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**UNIVERSITY OF ZAGREB
SCHOOL OF MEDICINE**

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ACUTE AORTIC DISSECTION

GRADUATION THESIS



Zagreb, 2018

This graduation paper was made at the Acute Cardiac Care Unit in the Department of Cardiology, Sisters of Charity University Hospital Centre Zagreb under supervision of Nikola Bulj, M.D. PhD University of Zagreb School of Medicine and Sisters of Charity University Hospital Centre Zagreb, and was submitted for evaluation in the academic year 2017/2018.

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SUMMARY

Title: Acute aortic dissection

Name: Azra Smajic

Acute aortic dissection is an acute state that potentially could be fatal. It is caused by the separation of two layers of the aortic wall and allowing blood flow to enter creating two lumens, one true lumen and one false.

The most common cause of acute aortic dissection are unregulated hypertension, smoking, aneurysms and male gender. There are also genetic predispositions as Marfan's syndrome and Ehlers-Danlos syndrome.

Clinical signs of acute aortic dissection are not always clear and that is why acute aortic dissection are often misdiagnosed. The most common symptoms described by patients are severe, sharp pain in the chest and the diagnoses should be suspicions from the anamnesis. One of the indications are usually the abruptness of the pain. Acute aortic dissection can proven by computed tomography.

Acute aortic dissections are classified into two groups. This is type A and type B. The importance of the classification is because this tells us about location of dissection and the management and treatment options. Acute aortic dissections are treated by surgery or by medication. Surgery procedure choice depend if the aortic valve is damaged or not. Bentall procedure, valve sparing aortic root replacement and thoracic endovascular aortic repair are three most common procedures used for aortic dissection repair.

Keywords: Acute aortic dissection, Tunica media, Hypertension, Classifications, Medication, Surgery.

Sažetak

Title: Akutna disekcija aorte

Ime: Azra Smajic

Akutna disekcija aorte je akutno stanje koje je potencijalno smrtonosno. Uzrok je razdvajanje slojeva aortne stijenke koje posljedično dozvoljava utok krvi te raslojavanje stijenke uz stvaranje dvaju lumena; pravi lumen i lažan lumen.

Najčešći uzroci akutne disekcije aorte je neregulirani krvni tlak, pušenje, aneurizmi i muški spol. Marfanov sindrom i Ehlers-Danlos sindrom su genetske predispozicije.

Klinički znakovi akutne disekcije aorte često se ne prepoznaju lako, što može dovesti do neispravne dijagnoze. Najčešći simptomi su opisani od pacijenata kao probadajuća oštra bol u prsima i dijagnoza bi se trebala posumnjati od anamneze. Jedan od indikacija je i iznenadna, naglo nastala bol. Akutna disekcija aorta u pravilu se dokazuje kompjuteriziranom tomografijom.

Akutna disekcija aorte se klasificira u dvije grupe. Tip A i tip B. Važnost klasifikacije je u tome što nam ona govori o lokalizaciji disekcije te o mogućnostima liječenja. Akutna disekcija aorte se liječi kirurški ili medikamentno. Izbor vrste kirurškog zahvata ovisi o tome da li je aortna valvula oštećena ili nije. Procedura po Bentallu, zamjena aortnog korijena uz poštedu valvule i torakalni endovaskularni postupak postavljanja aortnog stent-grafta su najčešće metode izbora za popravak aortne disekcije.

Ključne riječi: Akutna disekcija aorte, Tunica media, Krvni tlak, Klasifikacija, Medikamenti, Kirurgija.

1. Introduction

Acute aortic dissection is rare condition but life threatening. It has a lethality rate of 1 to 2% per hour after onset of symptoms in untreated patients. Acute aortic dissection is defined as the separation of the aortic wall layers. Tears enter in the space between the intima and media layer and form of a true and false lumen. This can ensue aortic rupture or impaired blood flow.

The incidence is higher in men and increasing with age. One of the known risk factors for acute aortic dissection is poorly controlled hypertension which occur in 60-75% of diagnosed individuals. Other occurring risk factors are pre-existing aortic diseases or bicuspid aortic valve disease, genetic diseases such as Marfan and Loeys-Dietz syndromes, history of previous cardiac surgery, trauma to the chest, cigarette smoking and intravenous drug abuse. [1]

The aorta arises from the left ventricle forming the arch and continuing as the descending aorta, until the bifurcation into common iliac arteries. The bifurcation is at the level of the sacroiliac joint. [2]

There are two types of classification for acute aortic dissection, Stanford and DeBakey.

There are no one sign or symptom that can positively identify acute aortic dissection and the clinical manifestations are diverse.

Treatment of acute aortic dissection is dependent on type and extension of the dissection. In type A aortic dissection surgery is the option and in type B aortic dissection will depend on if it is uncomplicated or complicated because medical treatment is an option. [1]

2. Risk factors

There are several recognized risk factors for developing acute aortic dissection. Men are more likely to develop acute aortic dissection than female concerning both type A and type B dissection. The mean age for the onset is around 65 years. Usually the patients with type B dissection are older than those with type A.

