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ACUTE TYPE A AORTIC DISSECTION AND DIABETES

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TIIVISTELMÄ

Santtu Sakari Heikurinen: Akuutti tyypin A aortan dissekaatio ja diabetes
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Diabeteksella on yhteys monien sydän- ja verisuonitautien patologiassa. Akuutti tyypin A aortan dissekaatio (ATAAD) on katastrofinen aorttasairaus, jonka kuolleisuus on eri lähteitten mukaan 60–80 % luokkaa. Tämän kirjallisuuskatsauksen tavoitteena on selvittää diabeteksen ja ATAAD:n suhdetta, ja sitä vaikuttaako esiintyvyydeltään kasvamassa oleva diabetes ATAAD:n patologiaan ja patogeneesiin.

Artikkeleiden haku toteutettiin PubMed tietokantaa käyttäen. Haussa oli mukana diabeteksen lisäksi hyperglykemia, joka on diabetesta sairastavilla tavanomainen oire, varsinkin tyypin 2:ta sairastavilla. Aineistona käytettiin vähäisen aikaisemman tutkimuksen vuoksi myös tutkimuksia, jotka käsittelivät tyypin B dissekaatiota, aortan aneurysmaa, tai ei spesifisesti mainittua dissekaatiota.

Kirjallisuuskatsauksessa havaittiin, että diabetekseen liittyy vähempi ATAAD:n esiintyvyys, mutta suurempi kuolleisuus. Dialyysin ja akuutin munuaisvaurion prevalenssit kasvavat diabeettisilla potilailla. Hyperglykemisillä potilailla on suurempi mahdollisuus pitkittyneeseen mekaaniseen ventilaatioon, sekä pidentynyt sydänkeuhkokoneen käyttö ja pitkittynyt aortan pihditys. Diabeteksella ei löytynyt yhteyttä neurologiseen toimintahäiriöön tai riskiin joutua uuteen operaatioon.

ATAAD:n patogeneesissä diabeteksen suojaavat vaikutukset lienevät liittyvän aortan mediakerroksen paksuuntumiseen, sekä monosyyttien merkittävään metalloproteiinaasikonsentraatioiden laskuun. Metalloproteiinaasitasojen nousua on havaittu dissekoituneessa aortan kudoksessa. Yksi tutkimus tosin löysi insuliiniresistenssin aiheuttavan korkeampia metalloproteiinaasitasoja, sekä frakmentoituneita ja pienempiä säikeitä elastisessa kerroksessa.

Avainsanat: aortan dissekaatio, diabetes, ATAAD

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ABSTRACT

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Diabetes has a known association in the pathology of cardiovascular diseases. Acute type A aortic dissection (ATAAD) is a disastrous condition that has a mortality rate between 60-80 % depending on the source. This literature review aimed to clarify the relationship between ATAAD and diabetes based on the current scientific information, and to see whether diabetes, which is increasing in prevalence, influences the pathology and pathogenesis of ATAAD.

The literature search was done using PubMed. In addition to diabetes, hyperglycaemia was also used as a search term, because it is common with diabetic individuals especially in type 2 diabetics. Due to limited number of previous studies, type B dissections, aortic aneurysms, and unspecified dissections were also used as a basis.

This review found that diabetes decreases the prevalence of ATAAD but raises the mortality rate. The prevalence of dialysis and acute kidney injury rise in diabetic patients. Hyperglycaemic patients have a raised risk for prolonged mechanical ventilation, as well as an increased cardiopulmonary bypass and aortic cross clamping time. No connection was found between neurologic dysfunction and the risk for reoperation in diabetic patients.

In the pathogenesis of ATAAD, the protective mechanism of diabetes seems to root from the increased thickness of aortic media, as well as a decrease in monocyte metalloproteinase concentration. A decrease in metalloproteinase concentration has been found in ATAAD tissues. Though, one study found an increase in the concentration of metalloproteinases, as well as fragmented and small fibres in the elastic layer.

Keywords: aortic dissection, diabetes, ATAAD

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ABBREVIATIONS AND ACRONYMS

AAA	Abdominal aortic aneurysm
AKI	Acute kidney injury
ATAAD	Acute type A aortic dissection
ATBAD	Acute type B aortic dissection
CI	Confidence interval
CRRT	Continuous renal replacement therapy
CT	Computed tomography
HR	Hazard ratio
MetS	Metabolic syndrome
MRI	Magnetic resonance imaging
OR	Odds ratio
TAAAD	Thoracic aortic aneurysms and dissections

1 INTRODUCTION

1.1 Aortic dissection

Acute aortic dissection is a disastrous condition, where blood flows in between the inner two thirds and the outer third of the aortic media separating the two layers. The separation creates a so-called false lumen which runs parallel to the true lumen. Typically, it is assumed that the dissection occurs when the intima layer is damaged, or weakened, by various factors and thus the pulsative blood flow breaches the intima layer and allows blood to flow inside the media layer. On the other hand, an outer theory has also been suggested where dissection occurs first in the aortic wall layer and then torn apart by reorganised blood flow. The initial tear can progress antegradely or retrogradely, and the false lumen may advance to many distal aortic branches such as cerebral and coronary arteries.

There are two commonly used classification systems regarding aortic dissection, the Stanford classification system and the DeBakey classification system. The Stanford system is divided to type A and type B. Type A consists of all the dissections where the false lumen spans the ascending aorta, and type B does not involve the ascending aorta. This paper will focus on the acute type A aortic dissection. It should be stated that the Stanford system does not express the intima tear site and thus the tear can originate anywhere along the dissected aortic path. The DeBakey system is divided into type I, II, III. Type I involves the ascending aorta and extends to at least the aortic arch. Type II involves only the ascending aorta. Type III derives from the left subclavian artery and extends distally along the descending aorta.

Major risk factors for aortic dissection include hypertension, advanced age (> 50 years), dyslipidemia, smoking, and certain genetic disorders, most of which are characterized by connective tissue abnormalities, such as Marfan syndrome. Type A aortic dissection often manifests as a sudden intense chest pain originating substernally or retrosternally. Characteristics that differentiate the chest pain of ATAAD and myocardial infarction is that the chest pain in ATAAD is often sudden, strongest at the start, and sharp by nature. The most accurate and swiftest way of confirming TAAD diagnosis is by computed tomography (CT) scanning. Counter arguments for CT scanning are poor renal function, possibly due to malperfusion and subsequent

acute kidney injury (AKI), and an allergy to iodinated dye. If a CT scan is not possible, then other imaging methods can be considered, such as magnetic resonance imaging (MRI). The goal of CT scanning is to locate and visualize the two lumens, the possible tear sites, and the magnitude of the dissection, thus enabling planning of surgical repair.

It has been estimated that the total mortality rate of ATAAD is 73 %. Aortic dissections can be differentiated into acute, subacute, and chronic, characterised by the time from onset of symptoms and the diagnosis. Acute is when the diagnosis is done within 14 days from the start of symptoms. If an urgent surgical repair is not performed, patients often die from dissection related complications such as aortic rupture, acute heartfailure, and pericardial tamponade. Further complications arise from possible malperfusions in end-organ arteries. A great example of this is acute kidney injury (AKI), which has been found in over 50 % of ATAAD patients.

Main treatment option for ATAAD is open surgery. Recent results have indicated that conservative techniques have better overall outcome regarding short-term (< 30-days) and long-term mortality (> 30-days). However, each situation is different and unique dissection characteristics must be recognised. Major postoperative complications succeeding ATAAD repair include major bleeding (and possible subsequent surgery), pericardial tamponade, stroke, acute kidney injury (AKI), and pneumonia. Long-term survival after ATAAD repair operation is 84-85 % at 5 years, 64-68 % at 10 years, and 38 % at 30 years. Short-term survival rate ranges from 5 % to 24 %, while the current average is around 17 %. [1]

1.2 Diabetes mellitus

Diabetes mellitus is a metabolic condition that is characterised by high plasma glucose concentration (hyperglycaemia). The high glucose concentration is caused by insufficient or absent insulin secretion by the β -cells of the pancreas, or insulin ineffectiveness to influence the target cells to transit GLUT-4 transporters to the cell membrane and thus enabling more effective glucose import into cells. It has been estimated that there are approximately 425 million diabetic patients worldwide, and thus diabetes carries an immense economic burden in addition to the lowered well-being of those affected by it.

