy PM, Loop FD, Cosgrove DM. Long-term effectiveness of operations for ascending aortic dissection. J ThoracCardiovascSurg 2000;119:946–62.

Sawhney NS, DeMaria AN and Blanchard, D.G. (2001) Aortic intramural hematoma: an increasingly recognized and potentially fatal entity. Chest 120(4): 1340–1346.

Schoeneich F, Rahimi A, Eide M et al. Transatrial left ventricular cannulation for arterial return in CABG with severe aortic calcification. Thorac cardiovasc Surg 2012; 60 - PP60

Slater EE. Aortic Dissection: Presentation and diagnosis. In: Doroghazi RM, Slater EE, eds. Aortic Dissection. New York: McGraw-Hill, 1983: 61–70.

Slater EE, DeSanctis RW. The clinical recognition of dissectingaortic aneurysm. Am J Med 1976; 60: 625–33.

Spittell PC, Spittell JA Jr, Joyce JW et al. Clinical featuresand differential diagnosis of aortic dissection: experience with236 cases (1980 through 1990). Mayo Clin Proc 1993; 68: 642–51.

Sun L, N. Liu, et al. (2006). "Clinical experience of simultaneous aortic operation andcoronary aortic bypass grafting." Zhongua Wai KeZaZhi 44(2): 76-79.

Svensson LG, Crawford ES. Aortic dissection and aorticaneurysm surgery: clinical observations, experimental investigationsand statistical analyses. Part II. Curr Probl Surg1992; 29: 913–1057.

Tan ME, Morshuis WJ, Dossche KM, Kelder JC, Waanders FG, Schepens MA. Long-term results after 27 years of surgical treatment of acute type a aortic dissection. Ann Thorac Surg. 2005;80:523-9.

Treasure T and M. J. Raphael (1991). "Investigation of suspected dissection of the thoracicaorta." The Lancet 338: 490 - 495.

Trimarchi S, Eagle KA, Nienaber CA et al ;International Registry of Acute Aortic Dissection Investigators. Role of age in acute type A aortic dissection outcome: report from the International Registry of Acute Aortic Dissection (IRAD).J.Thorac. Cardiovasc. Surg. 2010 Oct;140(4):784-9. doi: 10.1016/j.jtcvs.2009.11.014. Epub 2010 Feb 21.

Trimarchi S, C. Nienaber, et al. (2005). "Contemporary results of surgery in acute type Aaortic dissection: The International Registry of Acute Aortic Dissection experience." The journal of thoracic and cardiovascular surgery 129(1): 112-122.

Ueda Y, Miki S, Kusuhara K, Okita Y, Tahata T, Yamanaka K. Surgical treatment of aneurysm or dissection involving theascending aorta and aortic arch, utilizing circulatory arrestand retrograde cerebral perfusion. J Cardiovasc Surg 1990;31:553–8.

Uysal S, Lin HM, Fischer GW, et al. Selective cerebral perfusion for thoracic aortic surgery: association with neurocognitive outcome. J Thorac Cardiovasc Surg 2012;143:1205-12.

Von Segesser, L.K., Killer, I., Ziswiler, M., Linka, A., Ritter, M., Jenni, R. et al. (1994) Dissection of the descending thoracic aorta extending into the ascending aorta. A therapeutic challenge.J Thorac Cardiovasc Surg 108(4): 755–761.

Woywodt A, Stabroth C, Kadow K, Krupp G, Luft FC. The patient with low back pain and acute oliguric renal failure. Nephrology Dialysis Transplantation. 2000;15(4):544–546.

Yacoub MH, Gehle P, Chandrasekaran V, Birks EJ, Child A. and Radley-Smith, R. (1998) Late results of a valve-preserving operation in patients with aneurysms of the ascending aorta and root. J Thorac Cardiovasc Surg 115(5): 1080–1090.

Yamada E, Matsumura M, Kyo S, Omoto R. Usefulness of a prototype intravascular ultrasound imaging in evaluationof aortic dissection and comparison with angiographic study, transesophageal echocardiography, computed tomography, and magnetic resonance imaging. Am J Cardiol 1995; 75: 161–5.

Yan TD, Bannon PG, Bavaria J, et al. Consensus on hypothermia in aortic arch surgery. Ann Cardiothorac Surg 2013;2:163-168.

Danksagung

Ausdrücklich möchte ich mich bei Herrn Prof. Dr. med. J. Cremer, Direktor der Klinik für Herz- und Gefäßchirurgie des Universitätsklinikums Schleswig-Holstein / Campus Kiel, für die Möglichkeit, diese Arbeit an seiner Klinik durchführen zu können, bedanken.

Herrn Professor A. Haneya danke ich für die Themenstellung dieser Arbeit und die ausgezeichneten Möglichkeiten, diese zu bearbeiten, sowie für seine Hilfsbereitschaft, Großzügigkeit und Geduld, die er mir trotz seiner Belastung in Klinik und Forschung entgegenbrachte. Auch für die Durchsicht meiner Arbeit und die vielen Hinweise, die zur Vollendung derselben hilfreich waren, bin ich ihm sehr dankbar.

Ich bedanke mich sehr bei Frau Christine Friedrich für die gute Teamarbeit.

Besonderen Dank schulde ich meinen Eltern, meiner Frau und meiner Geschwister für ihre durchgehende Unterstützung bis zur Fertigstellung dieser Arbeit.