Hypertension is believed to be one of the more important risk factors because the presence in about 80% in affected patients. [3]

Another risk factor for acute aortic dissection and aneurysm is smoking. Smokers are twice as more affected than for non smokers. Aortic dilation is as we can see an increased risk but not essential but 60% of acute aortic dissection will occur at the diameter of 55mm. [4]

It is unclear whether atherosclerosis is involved in the development of acute aortic dissection but what has been seen is that atherosclerosis is more commonly present in type B dissections than in those of type A. [5]

Diabetes and obesity have no proven association with acute aortic dissection. [6]

Table 1: Risk factors for acute aortic dissection
Accepted from Swiss Medical Weekly, www.smw.ch*

Male sex
Age >65 years
Hypertension
Smoking
Aneurysm
Congenital disorders
Marfan syndrome
Loeys-Dietz syndrome
Vascular Ehlers-Danlos syndrome
Bicuspid aortic valve
Inflammatory disease
Aortitis
Giant cell arteritis
Takayasu arteritis
Systemic lupus erythematosus

* Gawinecka, j., Schönrrath, F., & von Eckardstein, A. (2017). Acute aortic dissection: pathogenesis, risk factors and diagnosis. *Swiss Medical Weekly*, 147(3334).

3. Predisposing factors

There are a few genetic diseases and conditions that are predisposing to acute aortic dissection. Marfan syndrome is a fibrillin 1 deficiency and animal models imply that FBN1 mutations causes morphological changes in vascular smooth muscle cells and releasing of matrix-degrading enzymes that causes elastolysis, fibre calcification and inflammation. Among patients with type A dissection and Marfan's syndrome at the age of 60 the prevalence is around 50%.

Ehlers-Danlos syndrome the vascular type is linked to defects in the synthesis of type 3 procollagen which regulates the type 1 collagen fibrillogenesis. When there is abnormal type 1 fibrillogenesis the vascular smooth muscle cell signalling end up in thinner intima media thickness which will eventually result in increased wall stress and higher risk of arterial dissection. [7]

Loeys-Dietz syndrome is as well associated with acute aortic dissection. The genes that are mutated are encoding growth factor β and form this syndrome.

Most common cardiovascular malformation is congenital bicuspid valve which is in general population occurring 1-2% and is a risk factor. The connection of aortic dissection and bicuspid valve are very similar to those that were described for Marfan's syndrome, meaning that vascular matrix remodelling is due to some deficits of components of elastin, emilin, fibrillin and increased release of matrix metalloproteinase. [8][9]

Mutations in the subsequent genes, as well as others have been linked to bicuspid valve and aortic complications. The genes discussed are NOTCH1 (familial and isolated and left ventricular outflow tract imperfections), TGF β -2 and ACTA2 (bicuspid aortic with familial aortic aneurysm). [10]

The prevalence of aneurysm and aortic dissection with a bicuspid valve and a higher age for acute aortic complications.

4. Anatomy of aorta

The aorta consists of 3 parts, the ascending aorta, the aortic arch and the descending aorta. The ascending aorta arises from the left ventricle initially starting behind the pulmonary trunk. The ascending aorta will then make a curve forming the aortic arch and continue posteriorly over the root of the left lung reaching all the way to T4 and then start descend on the left side anteriorly of the vertebral column as the descending aorta.

The first branches that are risen from the ascending aorta are right and left coronary arteries.

The aortic arch gives rise to vessels that are supplying head, neck and arms. It starts with the brachiocephalic trunk which is 2-3 cm long. The brachiocephalic trunk ascends obliquely towards the right over the trachea and divides to form the right common carotid and right subclavian artery. On the left part of the aortic arch the arteries emerging directly from the arch as the left common carotid artery and left subclavian artery. The aortic isthmus is formed from the level of the left subclavian artery to connect and become the descending aorta, which consist of the thoracic aorta and abdominal aorta. [2]

The aorta is an elastic artery, consisting of extracellular matrix, fibroblast-like cells, endothelial cells, intimal cells, nerves and smooth muscle. There are several layer of the vascular wall which is called tunica externa, tunica media and tunica intima. The tiny vessels feeding the tunica externa and tunica media are called vasa vasorum. They supply the aorta because of the thickness.

The largest components of the vascular wall is the tunica media. Inside the tunica media we can find smooth muscle and extracellular matrix. The key unit of the aorta is this elastic lamella which is these two combined. The role of the smooth muscle is to not dramatically change the diameter when the aorta is active but rather to keep the stiffness. The elastic matrix consist of elastic fibers, collagens aminoglycans and proteoglycans. [11][12]

5. Classification of dissection

Aortic dissection is can be classified by two ways. By Stanford classification or DeBakey.