In general, diabetes is classified into two types. Type 1 diabetes is an autoimmune disease where the bodies own cells, including CD8⁺-T-lymphocytes, are destroying the β -cells of the pancreas. This may be caused by a virus infection. The similarities in the virus antigen and the surface proteins in the pancreatic β -cells may lead to the cell's destruction, however, much of the function remains unclear. There is compelling evidence indicating that type 2 diabetes has a more pronounced genetic component compared to type 1 diabetes. A significant majority of individuals

diagnosed with type 2 diabetes have at least one parent who also has the condition. The proceeding of the condition is as follows: firstly, insulin effectiveness in the target tissue diminishes, which leads to increased insulin secretion by the pancreas. The diminishing of the insulin effectiveness is called insulin resistance, and the primary cause is the accumulation of ectopic fat. The initial increase in insulin secretion maintains proper glucose metabolism. However, as the insulin resistance progresses and the amount of insulin needed to maintain proper glucose metabolism increases, the β -cells struggle to keep up with the continuing rise in demand. Consequently, the β -cell insulin secretion diminishes and may shut down completely. Treatment of type 1 diabetes consist of insulin injections and close monitoring of the plasma glucose. The main treatment for type 2 diabetes is lifestyle change. The condition can even be reversed by increased exercise, weight loss and paying special attention to visceral fat, as well as abstinence from smoking. Possible medication, such as metformin and sitagliptin, and insulin injections can be considered depending on the patient's condition. [2]

Typical symptoms include glucosuria and subsequent polyuria. Polyuria then may cause polydipsia. A large amount of urinated glucose may cause tiredness and weight loss. An increased liability to infections is also characteristic to diabetes. Risks associated with diabetes include cardiovascular disease, diabetic retinopathy, and diabetic kidney disease. Diabetes is strongly connected with an increased cardiovascular disease risk. The risk is primarily increased by the same factors as non-diabetic individuals, such as raised LDL-cholesterol, hypertension, smoking and increased coagulation sensitivity. [3]

The exact mechanisms underlying vascular damage caused by hyperglycaemia are intricate and not completely elucidated. However, it is believed that elevated levels of intracellular glucose contribute to the generation of reactive oxygen species, which subsequently affect several essential downstream pathways. These pathways include polyol pathway flux, formation and formation of advanced glycation end products, activation of protein kinase C, and flux in the hexosamine pathway. [4] In addition, arteries from patients with diabetes are often harder and more calcified than those of patients without diabetes [5].

2 Methods and materials

Articles were searched from PubMed regarding diabetes and hyperglycaemia in association with acute type A aortic dissection. Search terms used were “aortic”, “type A”, “acute”, “dissection”, “diabetes”, and “hyperglycaemia”. Altogether, there were 109 articles (January 26th). Previous research on this topic is limited and thus the amount of conclusive literature is scarce. Additional articles concerning the epidemiologic of diabetes and TAAAD were searched with specific types of articles in mind. Due to limited number of previous studies, type B dissections, aortic aneurysms, and non-specific dissections were also used as a basis.

Initial search did not provide sufficient amount of information regarding the molecular and histological changes which occur in dissection pathological processes in diabetic patients, and thus this information needed to be found later on. Presently, the pathological process is not fully understood, however, there are interesting factors which contribute to aortic remodelling and thus possible dissections. Most of the research have been done with aortic aneurysm in mind, nevertheless, some research has also been directed on aortic dissection. The search terms were, in addition to the previous search terms, as follows: “histology”, “pathogenesis”, and “pathology”.

3 Results

3.1 Dissection prevalence

3.11 Positive correlation

In a case-control study by Prakash et al. the researchers used the 2006 and 2007 Nationwide inpatient sample (NIS) registry to identify discharge rates for thoracic aortic aneurysms and dissections (TAAAD). Using 2006 NIS data, they found that TAAAD cases (n = 8 877) were 40% less likely to have diabetes mellitus than control subjects (n = 27 069). After correcting for clinical risk factor differences, diabetes remained inversely associated with TAAAD (OR 0,48; CI 95 % (0,44–0,52)). In their model the only predictive factors, which were more significant than diabetes, were Marfan syndrome, valvular disease, and hypertension. The relationship between diabetes and TAAAD was slightly weaker in women than in men was also found (OR 0,66 vs. 0,52).

Interestingly, those with chronic diabetic complications were less likely to have TAAAD (OR 0,17; CI 95 % (0,12–0,23)) compared to those with diabetes without chronic complications. When the researchers replicated their findings using 2007 NIS data, 6 825 had TAAAD and 22 463 were control subjects, they found an inverse association between diabetes and TAAAD (OR 0,47; CI 95 % (0,43–0,51)). In addition, subjects with complicated diabetes had significantly lower prevalence of TAAAD (OR 0,26; CI 95 % (0,20–0,35)) than amongst subjects with uncomplicated diabetes (OR 0,50; CI 95 % (0,45–0,54)). [7]

An observational cohort study done in 2022 by Suzuki et al. used 3 358 293 individuals registered in a health check-up and claims database in Japan with a median age of 43 years. The researchers extracted the records of individuals enrolled in the database between 2005 and 2021. ICD-10 coding was used to extract disease status. This study aimed to clarify the association with hyperglycaemia, hypertension, and the possible risk for aortic aneurysm and aortic dissection. Interestingly, people with a history of cardiovascular disease and those using blood pressure or glucose-lowering medication were excluded. A correlation between the increase of fasting plasma glucose and the decrease of aortic dissection prevalence was found. Prediabetes (n = 568 501) was defined as fasting plasma glucose level of 100–125 mg/dl, and diabetes (n = 53 507) as fasting plasma glucose level of ≥ 126 mg/dl. After fasting plasma glucose exceeded 100 mg/dl the risk for aortic dissection (n = 1 095) started to decrease. Even people with stage 2 hypertension (systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg) when combined with an increased fasting plasma glucose showed notable decrease in dissection prevalence (normal fasting plasma glucose: HR 6,70; CI 95 % (5,62–7,98); diabetes: HR 2,90; CI 95 % (1,75–4,79)). When aortic dissection prevalence was compared with normal blood pressure and different fasting plasma glucose levels, HRs for normal fasting plasma glucose and diabetes were 1,00 (reference) and 0,77 (CI 95 % (0,28–2,07)), respectively. Indicating a lower aortic dissection prevalence with increased fasting plasma glucose levels. [8]

Avdic et al. gathered nearly three million Swedish subjects (type 2 diabetes n = 448 319, control subject group n = 2 251 015). For every patient with type 2 diabetes, five control subjects were selected at random from the Swedish Total Population Register, and matched for county, sex, and age. This study used the definition of type 2 diabetes as dietary treatment only or oral antihypoglycaemic medication, or in patients diagnosed with diabetes at the age of 40 years taking insulin with or without oral antihypoglycaemic medication. When the risk for aortic dissection between individuals with type 2 diabetes mellitus and control subjects were compared, the risk for aortic dissection was significantly lower in individuals with type 2 diabetes (HR 0,53; CI 95 % (0,42–0,65); $P < 0,05$). Throughout follow-up, there were 200 hospitalizations attributable to aortic dissection amid patients with type 2 diabetes compared to 2019 among the control subjects. The

unadjusted prevalence of aortic dissection was 5,6 per 100 000 person-years amid patients with type 2 diabetes and 11,2 per 100 000 person-years amid the control subjects. [9]

He et al. studied the association between diabetes and the risk of aortic dissection in Chinese population. This study differentiated between type A and type B aortic dissection. 2 160 aortic dissection patients were enrolled in the study and 4 320 control subjects were selected at random matched by age and gender. Type A and type B control groups had 1 722 and 2 598 subjects, respectively. Traumatic or iatrogenic aortic dissections were excluded, as well as subjects with prior aortic dissections. Diabetes was defined either by fasting plasma glucose levels of over 126 mg/dl, 2 hours post a 75-gram oral glucose tolerance test glucose levels of over 200 mg/dl, or by physician diagnosis. When patients with aortic dissection were divided into two groups, the diabetic group and the non-diabetic group, patients with diabetes were generally older ($P < 0,001$), had more hypertension ($P < 0,001$), and had a higher prevalence of peripheral vascular disease ($P < 0,001$). Overall prevalence of diabetes in control subjects and aortic dissection patients were (434/4 320, (10,0%) vs 102/2 160, (4,7 %), $P < 0,001$). Likewise, the prevalence of diabetes in type A and type B groups were lower than that of control A and control B groups (8,8 % vs. 2,9 % and 10,9 % vs. 5,9 %, $P < 0,001$). [10]

Yeh et al. studied acute aortic dissection in the elder population in Taiwan. 132 cases of spontaneous acute aortic dissection from a single centre were enrolled. The patients were divided into two groups: above 65 years of age (elderly) ($n = 38$; 45,8 %) and the non-elderly group ($n = 45$; 54,2 %). Elderly group had higher prevalence of hyperglycaemia (8 (17,8 %) vs 0 (0 %), $P < 0,01$) and type I acute aortic dissection (20 (44,4 %) vs 15 (39,5 %), $P < 0,01$). [11]

3.12 No correlation

Howard et al. examined the occurrence of acute aortic events in a population of 92 728 individuals in Oxfordshire, UK, from 2002 to 2012. Throughout the study period, a total of 173 events were observed in 155 patients. Among these, 54 patients experienced 59 thoraco-abdominal aortic dissections, while 101 patients had 114 ruptured or symptomatic aortic aneurysms. Among the 52 incident dissections, 37 (71.2%) were classified as Stanford type-A, and 15 (28.8%) as type-B. Two patients had experienced a type-A dissection prior to the study period, but they had subsequent type-A dissection (both surgically repaired) during the study period and were therefore considered recurrent events. The average age for acute aortic dissection was 72,0 years. Among the 52 patients with dissections, six had diabetes, but the statistical analysis ($P = 1,00$) did not indicate a significant association. Additionally, among the diabetic individuals, three had type-A dissection (out of 37 type-A patients) and three had type-B dissection (out of 15 type-B patients), with a p-value of 0,34. [12]

3.2 Early mortality

In this paper, early mortality will be defined as: death before getting to the hospital, during the time in the hospital prior surgery, during surgery, and 30 days after surgery.

3.21 Negative correlation

Spirito et al. studied the pre-operative risk factors for in hospital death after surgery of type A aortic dissection. From January 1985 to June 1998, 108 patients from a single centre were enrolled in this statistical analysis study. The majority of patients (89,9 %) experienced an acute type A aortic dissection, while 11,1 % had a chronic dissection. 86 patients out of 108 were discharged, and 22 died in the hospital. Univariate analysis found that 12 discharged patients (13,9 %) and 8 who died in the hospital (36,3 %) had diabetes ($P = 0,03$). Thus, indicating that diabetes could in fact be a risk factor for type A aortic dissection induced death. However, multivariate analysis found no correlation between diabetes and type A aortic dissection. [13]

Lau et al. studied conservative and extensive repair in patients who underwent ATAAD surgery. They reviewed their database for patients who underwent surgery for type I or type II dissections from 1997 to 2019. There were 343 patients of which 47 had diabetes. Operative mortality was determined as in-hospital and 30-day post-operation mortality. This study did not differentiate between operative mortality or other adverse events including, myocardial infarction, cerebrovascular accidents, need for dialysis, or the need for tracheostomy. They are all collectively included as major adverse events, which makes the mortality rate difficult to interpret. Univariate analysis for diabetes and major adverse events shows a significant correlation between the two (OR 3,39; CI 95 % (1,53-7,25); $P < 0,01$). Multivariate analysis strengthens the univariate analysis' result (OR 2,65; CI 95 % (1,08-6,26); $P = 0,03$). [14]

Yang et al. studied the relationship between systolic blood pressure and in-hospital mortality in ATAAD. 703 patients were enrolled from a single centre database between January 2014 and December 2018. Admission systolic blood pressure was measured from all patients at admission. 22 patients had diabetes. Univariate analysis did not reach statistical significance (22/703 (3,13 %); OR 1,39; CI 95 % (0,59-3,31); $P = 0,452$). An analysis of diabetes and systolic blood pressure rise per 10 increments was made and it was found that admission systolic blood pressure in non-diabetics had a higher association with in-hospital mortality (non-diabetic: 681/703; OR 0,90; CI 95 % (0,85-0,95); diabetic 22/703; OR 1,37; CI 95 % (0,94-2,01); $P = 0,020$). [15]

Lee et al. used statistical analysis to study ATAAD management and outcomes. The researchers used The Society of Thoracic Surgeons Adult Cardiac Surgery Database and enrolled 2 982 patients from 640 centres around north America who had received surgery for ATAAD between July 2011 and September 2012. There were 325 diabetic patients overall of which 59 used insulin and 266 did not. Diabetes was found to be a pre-operative risk factor for mortality (OR 1,48; CI 95 % (1,08-2,03); P = 0,0153). [16]

Pompilio et al. studied the determinants of early and late outcome after surgery for type A aortic dissection. 110 patients, who underwent surgery for spontaneous type A aortic dissection in a single centre, were enrolled. 87 out of 110 were discharged, and 23 had an in-hospital death. A total of 20 patients had diabetes. Univariate analysis found a correlation between insulin dependent diabetes and in-hospital mortality. 12 patients (13,7 %) with diabetes were discharged, 8 patients (34,7 %) had an in-hospital death (P = 0,03). However, multivariate analysis showed no statistical significance between diabetes and in-hospital death. [17]

Dumfarth et al. studied the relationship between immediate surgery in ATAAD and neurologic dysfunction. The researchers conducted a review of an institutional database and enrolled 338 patients with ATAAD between 2000 and 2017. While diabetes (n = 26) seemed to not be a risk factor for new postoperative neurologic injuries (OR 1,196; CI 95 % (0,429-3,335); P = 0,732), it did correlate with a higher 30-day mortality rate (OR 3,275; CI 95 % (1,405-7,632); P = 0,006). [18]

Niu et al. studied metabolic syndrome and its association with acute type B aortic dissection (ATBAD) after a thoracic endovascular aortic repair. In this paper metabolic syndrome (MetS) is defined as per the American National Cholesterol Education Program criteria, as the presence of 3 or more of the following: BMI > 30 kg/m², fasting plasma triglyceride > 150 mg/dL, HDL < 50 mg/dL for women and < 40 mg/dL for men, fasting blood glucose > 100 mg/dL, systolic blood pressure > 130 mmHg, diastolic blood pressure > 85 mmHg, and previously diagnosed type 2 diabetes. 683 patients with acute type B aortic dissection who underwent thoracic endovascular aortic repair were enrolled between January 2015 and January 2021. Patients without in-hospital complications were enrolled into the no complications group, and those with in-hospital complications were enrolled into the poor outcome group. The in-hospital complications encompassed various categories, including all-cause death and complications related to deployment, implantation, and systemic factors. These complications comprised endograft migration or infection, ruptured aneurysms, erosion of the device through the walls of the aorta or iliac arteries, obstruction of endograft limbs during the operation, intraoperative bleeding requiring transfusion, haematoma at the access site, aortic dissection, dissection or thrombosis of the access artery, arterial perforation or rupture, and the development of false aneurysms. Additionally, complications such as cerebrovascular events, pulmonary issues, cardiac problems, and renal insufficiency were also

observed during the in-hospital period. Based on the number of MetS diagnostic components, the patients were categorized into six groups. These groups consisted of 32 (4.7 %) (group 0), 244 (35.7 %) (group 1), 244 (35.7 %) (group 2), 121 (17.7 %) (group 3), 35 (5.1 %) (group 4), and 8 (1.1 %) (group 5). Diabetes was found to be a factor for in-hospital complications overall (poor outcome 24/90; no complications 77/594; $P = 0,001$), MetS (poor outcome 18/44; no complications 26/120; $P = 0,014$), and non-MetS (poor outcome 6/46; no complications 51/474; $P = 0,636$), as well as fasting plasma glucose overall (poor outcome 39/90; no complications 185/594; $P = 0,022$), MetS (poor outcome 32/44; no complications 83/120; $P = 0,659$), and non-MetS (poor outcome 7/46; no complications 102/474; $P = 0,316$). When divided into the six MetS groups diabetes was found to have a significant connection: group 0 (0/32), group 1 (13/244), group 2 (44/244), group 3 (27/121), group 4 (13/35), group 5 (4/8), $P < 0,001$. When individual MetS components were compared regarding in-hospital complications, diabetes was found to be a significant factor (poor 24/101; good 77/101; OR 2,135 CI 95 % (1,192-3,824); $P = 0,011$). When fasting plasma glucose level was studied individually no statistical significance was found with the exception of $5,12 < x \leq 5,49$ mg/dL level (poor 14/173; good 159/173; OR 0,422 CI 95 % (0,191-0,931); $P = 0,033$). Multivariate analysis of the individual MetS components showed a correlation with fasting plasma glucose levels (OR 1,602 CI 95 % (0,985-2,605); $P = 0,057$). However, it should be kept in mind that this study focuses on ATBAD and not ATAAD, but it is in keeping with ATAAD research and should be noted. [19]