Stanford classification consist of type A and type B. Type A dissection shows the involvement of ascending aorta independent of site of the tear and if the distal part is included. Type B dissection shows the involvement of the aortic arch and/or the descending aorta without including the ascending aorta.

Debakey classification goes this way. Type I dissection involves ascending to descending aorta meaning the whole aorta. Type II dissection include the ascending and or the the aortic arch without descending aorta. Type III will only involve the descending aorta.

There has to be a classification based on the clinical status. Then we mention the hyperacute which means that 24 or less hours have passed since the beginning of incidence, acute from 2-7 days, subacute 8-30 days and chronic more than 30 days.
[13]

Classification and identification is one of the key parts in aortic dissection because based on what class the aortic dissection is further treatment is appropriately decided.

Treatments will be described in a later section.

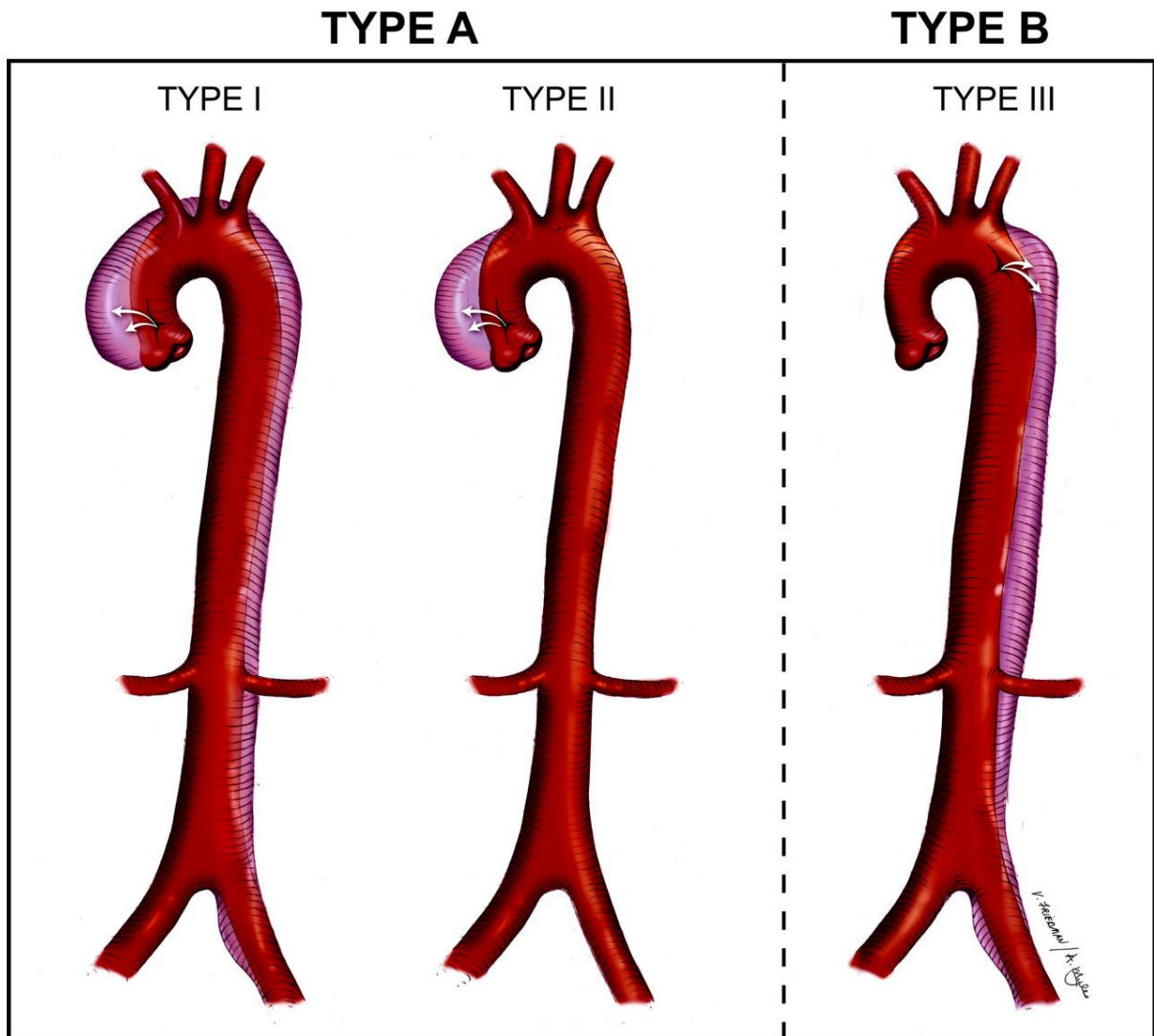


Figure 1. Classification schemes of acute aortic dissection. Reprinted from Acute Aortic Dissection with permission from Braverman et al.



Figure 2. Contrast computed tomography scan demonstrating acute type A aortic dissection with enlargement of the ascending aorta and intimal flap (arrow) in the ascending and descending aorta. Both the true lumen (TL) and false lumen are opacified with contrast in this example.