Helder et al. aimed to study the relationship between ascending aorta-only operations versus those including the arch. A database query was done at the Society of Thoracic Surgeons database searching for patients who underwent ATAAD surgery between 2004 and 2016. Patients were divided into two groups according to the magnitude of the aortic resection: ascending aorta only, or ascending aorta and partial or total arch replacement. A total of 25 462 patients were enrolled. Patient distribution in the two groups was 13 741 and 11 721 of ascending aorta only and any arch procedure, respectively. Univariate and multivariate analysis yielded a result, which indicated an increased 30-day mortality with diabetes (OR 1,43; CI 95 % (1,29-1,58)) and (OR 1,25; CI 95 % (1,11-1,40)), respectively. They also reviewed the updated database from July 1, 2014, to December 31, 2016. Updates to the database included additional information on arch procedures and circulatory arrest. Between 2014 and 2016 diabetic patients undergoing circulatory arrest had a higher 30-day mortality in univariate and multivariate analysis (OR 1,45; CI 95 % (1,21-1,73)) (OR 1,20; CI 95 % (0,97-1,47)), respectively, though multivariate analysis did not reach statistical significance. [20]

Ong et al. aimed to validate that severe acidosis with or without malperfusion is a notable predictor of operative mortality in patients with ATAAD. A single centre database was used to extract the necessary data from 1997 to 2018. In addition, supplementary data was obtained from electronic

medical records to gather patient laboratory values for 2 weeks prior surgery. A total of 298 patients underwent surgical repair for ATAAD, 33 of which had diabetes (11,2 %). No comorbidities in patients with diabetes were stated. Univariate analysis found diabetes to be a risk factor for operative mortality. Similarly, multivariate logistics regression analysis identified diabetes as a risk factor (OR 4,2; CI 95 % (1,3-13,3); P = 0,015). [21]

Lannacone et al. studied how malperfusion in ATAAD patients influence different outcomes. A single centre database search was performed. A total of 336 patients underwent surgery for ATAAD between 1997 and 2019. 239 patients had no evidence of malperfusion, in contrast, to the 97 who had. Diabetes was not a risk factor for the incidence of malperfusion (overall 47/336 (14,5 %); no malperfusion 37/239 (16,2 %); malperfusion 10/97 (10,4 %); P = 0,237). In both univariate and multivariate analysis, diabetes was found to be a risk factor for adverse events which included operative mortality, myocardial infarction, cerebrovascular incidents, dialysis, and tracheostomy (univariate analysis: OR 3,39; CI 95 % (1,53–7,25); P = 0,002; multivariate analysis: OR 3,17; CI 95 % (1,28–7,85); P = 0,013). Operative mortality was characterized as the mortality rate that encompassed both in-hospital deaths and deaths occurring within 30 days of the operation. [22]

3.22 No correlation

Howard et al. found no difference between groups of immediate death and survived to admission in diabetic patients (1/18 (5,6 %); 2/19 (10,5 %); P = 1,00) [12]. Neither did He et al. find any statistical difference between diabetic and non-diabetic patients. Mortality in diabetic and non-diabetic patients (223/2058, 14/102, P = 0,333), (167/836, 8/25, P = 0,203), (56/1222, 6/77, P = 0,261) for overall, type A, and type B, respectively. [10]

Lin et al. aimed to study admission hyperglycaemia as a prognostic factor for ATAAD. 820 patients who underwent ATAAD repair between January 2014 and June 2020 were enrolled. 86 were excluded, interestingly, 32 diabetic patients among them. After exclusion criteria were utilised, 734 patients were accepted into the study. Excluding criteria included diabetes, autoimmune disease, fever, tumour, steroid or another immunosuppressant recipient. Hyperglycaemia was defined as admission blood glucose > 140 mg/dL. Regardless of the admission plasma glucose criteria, normal blood glucose group had significantly lower glucose levels than the hyperglycaemic group: 100,62 (95,22-116,64) and 157,14 (148,32-190,25), respectively. 531 (72,3 %) patients had normal blood glucose levels and 203 (27,7 %) had hyperglycaemia. The study found no correlation between the two groups and in-hospital mortality (normal blood glucose group: 108/531 (20,3 %); hyperglycaemia group 47/203 (23,2 %); P = 0,403). This study also covered some other in-hospital outcome differences between the two groups such as acute kidney injury and pulmonary infection, but found no statistical difference between the two groups. [23]

Ogami et al. performed a national database analysis with a focus on proximal aortic repair in dialysis patients. They used The United States Renal Data System to search for patients who received dialysis for end-stage renal disease and underwent proximal aortic replacement between April 1987 and August 2015. A total of 726 patients were identified 461 of which had an aortic dissection. 57 patients overall had diabetes 41 of which survived. They excluded renal transplant recipients, non-dialysis patients on the renal transplant waiting list, individuals below 18 years of age, and those who had dialysis induction after surgery. Perioperative mortality was defined as occurrence of in-hospital or 30-day mortality. No correlation was found in multivariate analysis between diabetes and perioperative mortality (OR 1,4; CI 95 % (0,8-2,4); P = 0,24). Nor did the univariate analysis find any statistical significance between diabetes and perioperative mortality (OR 1,46; CI 95 % (0,72-2,87); P = 0,3). [25]

3.3 Late mortality

3.31 Negative correlation

Brown et al. studied the impact of prior versus first-time sternotomy in ATAAD. The study used an observational single centre database between 2007 and 2021. A total of 601 patients with ATAAD were enrolled. 529 had a first-time sternotomy versus 72 had a reoperative sternotomy. No specific data regarding diabetes and follow-up times are given, however, median follow-up time was 4,6 years. Overall survival rate was lower in patients with diabetes (HR 1,94; CI 95 % (1,27-2,96); P = 0,002). [19]

3.32 Positive correlation

In the study by Avdic et al. type 2 diabetes patients exhibited higher unadjusted survival rates following aortic dissection compared to control subjects at various time points. The survival rates for type 2 diabetes patients after hospitalization for aortic dissection were at 3 months, 77,86 % (CI 95 %; 72,43–82,35) at 1 year, 73,80 % (CI 95 %; 68,13–78,62) and at 2 years, 67,02 % (CI 95 %; 61,05–72,28). In contrast, the corresponding survival rates for control subjects were at 3 months, 72,98 % (CI 95 %; 71,17–74,70) at 1 year, 68,49 % (CI 95 %; 66,60–70,30) and at 2 years, 62,94 % (CI 95 %; 60,98–64,83). There was no significant difference in the risk of mortality after aortic dissection between the type 2 diabetes group and control subjects up to a period of 2 years, with an unaltered risk (HR 1,07; CI 95 % (0,85–1,34); P = 0,5859). [9]

3.4 Follow-up surgeries

In the study by Lau et al. diabetes was not found to be a factor for late reoperations (univariate analysis: HR 0,36; CI 95 % (0,05-2,70); P = 0,32; multivariate analysis: -). Reoperations consisted of the aortic valve, proximal aorta, and distal aorta operations. No specific mention is made about the timeframe of the late reoperations. [14]

3.5 Different surgical techniques and procedures regarding survival rate

Crawford et al. studied the relationship between ATAAD, specifically DeBakey type I, and the survivorship of ascending aorta only or arch-included procedures. From 1968 to May 1989, a total of 82 patients underwent surgery within 14 days following the onset of an acute aortic dissection affecting the ascending aorta. Seven patients had diabetes and the univariate analysis regarding 30-day survival rate showed no statistical significance (P = 0,13). The survival-rate between diabetic and non-diabetic patients in ascending aorta only replacing procedures mildly favoured the non-diabetic patients. In arch and ascending aorta replacement procedures the difference between the groups grew significantly, again favouring the non-diabetic patients. The cut-off point for both procedure extents was 14 years and the trend stayed the same throughout the entirety of the follow-up time. [18]

In the study by Lau et al. 47 patients had diabetes, 39 had conservative and 8 had an extensive procedure done (P = 0,07). When hemiarch and total arch procedures were compared no statistical difference was found between the two (hemiarch: 41/298; total arch: 6/45; P = 1,00). In contrast to the arch procedures, root-sparing and root replacement techniques had a significant difference in prevalence (root-sparing: 45/276; root replacement: 2/67; P = 0,007). This is likely because of root replacement is a more intricate procedure that necessitates considerably longer periods of bypass and cross-clamping times compared to root-sparing techniques. The author expressed a preference for reserving more extensive surgical interventions in the root and arch for lower-risk patients whom they believe have a higher likelihood of requiring future reoperation. [14]

3.6 Ventilator, cardiopulmonary bypass, and cross-clamping time

Lin et al. found a correlation with hyperglycaemia and prolonged mechanical ventilation (> 48 hours) 270/531 (53,3 %) and 121/203 (59,6 %) (P = 0,040), respectively. Hyperglycaemic group had longer cardiopulmonary bypass and aortic cross-clamping time (normal: 149,0 (125,0–185,0); hyperglycaemic: 158,0 (130,0–202,0) (minutes); P = 0,048) and (normal: 64,0 (4,0–96,0);

hyperglycaemic: 71,0 (50,0–107,0) (minutes); $P = 0,023$), respectively. Adjusted logistic regression analysis found no association between cardiopulmonary bypass and cross-clamping time with hyperglycaemic prolonged mechanical ventilation. (cardiopulmonary bypass time: OR 1,00; CI 95 % (0,097-1,004); $P = 0,896$) (cross-clamping time: OR 1,003; CI 95 % (0,998-1,008); $P = 0,185$). [23]

3.7 Dialysis and Acute kidney injury

Ogami et al. found in multivariate analysis that diabetes had a significant influence on 10-year dialysis mortality prevalence (HR 1,75; CI 95 % (1,2-2,57); $P = 0,004$). Univariate analysis also found a significance in perioperative dialysis mortality prevalence with diabetes (OR 2,94; CI 95 % (1,27-6,8); $P = 0,02$). [25]

Arnaoutakis et al. aimed to validate the relationship between postoperative acute kidney injury (AKI) and type A aortic dissection on in-hospital and long-term outcomes. Patients who underwent type A aortic dissection surgical repair from 2011 and 2021 were identified in the International Registry of Acute Aortic Dissection database. Patients younger than 18 years were not included in the database. 3 307 patients were identified. Diabetes had a significant post-operative AKI association (AKI: 102/761 (15,7 %); non-AKI; 251/2 546 (11,2 %); $P < 0,001$). Multivariate analysis showed similar results (OR 1,58; CI 95 % (1,05-2,39); $P = 0,03$). [26]

Chen et al. studied the risk factors for continuous renal replacement therapy (CRRT) and in-hospital mortality in patients with ATAAD. The researchers used a single centre database to collect medical records and laboratory results. They excluded the patients who had received kidney transplantation, had incomplete data, had received maintenance dialysis within the last month or were on dialysis before surgery, as well as those who had died within 24 h of admission to the hospital. 432 patients over 18 years of age, who underwent surgery for ATAAD between March 2009 and June 2021, were enrolled. Patients were divided into CRRT and non-CRRT groups. AKI definition Acute kidney injury was defined based on the KDIGO criteria: an increase in serum creatinine levels of over 0.3 mg/dl within 48 hours, or an over 1,5-fold rise from the baseline level, which is known or suspected to have occurred in the previous 7 days, or a urine output of less than 0.5 ml/kg/h for 6 consecutive hours. Diabetes was a significant factor for CRRT (non-CRRT 11/369 (3,0 %); CRRT 9/63 (14,3 %); $P = 0,000$). Multivariate analysis also indicated that diabetes was a significant risk factor for CRRT (OR 6,868; CI 95 % (2,182-21,621); $P = 0,001$). However, diabetic patients with CRRT had no statistical difference in survival rate (non-survivor 6/29 (20,7 %); survivor 3/34 (8,8 %); $P = 0,180$). [27]

3.8 Molecular and histological changes

Zhang et al. aimed to use single-cell RNA sequencing to distinguish macrophage heterogeneity in ATAAD tissues. A total of nine ascending aorta samples were collected consisting of six ATAAD and three heart transplant donor samples. A cell proportion analysis found that ATAAD group had a considerably higher proportion of macrophages (24,51 % vs 13,69 %) and a significantly lower proportion of endothelial cells (5,72 % vs 8,51 %), mesenchymal cells (2,38 % vs 4,70 %) and fibroblasts (10,92 % vs 16,13 %). A macrophage transcriptome analysis showed an increased expression of chemokines CCL2 (C-C Motif Chemokine Ligand 2), CCL20, S100A8 (S100 Calcium Binding Protein A8) and S100A9 in ATAAD tissues. A significant proportion of the genes that exhibited differential expression were linked to activities such as neutrophil degranulation, immune system processes, and regulation of transcription, including positive regulation of transcription by RNA polymerase II. Using the area under curve values of 33 regulons, the t-SNE dimensionality reduction analysis was conducted based on cell type and disease grouping. The findings revealed a higher presence of macrophage-related regulons in aortic dissection tissues than in normal tissues. The t-SNE plots, which were generated based on area under curve values, gene set activity, and expression, demonstrated a strong association between SPI1 and CEBPB, two crucial transcription factors, with macrophage activity. These observations suggest that SPI1 and CEBPB may play a role in the development of aortic wall lesions in aortic dissection tissue by promoting macrophage polarization and triggering their pro-inflammatory effects. The aortic macrophages were sorted into five subgroups based on different expressed genes. The proportions of pro-inflammatory macrophages (CXCL5, CXCL8, CCL7, PPBP), interferon-mediated macrophages (APOC1, APOE, LPL, FABP4, FABP5), and lipid-metabolism-related macrophages (IFI6, IFI44L, IFIT2, XAF1) were higher in ATAAD tissues. Genes involved in extracellular matrix repair, VCAN, FN1, and TIMP1 for instance, were found to be considerably more expressed in ATAAD tissue macrophages. Moreover, a reduction in communication between vascular smooth muscle cells and macrophages via fibronectin 1 was reduced. In addition, the interaction between fibronectin 1, which exists as a dimeric or multimeric form in the cell surface and extracellular matrix, and its receptor was observed to be weaker among smooth muscle cells in ATAAD tissue as compared to normal tissue. In ATAAD tissue, stronger ligand-receptor interactions were observed between macrophages and other major cells compared to normal tissue. The study identified that the communication between macrophages and T cells, endothelial cells, and smooth muscle cells in ATAAD tissues was predominantly linked to the increased binding of complement C5a receptor 1 to ribosomal protein S19. Matrix metalloproteinase 2 (MMP2) and MMP9 expression were increased in ATAAD tissues. The aortic dissection group showed a significant breakage of elastic and collagen fibres in the aortic wall tissue, along with a thickening of the intima, possibly indicating an ongoing inflammatory response and an increase in secretory units. Additionally, HE-staining

revealed that smooth muscle cells in the media of aortic dissection tissue had lost their regular arrangement order and complete cell morphology. Immunohistochemical staining for monocyte (CD14) and macrophage (CD68, CD86, and CD163) markers indicated a build-up of macrophages in the aortic wall tissue of the aortic dissection group. CD14 staining showed a significant increase in the concentration of monocytes in the intima, tear site of the media, and adventitia. Moreover, positive staining of macrophages was stronger in aortic dissection tissues than in normal tissues, as seen by the staining of CD68, CD86, and CD163. Further, four-plex multiplex immunofluorescence assay and protein blotting experiments verified the elevated expression levels of MMP9, MMP2, CD163, and CD68 in aortic dissection tissues. The fluorescence intensity of MMP9 and MMP2 was significantly higher in the ascending aortic wall of aortic dissection patients than in normal ascending aortic tissue, and the fluorescence was primarily concentrated in the intima (MMP9) and tear sites (MMP2) of the aortic wall of aortic dissection tissue. CD163 and CD68, the macrophage markers, were also expressed more strongly in aortic dissection tissues than in normal tissues. The Western blot analysis of protein extracted from ascending aorta tissue showed that the expression levels of MMP9, MMP2, CD163, and CD68 were higher in aortic dissection tissue than in normal aortic tissue. [28]

Golledge et al. focused on the impact of diabetes and glycation on the expansion of abdominal aortic aneurysm and the interactions between extracellular matrix and monocytes. This chapter will only focus on the extracellular matrix and monocyte interactions as abdominal aortic aneurysm is not a focal point in this review. They utilized a decellularized sheep aortic media to create a healthy aortic extracellular matrix model, and decellularized atherosclerotic media collected from patients undergoing an aortic bypass. Resting monocytes exhibited a slight increase in MMP-9 secretion but no changes in MMP-2 and interleukin 6 after being incubated with glycated monomer collagen. Meanwhile, activated monocytes showed no change in MMP secretion when exposed to glycated monomer collagen, but a significant decrease in MMPs and interleukin 6 secretion was observed when exposed to glycated collagen lattices. Moreover, activated monocytes and human peripheral blood monocytes exposed to glycated collagen lattices exhibited a marked reduction in MMP-9 secretion, along with a decrease in MMP-2 (for peripheral blood monocytes) and interleukin 6 (for monocytes) secretion. Cross-linked collagen lattices had similar effects as glycated collagen lattices on activated monocytes and peripheral blood monocytes, reducing MMP-9 and MMP-2 secretion markedly. [29]