Reprinted from Acute aortic dissection with permission from Braverman et al.

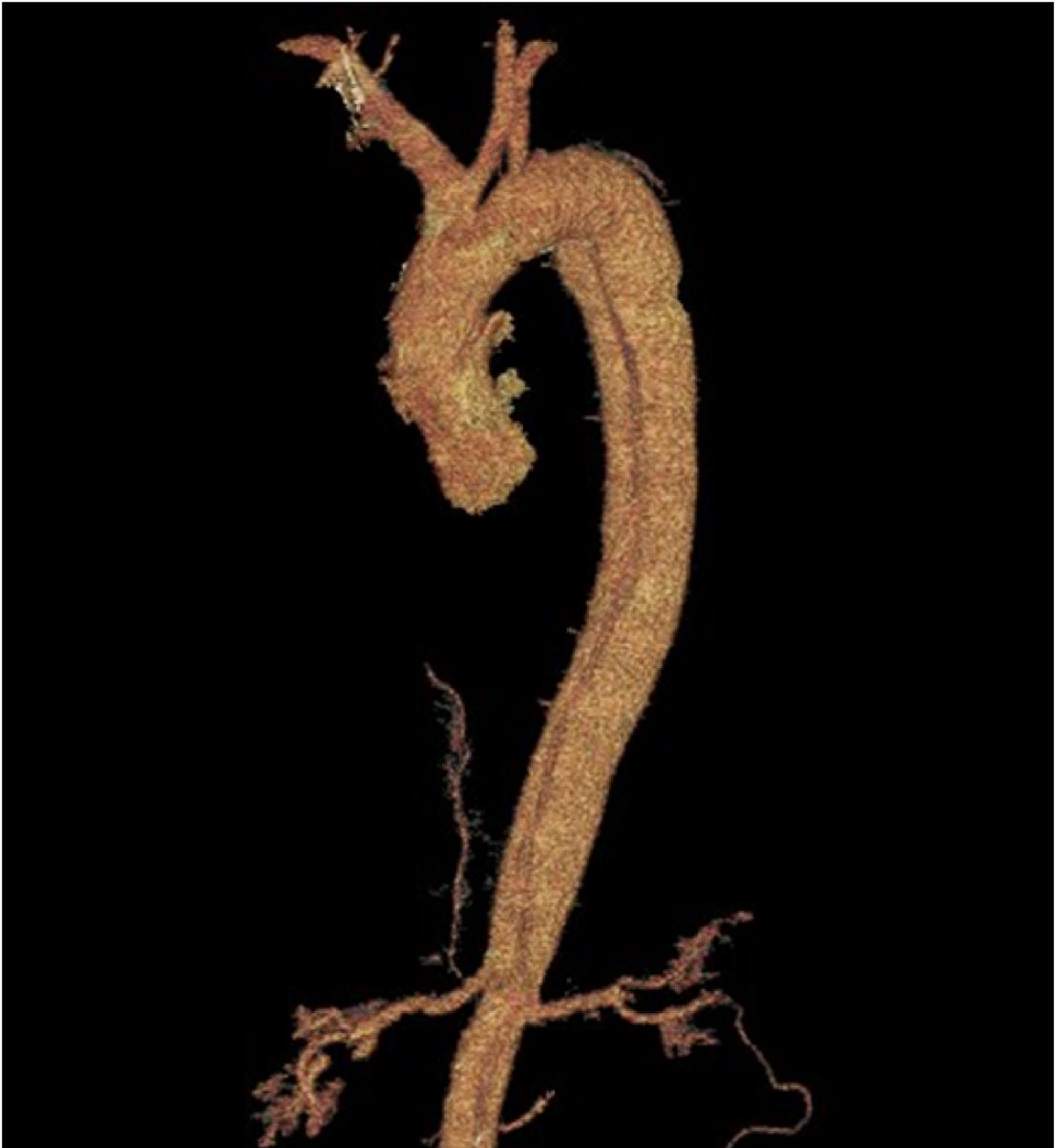


Figure 3. Uncomplicated acute type B aortic dissection. Reprinted from Uncomplicated Acute type B Aortic Dissection: Selection Guidelines for TEVAR. Emilia et al.

6. Pathophysiology

Aortic dissection result from a tear in the aorta in the intima layer and expose the medial layer with highly pulsatile blood flow. The most frequent site of tear in the intima are the segments of the aorta that are exposed to the greatest shear stress. These sites are the ascending or the proximal part of the descending aorta. The outcome of this is separation of the wall layers and a formation of false lumen. From the false lumen the blood can re-entry to the true lumen. [3]

The false lumen can potentially end blindly in a cul-de-sac and create a blood clot. If the thrombosis occur in the the early stage the thrombosed false lumen is smaller than the true lumen but if the thrombosis occur in the later stage the false lumen may become larger than the true lumen. Since the false lumen can grow because of the blood clotting it can compress the true lumen and create a decrease in systemic perfusion. The dissection can also spread to the coronary arteries. [14][15]

Aortic rupture is life threatening which occur if the adventitia disrapture. Aortic disruption leads to rapid blood loss and death. [3]

Looking at the molecular level aortic dissection is the consequence of remodelling of the aortic wall structure as a reaction of inflammation and extracellular matrix degradation. Macrophages that are activated and infiltrating the tunica media are secreting matrix metalloproteinases and proinflammatory cytokines. The collagen and elastin fibers are degraded rapidly by metalloproteinase-9 and metalloproteinase-12. These metalloproteinases are involved in the connection of Marfan's syndrome and aortic dissection.