Dua et al. conducted a study to investigate how hyperglycaemia affects the progression of abdominal aortic aneurysm (AAA) by examining the levels of plasminogen activator inhibitor-1 (PAI-1) and the subsequent reduction in the generation of plasmin. The method of inducing experimental AAA in mice through intra-aortic elastase infusion was used on both diabetic and control mice. In hyperglycaemic mice, PAI-1 expression was found to be increased both

systemically and within the aortic wall. Plasma PAI-1 levels were significantly higher in diabetic-AAA mice compared to AAA mice, both at baseline and after elastase infusion. Following elastase infusion, PAI-1 expression increased at post-operative day in both groups, but subsequent plasma levels returned to near baseline. Aortic PAI-1 gene expression was also increased in diabetic-AAA mice prior to elastase infusion. However, hyperglycaemia led to a reduction in aortic macrophage and MMP-9 expression. Immunohistochemical analysis showed that diabetic-AAA mice had a lower number of MAC-2 and MMP-9-stained cells per cross sectional area compared to AAA mice at 14 days post-operation. The combination of plasmin and α 2-antiplasmin forms a complex called PAP, which is commonly used to assess plasmin generation. In diabetic-AAA mice, PAP complexes were consistently lower compared to AAA mice at all time points following elastase infusion of AAA. [30]

Åstrand et al. studied the aortic wall stress in diabetic patients. The study involved 39 patients diagnosed with type 1 diabetes a mean age of 43,3 years. Additionally, there were 46 healthy controls who were matched in terms of age and sex with a mean age of 44,4 years. The controls did not smoke and had no family history of aneurysmal disease. They also had no previous history of cardio-pulmonary, cerebrovascular, or peripheral vascular disease and were not taking any prescription medication. Intima-media thickness in the abdominal aorta was larger by 22 % in diabetic patients ($P < 0,001$). A 20 % reduction in aortic wall stress was also observed ($P < 0,001$). [31]

Croccia et al. studied how different cardiovascular risk factors affect the thoracic aorta size in patients who had surgery for ATAAD. Electrocardiography-gated computed tomography angiography follow-up was conducted on 18 patients with a history of aortic repair. The mean age of the patients was 64 years. Measurements of aortic systolic and diastolic diameter and cross-sectional area were taken at four different levels: 1 cm proximal (level A) and 1 cm (B), 3 cm (C), and 10 cm (D) distal to the origin of the left subclavian artery. 7 patients had diabetes which was controlled with oral therapy. Significant differences in diameter and area change were observed only at level D in relation to diabetes. Among diabetic patients, the absolute diameter change at level D was 3.7 ± 3 mm ($P = 0,05$) with a percentage change of $10,4 \pm 6.8$ % ($P = 0,03$). In contrast, nondiabetic patients showed an absolute diameter change of $0,9 \pm 0,7$ mm, and a percentage change of $2,9 \pm 2$ %. Additionally, the percentage area change differences reached statistical significance, with a percentage area change of $21,5 \pm 12.8$ % among diabetic patients and $8,5 \pm 6.4$ % ($P = 0,04$) among nondiabetic patients. [32]

Zheng et al. studied insulin resistance and the prevalence of aortic dissection. The researchers used statistical analysis to determine the proportion of abnormally glycosylated haemoglobin (HbA1c $> 5,7$ %) in individuals with aortic dissection. They also compared the difference of mRNA

and protein expression of GLUT1 transporters between people with normal range of HbA1c and those with aortic dissection. Information from cardiac surgery patients with aortic dissection at a single centre between July 2017 and June 2020 were collected. Patient exclusion criteria included Marfan syndrome, aortic arteritis, type 1 diabetes, a history of syphilis, as well as no HbA1c testing upon admission. Out of the 3 185 participants identified, 552 patients fulfilled the criteria. Normal thoracic aorta tissue from heart transplant donors was discarded during the operation. The thoracic aorta tissues of the aortic dissection groups were obtained from the tissues removed during thoracic aortic replacement surgery. Among the patients, the percentages for different HbA1c levels were: HbA1c $\geq 6,5$ accounted for 8,7 %, HbA1c $< 5,7$ accounted for 41,67 %, and $6,5 > \text{HbA1c} \geq 5,7$ accounted for 49,64 %. Based on the diagnostic criteria for insulin resistance, it was determined that the majority of the patients with aortic dissection also exhibited insulin resistance. In order to elucidate the connection between aortic dissection and insulin resistance, they employed quantitative PCR to analyse the expression of GluT1 in vascular smooth muscle cells of the ascending aorta. The findings revealed a notable decrease in mRNA expression of GluT1 in patients with aortic dissection ($P < 0,0001$). By utilizing western blot technology, they further observed a significant reduction in GluT1 levels in thoracic aortic smooth muscle cells of aortic dissection patients compared to individuals without the condition ($P < 0,01$). Additionally, immunofluorescence experiments confirmed the reduction of GluT1 in aortic dissection patients. [33]

Zheng et al. also created two mouse (*apoE^{-/-}*) groups by random division of all mice, with one group being fed a normal diet (control group) while the other group was given a 60% high-fat diet. Aortic dissection was induced with beta-aminopropionitrile, which is an agent to induce thoracic aortic dissections, as well as angiotensin II infusion [34]. Out of the 14 mice in the insulin resistance group, 13 were found to have aortic dissection, and 8 of those had already succumbed to aortic dissection before the administration of angiotensin-II. Meanwhile, in the normal diet group, 6 out of 14 mice were diagnosed with aortic dissection, and 2 of them had died due to aortic dissection prior to the implantation of the angiotensin-II pump. The insulin resistant group of mice showed a higher number of smooth muscle cells with a disordered arrangement and thinner basement membranes when compared to the control group. Additionally, the extracellular matrix was found to be increased, while the elastic fibre layer exhibited smaller, fragmented fibres with reduced thickness. Furthermore, the density of collagen fibres was observed to be higher in the insulin resistant group. In the insulin resistant group, the protein expression of osteopontin, MMP2, and MMP9 was found to be significantly higher $P < 0,05$, $P < 0,01$, $P < 0,001$, respectively, while that of transgelin and alpha smooth muscle actin was significantly lower $P < 0,01$, $P < 0,01$, respectively. [33]

3.9 Neurological dysfunction

Eusanio et al. studied different cannulation strategies on in-hospital outcomes with aortic arch surgery. 473 patients overall had an aortic arch operation in a single centre between November 1996 to March 2011. 8 diabetic patients had a central cannulation and 14 had femoral cannulation. Multivariate analysis found diabetes to be an independent predictor of permanent neurologic dysfunction (OR 6,6; P = 0,007). [35]

Haldenwang et al. studied pre- and intraoperative factors leading to neurologic complications and early mortality following ATAAD surgery. 122 patients, with a mean age of 58,6 years, underwent ATAAD surgery in a single centre from 2003 to 2010. 16 patients had diabetes (13,1 %). Univariate analysis did not find a statistical correlation between diabetes and postoperative temporary neurologic dysfunction (P = 0,088). Multivariate analysis, on the other hand, found diabetes to be a risk factor for temporary neurologic dysfunction (OR 3,95; CI 95 % (1,18–13,24); P = 0,026). [36]

Dumfarth et al. did not find diabetes to be a risk factor for new postoperative neurologic injuries (OR 1,196; CI 95 % (0,429-3,335); P = 0,732), nor did they find any statistical significance between diabetes and preoperative neurologic dysfunction (with preoperative neurologic dysfunction: 5/50 (10 %); without preoperative neurologic dysfunction: 21/288 (7,3 %); P = 0,507). [18]

Helder et al. found no correlation between permanent postoperative stroke and diabetes neither in the univariate nor the multivariate analysis (univariate: OR 1,00; CI 95 % (0,86-1,17); multivariate: OR 1,03; CI 95 % (0,87-1,21)). The same trend continues in the updated database between the years 2014-2016 (univariate: OR 1,11; CI 95 % (0,86-1,43); multivariate: OR 1,14; CI 95 % (0,86-1,50). [20]

4 DISCUSSION

While relatively little research has been made regarding diabetes and ATAAD, both subjects have received a fair amount of research independently, especially diabetes. As the prevalence of diabetes is constantly rising, the possible complications coming along with it should be further studied and identified [6]. While diabetes is a well-known risk factor for cardiovascular diseases, it seems that diabetes and potential hyperglycaemia may reduce the prevalence of aortic dissections [3,7-11].

Although the literature on the relationship between diabetes and ATAAD is scarce, certain conclusions can be made. Firstly, it seems diabetic patients have a lower prevalence of ATAAD than patients without it [7-11]. Secondly, early mortality seems to be higher with diabetic individuals [13-22]. Thirdly, dialysis and AKI prevalence seems to rise with diabetics [26,27]. Other information regarding their relationship seems inconclusive and requires further research.

Overall, it would seem that diabetes lowers the prevalence of ATAAD. Even raised fasting plasma glucose levels have a protective function in the ATAAD pathogenesis. Though the mechanisms in the pathogenesis are somewhat elusive, there are some interesting characteristics. Such as the increased aortic media thickness [31]. And the activated monocytes having significant decrease in MMPs and interleukin 6 secretion when exposed to glycated collagen lattices [29]. Regardless, it should be noted that even in this review, the pathogenesis is controversial, and some research findings contraindicate others.

When it comes to mortality, evidence is more conclusive. Diabetes raises the odds for unfavourable outcomes at least in the short term [13-22]. The evidence for long-term negative outcomes remains inconclusive, much of it is for the reason of insufficient amount of research on that area [9,19]. Dialysis and AKI have a longer duration and higher prevalence in diabetic patients overall [26,27]. Even dialysis induced mortality was raised in diabetic patients [25]. Furthermore, there is no clear consensus whether diabetes induces neurological dysfunction in ATAAD patients [18,20,35,36]. Moreover, there is no evidence that diabetes is a risk factor for reoperations. One study found that diabetic patients have significantly fewer root replacement surgeries. The authors' surgical doctrine regarding this is that extensive surgeries should be saved for those who are lower-risk patients whom the author believes to have a higher likelihood of requiring future reoperation. This may indicate that the diabetic patients are in worse condition overall or that for any number of reasons diabetic patients have not needed an extensive surgery. [14] Additionally, hyperglycaemia may increase the prevalence of prolonged mechanical ventilation, as well as lengthen the cardiopulmonary bypass and aortic cross-clamping times [23].

Initial search did not provide sufficient amount of information regarding the molecular and histological changes which occur in dissection pathological processes in diabetic patients, and thus this information needed to be found later on. Presently, the pathological process is not fully understood, however, there are interesting factors which contribute to aortic remodelling and thus possible dissections. Most of the research have been done with aortic aneurysm in mind, nevertheless, some research has also been directed on aortic dissection. Though, it needs to be addressed that while the mechanisms that contribute to the pathological formation of aneurysms have something in common with dissections, such as an increase in MMP expression for instance, these two diseases are not the same and should be kept separate to a certain extent [28,29,33].

The prevalence of diabetes is rising globally [6]. Furthermore, aging population in many developed countries may increase the prevalence of ATAAD [1]. When both are increasing in prevalence, it is vitally necessary that the relationship between the two is studied and addressed. Gaining better understanding of their possible correlation, may open new areas for possible treatment and prevention. Finally, there has been quite a bit more research done on prevalence and mortality compared to the differences in surgical techniques, for instance. Though, the number of studies in these areas may be greater, it is still very little, and they need to be studied further.

TABLES

Article	Sample size	Findings	Issues and comments
Prevalence / positive correlation			
Prakash et al. 2014	<p>2006: 8 877 patients with TAAAD, and 27 069 control subjects.</p> <p>2007: 6 825 TAAAD patients, and 22 463 control subjects</p>	<p>2006 NIS data: TAAAD cases were 40% less likely to have diabetes mellitus than control subjects. After correcting for clinical risk factor differences, diabetes remained inversely associated with TAAAD (OR 0,48; CI 95 % (0,44–0,52)). In their model the only predictive factors, which were more significant than diabetes, were Marfan syndrome, valvular disease, and hypertension. The relationship between diabetes and TAAAD was slightly weaker in women than in men was also found (OR 0,66 vs. 0,52). Interestingly, those with chronic diabetic complications were less likely to have TAAAD (OR 0,17; CI 95 % (0,12–0,23)) compared to those with diabetes without chronic complications. 2007 NIS data: they found an inverse association between diabetes and TAAAD (OR 0,47; CI 95 % (0,43–0,51)). In addition, subjects with complicated diabetes had significantly lower prevalence of TAAAD (OR 0,26; CI 95 % (0,20–0,35)) than amongst subjects with uncomplicated diabetes (OR 0,50; CI 95 % (0,45-0,54)).</p>	

Suzuki et al. 2022	Normal fasting plasma glucose (n = 2 736 285) Prediabetes (n = 568 501) Diabetes (n = 53 507)	After fasting plasma glucose exceeded 100 mg/dl the risk for aortic dissection started to decrease. Even people with stage 2 hypertension (systolic blood pressure \geq 140 mmHg or diastolic blood pressure \geq 90 mmHg) when combined with an increased fasting plasma glucose showed notable decrease in dissection prevalence (normal fasting plasma glucose: HR 6,70; CI 95 % (5,62-7,98); diabetes: HR 2,90; CI 95 % (1,75-4,79)). When aortic dissection prevalence was compared with normal blood pressure and different fasting plasma glucose levels, HRs for normal fasting plasma glucose and diabetes were 1,00 (reference) and 0,77 (CI 95 % (0,28-2,07)), respectively. Indicating a lower aortic dissection prevalence with increased fasting plasma glucose levels.	People with a history of cardiovascular disease and those using blood pressure or glucose-lowering medication were excluded.
Avdic et al. 2018	Type 2 diabetes n = 448 319, control subject group n = 2 251 015	The risk for aortic dissection was significantly lower in individuals with type 2 diabetes (HR 0,53; CI 95 % (0,42- 0,65); P < 0,05). Throughout follow-up, there were 200 hospitalizations attributable to aortic dissection amid patients with type 2 diabetes compared to 2019 among the control subjects. The unadjusted prevalence of aortic dissection was 5,6 per 100 000 person-years amid patients with type 2 diabetes and 11,2 per 100 000 person-years amid the control subjects.	
He et al. 2015	2 160 aortic dissection patients and 4 320 control subjects	Overall prevalence of diabetes in control subjects and aortic dissection patients were (434/4 320, (10,0%) vs 102/2 160, (4,7 %), P < 0,001). Likewise, the prevalence of diabetes in type A and type B groups were lower than that of control A and control B groups (8,8 % vs. 2,9 % and 10,9 % vs. 5,9 %, P < 0,001).	Traumatic or iatrogenic aortic dissections were excluded, as well as subjects with prior aortic dissections.

Yeh et al. 2012	The patients were divided into two groups: above 65 years of age (elderly) (n = 38; 45,8 %) and the non-elderly group (n = 45; 54,2 %).	Elderly group had higher prevalence of hyperglycaemia (8 (17,8 %) vs 0 (0 %), P < 0,01) and type I acute aortic dissection (20 (44,4 %) vs 15 (39,5 %), P < 0,01).	There is no specific statistics about the correlation of diabetes and acute aortic dissection
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No correlation			
Howard et al. 2013	Among the 52 incident dissections, 37 (71.2%) were classified as Stanford type-A, and 15 (28.8%) as type-B. Six had diabetes.	Among the 52 patients with dissections, six had diabetes, but the statistical analysis (P = 1.00) did not indicate a significant association. Additionally, among the diabetic individuals, three had type-A dissection (out of 37 type-A patients) and three had type-B dissection (out of 15 type-B patients), with a p- value of 0,34.	It should be noted that the diabetic sample size is severely limited, and thus the utility of the study is questionable.

Early mortality / negative correlation			
Spirito et al. 2001	108 patients	Univariate analysis found that 12 discharged patients (13,9 %) and 8 who died in the hospital (36,3 %) had diabetes (P = 0,03). However, multivariate analysis found no correlation between diabetes and type A aortic dissection.	Old study (From January 1985 to June 1998)
Lau et al. 2022	343 patients of which 47 had diabetes	Univariate analysis for diabetes and major adverse events shows a significant correlation between the two (OR 3,39; CI 95 % (1,53-7,25); P < 0,01). Multivariate analysis strengthens the univariate analysis' result (OR 2,65; CI 95 % (1,08-6,26); P = 0,03).	This study did not differentiate between operative mortality or other adverse events including, myocardial infarction, cerebrovascular accidents.
Yang et al. 2021	703 patients of which 22 had diabetes	Univariate analysis did not reach statistical significance (22/703 (3,13 %); OR 1,39; CI 95 % (0,59-3,31); P = 0,452). An analysis of diabetes and systolic blood pressure rise per 10 increments was made and it was found that admission systolic blood pressure in non- diabetics had a higher association with in-hospital mortality (non-diabetic: 681/703; OR 0,90; CI 95 % (0,85-0,95); diabetic 22/703; OR 1,37; CI 95 % (0,94-2,01); P = 0,020).	
Lee et al. 2018	2 982 patients of which 325 had diabetes and 59 of them used insulin	Diabetes was found to be a pre-operative risk factor for mortality (OR 1,48; CI 95 % (1,08-2,03); P = 0,0153).	