It is important to keep in mind that it is not only the increase of activity of metalloproteinases but the imbalance between them and the inhibitors called tissue inhibitors. [16][17]

Vascular endothelial neogenesis might also be involved in the aortic wall remodelling causing the dissection. Primarily VEGF is responsible for vasculogenesis and angiogenesis but it also promotes proinflammatory actions. [18]

Arterial hypertension that is the silent attacker mentioned previously and one of the main risk factors of aortic dissection. In can act indirectly as a proinflammatory

activator by recruiting macrophages. Patients with hypertension show higher level of proinflammatory molecules such as metalloproteinase-9, metalloproteinase-2 macrophage chemoattractant protein-1, VEGF and interleukin-6. These all lead eventually to matrix degradation and finally aortic dissection. [19][20]

7. Clinical signs and symptoms

Acute aortic dissection will manifest in most patients as a sudden onset of severe anterior chest pain. The location of the pain points to where the origin of the dissection is. The most frequently reported symptom is severe ripping, sharp chest and or back pain occurring up to 85%. The presentation described above is mostly described with aortic dissection type A. Type B will be presented as pain in the back or abdomen.

The abruptness of the onset is the most specific symptom for acute aortic dissection. There can be dissections with no pain as a symptom and these are extremely difficult to diagnose so they tend to be missed. [1] Painless dissections are more common in Marfan's syndrome and in neurologic complications from the disease. The anterior chest pain may mimic the pain described when myocardial infarction is the diagnosis and this happens because the dissection in the ascending aorta or the arch of the aorta and interfering the flow to the coronary arteries. Neck and jaw pain indicate that the dissection is involving the aortic arch.

If there is tearing pain or ripping pain in the interscapular area the most likely cause is dissection of the descending aorta.

Aortic dissection could be suspected in patients with symptoms of myocardial infarction but with normal electrocardiographic (ECG) findings.

In 20% of cases there are neurological deficits. In approximately 5% syncope is present and may be the result of increased vagal tone, hypovolemia or dysrhythmia. Cerebrovascular accident (CVA) symptoms include hemiplegia, hemiparesis and hemianesthesia.

Cardiovascular manifestation include congestive heart failure secondary to acute aortic regurgitation, including dyspnea and orthopnea. [21]

8. Diagnosis

Diagnosis is made by clinical picture and imaging. Acute aortic dissection is a dynamic process and the spectrum of clinical presentation is wide. As mentioned above the symptoms that are most commonly described by patients are not symptoms specifically for the acute aortic dissection but the abruptness is one of the leading complains that should raise the suspicion. [22]

Chest radiography and 12-lead electrocardiogram may be the first method imaging technique but the majority of patients do not show any abnormalities in these examinations.

Transthoracic echocardiography (TTE) is a non-invasive and rapid assessment of several aortic segments. The disadvantage is that the sensitivity is limited which mean that even if negative results aortic dissection can not be excluded. Other disadvantages are patients with pulmonary emphysema, obesity and those on mechanical ventilation [23].

There are three imaging techniques that have high sensitivity and specificity and those are transesophageal echocardiography (TOE), contrast-enhanced computed tomography (CT) and magnetic resonance imaging (MRI) [24].

The portable TOE is an asset in the emergency department in patient that are hemodynamically unstable but TOE is a technique that needs an experienced observer otherwise false negatives are of high risk.

MRI is the most precise but rare used imaging technique since its lack of availability. [25]

Contrast-enhanced CT is the most used imaging technique and provides fast image. The only disadvantage is the ionising radiation and allergic reaction to the contrast as well as renal failure [26].

9. Types of surgery

There are four types of surgery treatments for aortic dissection type A but here is going to be discussed three of them, Bentall procedure, valve sparing aortic root replacement and thoracic endovascular aortic repair.

The Bentall procedure is a surgical procedure where there is a graft replacement of the aortic valve, aortic root and the ascending aorta followed by the re-implantation of the coronary arteries into the graft. The Bentall procedure was first described in 1968. [27] Although being used for many years, achieved ultimate goals and saved lives the procedure still lose the native valve which leaves us with two options, either mechanical or bioprosthetic valve. For younger patients none are ideal because with the former the patient is facing lifelong anticoagulation therapy or the risk for reoperation due to the degeneration of the bioprosthetic valve. [27]

The valve sparing aortic root replacement meaning the replacement of the root without the replacement of the valve. There are two main techniques, reimplantation (David procedure) and remodeling (Yacoub procedure). [28]

The valve sparing aortic root is more time consuming and technically more complex but it has shown to be more long-term favorable as well as lower rates of mortality, lower reintervention, less postoperative complications and the avoidance of anticoagulation therapy. [29]

A paper written by Yang et al. that compared the short-term and midterm outcomes after the David and Bentall procedure showed that the David procedure is more technically challenging and more time consuming as documented by longer cardiopulmonary bypass and cross clamp time. Even with these challenges there are only a few adverse effect. What is interesting is that in this paper the David procedure was chosen on the significant younger patients with less hypertension. [30]

Thoracic endovascular aortic repair is a procedure that comprises of placement of an expandable stent graft within the aorta without operating the aorta directly. [31]

10. Treatment of Type A and Type B

The treatment and management will depend on the anatomical location of the dissection and what type it is.

Acute type A aortic dissection has a high mortality rate, up to 1-2%/hour directly after onset of first symptom, even up to 50% within 48 hours if it is not operated on. The treatment of choice is emergency surgical intervention and this is associated with the most favorable outcomes even in patients that present with unfavorable condition with major comorbidities.

The mortality rate can vary from hospital to hospital up to 25% according to the International Registry of Acute Aortic Dissection. Although being so high it is better than conservative treatment which carries a mortality rate of 60%. [32]

When the diagnosis of type A dissection is made there are some crucial steps to follow. The patient should be taken to an emergency department and the focus should be to reduce the shear stress on the aorta. This is made by controlling blood pressure, heart rate and pain controlling.

When the patient is transported to the tertiary center immediate surgery should be done. Depending on the extension of the aortic dissection either valve replacement technique or a valve sparing that was discussed in previous section. [33]

Type B aortic dissection is different from type A dissection because it is divided by either uncomplicated or complicated dissection.

Complicated type B dissection are the ones with recurrent pain, uncontrolled hypertension although on treatment, early aortic expansion and malperfusion and signs of rupture as hemothorax or hematoma of mediastinum.

Most type B dissections are uncomplicated meaning having none of the former mentioned. The International Registry of Acute Aortic Dissection suggest that uncomplicated type B dissection should be treated medically rather than surgically. Medical treatment including pain control, blood pressure and heart rate control and monitoring if there is any progression. This is a similar manner to the first step in type A dissection.[34]

Complicated type B aortic dissection is different in treatment, it requires urgent intervention to restore the perfusion and and restore the flow in the true lumen. Since open surgical repair is extremely demanding and have high in-hospital mortality the preferred approach is thoracic endovascular aortic repair.

Patient that underwent thoracic endovascular surgery should be followed up first year after surgery regularly to exclude any complication, this is made by either computed tomography (CT) or magnetic resonance imaging (MRI) within 6 months and 12 months. [35]

11. Discussion

Acute aortic dissection which is always acute and always have to be considered. Still knowing the facts and pathophysiology of acute aortic dissection the mortality is still high preoperatively and postoperatively. Acute aortic dissection is not common but it is not rare either and the question remaining for years why the outcomes are not as promising as it could be considering the knowledge and the amount papers published on the subject.

All the risk factors are not specific for only acute aortic dissection but can be risk factors for a number of diagnosis. If patients have any of the predisposing factors such as Marfan's syndrome, Ehlers-Danlos syndrome or Loeys-Dietz syndrome where all the risk factors such be avoided such as smoking and hypertension perhaps these patients should be well informed that they are in higher risk of acute aortic dissections and any of the previously mentioned symptoms should be examined by a physician. If not in the category of the predisposing factors the diagnosis of acute aortic dissection is likely not considered in the differential diagnosis.

What are common practice in today's developed countries are using non-invasive methods before proceeding to invasive which is logical, less expensive and safe for patients. A patient coming with chest pain is to be examined thoroughly.

Echocardiogram is one of the first non-invasive methods being used as diagnostics and for acute aortic dissection and in an ECG the results will be mostly unspecific. This being the exclusion point for plenty other diagnosis we should have in mind that acute aortic dissection may be a player in the field. Another procedure which also belongs to the non-invasive is transthoracic echocardiography. What was mentioned in previous section is that this is a procedure which has a debatable sensitivity and the outcome of not recognizing acute aortic dissection is far more dangerous than just using the TTE as a sole diagnostic tool.

Contrast-enhanced CT will be the imaging technique that diagnose acute aortic dissection almost perfectly but what can not be forgotten is that the kidneys are not spared, especially if the patients have kidney renal or other renal condition.

When diagnosed and identified what type of dissection the treatments are chosen. In practice the first step in both dissection type A and type B, initially the aim is to control the heart rate, blood pressure and pain. Intravenous beta blockers on low dose so more arterial vasodilators can be added if needed. Oral antihypertensives are usually introduced the first 24 hours.

If the acute aortic dissection is of type A the further process must be to detect if the valve is affected or spared. When the valve is affected Bentall procedure is the only way and have been now used for quite some time and with the progression of modern medicine this procedure is not as fatal as when first described. The dilemma for valve option for young and old population is not most obvious. Mechanical valves are being used as well as prosthetic but the both the adverse effects are present. If the acute aortic dissection is of the type A and valve sparing both the Daid and Yacoub procedures have been described with promising results.

Type B are depending on if it is complicated or uncomplicated.

Why type B acute aortic dissection is preferably not operated on is because the studies has shown that the risk for recovery is higher when treated medically that with surgery. The reason is not known.

12. Conclusion

Acute aortic dissections remain an emergency where the short term and long term morbidity and mortality is still unacceptably high. The recent technology is improving the outcomes but perhaps not in the rates we want to and the rates we are expecting. The connecting steps are the time of the diagnosis and the direct imaging and conformation to the time of the operation.

What can not be forgotten is that this emergency condition is not the most common and not the primary diagnosis that the physician have in mind.

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References

- [1] Redfern E, Callaway M, Zakkar M, Bryan A. Improving outcomes in acute aortic dissection. *British Journal of Hospital Medicine*. 2017;78(6):320-326.
- [2] Fritsch H, Kühnel W. *Color atlas of human anatomy*. 5th ed. Stuttgart: Thieme; 2015. Vol.2: 44-45.
- [3] Gawinecka, j., Schönrrath, F., & von Eckardstein, A. (2017). Acute aortic dissection: pathogenesis, risk factors and diagnosis. *Swiss Medical Weekly*, 147(3334).
- [4] Pape L, Tsai T, Isselbacher E, Oh J, O'Gara P, Evangelista A et al. Aortic Diameter ≥ 5.5 cm Is Not a Good Predictor of Type A Aortic Dissection: Observations From the International Registry of Acute Aortic Dissection (IRAD). *Circulation*. 2007;116(10):1120-1127.
- [5] Tsai T, Trimarchi S, Nienaber C. Acute Aortic Dissection: Perspectives from the International Registry of Acute Aortic Dissection (IRAD). *European Journal of Vascular and Endovascular Surgery*. 2009;37(2):149-159.
- [6] Howard D, Banerjee A, Fairhead J, Perkins J, Silver L, Rothwell P. Population-Based Study of Incidence and Outcome of Acute Aortic Dissection and Premorbid Risk Factor Control: 10-Year Results From the Oxford Vascular Study. *Circulation*. 2013;127(20):2031-2037.
- [7] Boutouyrie P. Increased Carotid Wall Stress in Vascular Ehlers-Danlos Syndrome. *Circulation*. 2004;109(12):1530-1535.
- [8] Fondard O, Detaint D, Iung B, Choqueux C, Adle-Biassette H, Jarraya M et al. Extracellular matrix remodelling in human aortic valve disease: the role of matrix metalloproteinases and their tissue inhibitors. *European Heart Journal*. 2005;26(13):1333-1341.11.

- [9] Fedak P, de Sa M, Verma S, Nili N, Kazemian P, Butany J et al. Vascular matrix remodeling in patients with bicuspid aortic valve malformations: implications for aortic dilatation. *The Journal of Thoracic and Cardiovascular Surgery*. 2003;126(3):797-805.
- [10] Andreassi M, Della Corte A. Genetics of bicuspid aortic valve aortopathy. *Current Opinion in Cardiology*. 2016;31(6):585-592.
- [11] Ritman, E; Lerman,A (2007). "The dynamic vasa vasorum". *Cardiovascular Research*. 75 (4):649-658.
- [12] Lech, C; Swaminathan, A (November 2017). "Abdominal Aortic Emergencies".*Emergency Medicine Clinics of North America*. 35 (4): 847-67.
- [13] Stephen Hauser., Dennis Kasper., Anthony Fauci., Dan Longo., J. Jameson., Joseph Loscalzo. *Harrison's Manual of Medicine, 18th Edition*. 18th ed. McGraw-Hill; 2013.887-888.
- [14] Vilacosta I, Aragoncillo P, Canadas V, San Roman JA, Ferreiros J, Rodriguez E. Acute aortic syndrome: a new look at an old conundrum.*Postgrad Med J*. 2010;86(1011):52–61.
- [15] White A, Broder J, Mando-Vandrick J, Wendell J, Crowe J. Acute aortic emergencies--part 2: aortic dissections. *Adv Emerg Nurs J*.2013;35(1):28–52.
- [16] Koullias G, Ravichandran P, Korkolis D, Rimm D, Elefteriades J. Increased Tissue Microarray Matrix Metalloproteinase Expression Favors Proteolysis in Thoracic Aortic Aneurysms and Dissections. *The Annals of Thoracic Surgery*. 2004;78(6):2106-2110.
- [17] Manabe T, Imoto K, Uchida K, Doi C, Takanashi Y. Decreased Tissue Inhibitor of Metalloproteinase-2/Matrix Metalloproteinase Ratio in the Acute Phase of Aortic Dissection. *Surgery Today*. 2004;34(3):220-225.

- [18] Del Porto F, di Gioia C, Tritapepe L, Ferri L, Leopizzi M, Nofroni I et al. The Multitasking Role of Macrophages in Stanford Type A Acute Aortic Dissection. *Cardiology*. 2013;127(2):123-129.
- [19] Chae C, Lee R, Rifai N, Ridker P. Blood Pressure and Inflammation in Apparently Healthy Men. *Hypertension*. 2001;38(3):399-403.
- [20] Stumpf C, Jukic J, Yilmaz A, Raaz D, Schmieder R E, Daniel W G, et al. Elevated VEGF-plasma levels in young patients with mild essential hypertension. *Eur J Clin Invest*. 2009;39(1):31–6
- [21] SPITTELL P, SPITTELL J, JOYCE J, TAJIK A, EDWARDS W, SCHAFF H et al. Clinical Features and Differential Diagnosis of Aortic Dissection: Experience With 236 Cases (1980 Through 1990). *Mayo Clinic Proceedings*. 1993;68(7):642-651.
- [22] M sz ros I, M rocz J, Szl vi J, Schmidt J, Torn ci L, Nagy L, et al. Epidemiology and clinicopathology of aortic dissection. *Chest*. 2000;117(5):1271–8.
- [23] Meredith E, Masani N. Echocardiography in the emergency assessment of acute aortic syndromes. *European Journal of Echocardiography*. 2009;10(1):i31-i39.
- [24] Shiga T, Wajima Z, Apfel C, Inoue T, Ohe Y. Diagnostic Accuracy of Transesophageal Echocardiography, Helical Computed Tomography, and Magnetic Resonance Imaging for Suspected Thoracic Aortic Dissection. *Archives of Internal Medicine*. 2006;166(13):1350.
- [25] 2014 ESC Guidelines on the diagnosis and treatment of aortic diseases. *European Heart Journal*. 2014;35(41):2873-2926.
- [26] Bentall H, De Bono A. A technique for complete replacement of the ascending aorta. *Thorax*. 1968;23(4):338-339.

[27] Alhadi F, Ius F, Koigeldiyev N, Fleissner F, Stiefel P, Kaufeld T et al. Is Bentall Procedure Still the Gold Standard for Acute Aortic Dissection with Aortic Root Involvement?. *The Thoracic and Cardiovascular Surgeon*. 2015;64(02):116-123.

[28] David T. The aortic valve-sparing operation. *J Thorac Cardiovasc Surg* 2011;141:613–5.

[29] Erasmi A, Stierle U, Bechtel J, Schmidtke C, Sievers H, Kraatz E. Up to 7 years' experience with valve-sparing aortic root remodeling/reimplantation for acute type a dissection. *The Annals of Thoracic Surgery*. 2003;76(1):99-104.

[30] Yang B, Patel H, Sorek C, Hornsby W, Wu X, Ward S et al. Sixteen-Year Experience of David and Bentall Procedures in Acute Type A Aortic Dissection. *The Annals of Thoracic Surgery*. 2018;105(3):779-784.

[31] Moulakakis K, Mylonas S, Dalainas I, et al. Management of complicated and uncomplicated acute type B dissection. A systematic review and meta-analysis. *Ann Cardiothorac Surg* 2014; 3: 234-46

[32] Hagan P, Nienaber C, Isselbacher E, Bruckman D, Karavite D, Russman P et al. The International Registry of Acute Aortic Dissection (IRAD). *JAMA*. 2000;283(7):897.

[33] Hiratzka L, Bakris G, Beckman J, Bersin R, Carr V, Casey D 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: Executive Summary: A Report of the 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, and Society for Vascular Medicine. *Circulation*. 2010;121(13):1544-1579.

[34] Fattori R, Tsai T, Myrmet T, Evangelista A, Cooper J, Trimarchi S et al. Complicated Acute Type B Dissection: Is Surgery Still the Best Option?. *JACC: Cardiovascular Interventions*. 2008;1(4):395-402.

[35] Raudkivi P, Williams J, Monro J, Ross J (1989) Surgical treatment of the ascending aorta. Fourteen years experience with 83 patients. *J Thorac Cardiovasc Surg* 98(5 Pt 1): 675–682.

Biography

Azra Smajic was born in Nykyrka, Sweden. In Gothenburg she finished both primary and secondary school. Her dream was always to study in Croatia since her parents are refugees from Bosnia and Hercegovina. In 2012 she enrolled in the University of Zagreb, School of Medicine, Medical Studies in English.

During her studies she did internship in Sweden in Karlskrona in psychiatry.

Hobbies include handball, playing piano and spending time with friends and family.

She is fluent in English, Swedish, Croatian and French.