Pompilio et al. 2001	110 patients of which 20 had diabetes	Univariate analysis found a correlation between insulin dependent diabetes and in-hospital mortality. 12 patients (13,7 %) with diabetes were discharged, 8 patients (34,7 %) had an in-hospital death (P = 0,03). However, multivariate analysis showed no statistical significance between diabetes and in-hospital death.	A discrepancy in diabetic patient number
Dumfarth et al. 2020	338 patients of which 26 had diabetes	While diabetes seemed to not be a risk factor for new postoperative neurologic injuries (OR 1,196; CI 95 % (0,429- 3,335); P = 0,732), it did correlate with a higher 30-day mortality rate (OR 3,275; CI 95 % (1,405- 7,632); P = 0,006).	
Niu et al. 2023	683 patients with ATBAD who underwent thoracic endovascular aortic repair	Diabetes was found to be a factor for in-hospital complications overall (poor outcome 24/90; no complications 77/594; P = 0,001), MetS (poor outcome 18/44; no complications 26/120; P = 0,014), and non-MetS (poor outcome 6/46; no complications 51/474; P = 0,636), as well as fasting plasma glucose overall (poor outcome 39/90; no complications 185/594; P = 0,022), MetS (poor outcome 32/44; no complications 83/120; P = 0,659), and non-MetS (poor outcome 7/46; no complications 102/474; P = 0,316). When divided into the six MetS groups diabetes was found to have a significant connection: group 0 (0/32), group 1 (13/244), group 2 (44/244), group 3 (27/121), group 4 (13/35), group 5 (4/8), P < 0,001. When individual MetS components were compared regarding in-hospital complications, diabetes was found to be a significant factor (poor 24/101; good 77/101; OR 2,135 CI 95 % (1,192-3,824); P = 0,011). When fasting plasma glucose level was studied individually no statistical significance was found with the exception of 5,12 < x ≤ 5,49 mg/dL level (poor 14/173; good 159/173; OR 0,422 CI 95 % (0,191-0,931); P = 0,033). Multivariate analysis of the individual MetS components showed a correlation with fasting plasma glucose levels (OR 1,602 CI 95 % (0,985- 2,605); P = 0,057).	Focuses on ATBAD treated with thoracic endovascular aortic repair

Helder et al. 2020	25 462 patients. 13 741 and 11 721 of ascending aorta only and any arch procedure, respectively.	<p>Univariate and multivariate analysis yielded a result, which indicated an increased 30-day mortality with diabetes (OR 1,43; CI 95 % (1,29-1,58)) and (OR 1,25; CI 95 % (1,11-1,40)), respectively.</p> <p>They also reviewed the updated database from July 1, 2014, to December 31, 2016. Updates to the database included additional information on arch procedures and circulatory arrest. Between 2014 and 2016 diabetic patients undergoing circulatory arrest had a higher 30-day mortality in univariate and multivariate analysis (OR 1,45; CI 95 % (1,21-1,73)) (OR 1,20; CI 95 % (0,97-1,47)), respectively, though multivariate analysis did not reach statistical significance.</p>	No specific mention is made about the number diabetic patients
Ong et al. 2020	298 patients of which 33 had diabetes	Univariate analysis found diabetes to be a risk factor for operative mortality. Similarly, multivariate logistics regression analysis identified diabetes as a risk factor (OR 4,2; CI 95 % (1,3-13,3); P = 0,015).	
Lannacone et al. 2020	336 patients of which 47 had diabetes	In both univariate and multivariate analysis, diabetes was found to be a risk factor for adverse events which included operative mortality, myocardial infarction, cerebrovascular incidents, dialysis, and tracheostomy (univariate analysis: OR 3,39; CI 95 % (1,53–7,25); P = 0,002; multivariate analysis: OR 3,17; CI 95 % (1,28–7,85); P = 0,013).	

No correlation			
Howard et al. 2013	Among the 52 incident dissections, 37 (71.2%) were classified as Stanford type-A, and 15 (28.8%) as type-B. Six had diabetes.	No difference between groups of immediate death and survived to admission in diabetic patients (1/18 (5,6 %); 2/19 (10,5 %); P = 1,00)	
He et al. 2015	2 160 aortic dissection patients and 4 320 control subjects	Mortality in diabetic and non-diabetic patients (223/2058, 14/102, P = 0,333), (167/836, 8/25, P = 0,203), (56/1222, 6/77, P = 0,261) for overall, type A, and type B, respectively.	
Lin et al. 2022	734 patients	The study found no correlation between the two groups and in-hospital mortality (normal blood glucose group: 108/531 (20,3 %); hyperglycaemia group 47/203 (23,2 %); P = 0,403).	No diabetic patients were included
Ogami et al. 2021	726 patients were identified of which 461 had an aortic dissection. 57 patients overall had diabetes of which 41 survived	No correlation was found in multivariate analysis between diabetes and perioperative mortality (OR 1,4; CI 95 % (0,8-2,4); P = 0,24). Nor did the univariate analysis find any statistical significance between diabetes and perioperative mortality (OR 1,46; CI 95 % (0,72-2,87); P = 0,3).	

Late mortality / negative correlation			
Brown et al. 2022	601 patients with ATAAD 529 had a first-time sternotomy versus 72 had a reoperative sternotomy. (the number of diabetic patients is not specified)	Overall survival rate was lower in patients with diabetes (HR 1,94; CI 95 % (1,27-2,96); P = 0,002).	No specific data regarding diabetes and follow-up times are given, however, median follow-up time was 4,6 years.

Positive correlation			
Avdic et al. 2018	Type 2 diabetes: n = 448 319, control subject group: n = 2 251 015	The survival rates for type 2 diabetes patients after hospitalization for aortic dissection were at 3 months, 77,86 % (CI 95 %; 72,43–82,35) at 1 year, 73,80 % (CI 95 %; 68,13–78,62) and at 2 years, 67,02 % (CI 95 %; 61,05–72,28). In contrast, the corresponding survival rates for control subjects were at 3 months, 72,98 % (CI 95 %; 71,17–74,70) at 1 year, 68,49 % (CI 95 %; 66,60–70,30) and at 2 years, 62,94 % (CI 95 %; 60,98–64,83). There was no significant difference in the risk of mortality after aortic dissection between the type 2 diabetes group and control subjects up to a period of 2 years, with an unaltered risk (HR 1,07; CI 95 % (0,85–1,34); P = 0,5859).	

Follow-up surgeries			
Lau et al. 2022	343 patients of which 47 had diabetes	Diabetes was not found to be a factor for late reoperations (univariate analysis: HR 0,36; CI 95 % (0,05-2,70); P = 0,32; multivariate analysis: -)	

Different surgical techniques			
Crawford et al. 1992	82 patients of which 7 had diabetes	The univariate analysis regarding 30-day survival rate showed no statistical significance (P = 0,13). The survival-rate between diabetic and non-diabetic patients in ascending aorta only replacing procedures mildly favoured the non-diabetic patients. In arch and ascending aorta replacement procedures the difference between the groups grew significantly, again favouring the non-diabetic patients. The cut-off point for both procedure extents was 14 years and the trend stayed the same throughout the entirety of the follow-up time.	The cut-off point for both procedure extents was 14 years and the trend stayed the same throughout the entirety of the follow-up time. The number of patients in this study was quite limited, however, it is in keeping with many of the larger sample size studies.
Lau et al. 2022	47 patients had diabetes, 39 had conservative and 8 had an extensive procedure done	When hemiarch and total arch procedures were compared no statistical difference was found between the two (hemiarch: 41/298; total arch: 6/45; P = 1,00). In contrast to the arch procedures, root-sparing and root replacement techniques had a significant difference in prevalence (root-sparing: 45/276; root replacement: 2/67; P = 0,007).	

Ventilator, cardiopulmonary bypass, and cross clamping time			
Lin et al. 2022	734 patients	<p>A correlation with hyperglycaemia and prolonged mechanical ventilation (> 48 hours) 270/531 (53,3 %) and 121/203 (59,6 %) (P = 0,040), respectively. Hyperglycaemic group had longer cardiopulmonary bypass and aortic cross-clamping time (normal: 149,0 (125,0–185,0); hyperglycaemic: 158,0 (130,0–202,0) (minutes); P = 0,048) and (normal: 64,0 (4,0–96,0); hyperglycaemic: 71,0 (50,0–107,0) (minutes); P = 0,023), respectively. Adjusted logistic regression analysis found no association between cardiopulmonary bypass and cross-clamping time with hyperglycaemic prolonged mechanical ventilation. (cardiopulmonary bypass time: OR 1,00; CI 95 % (0,097-1,004); P = 0,896) (cross-clamping time: OR 1,003; CI 95 % (0,998-1,008); P = 0,185).</p>	

Dialysis and AKI			
Ogami et al. 2021	726 patients were identified of which 461 had an aortic dissection. 57 patients overall had diabetes of which 41 survived	Multivariate analysis that diabetes had a significant influence on 10-year dialysis mortality prevalence (HR 1,75; CI 95 % (1,2-2,57); P = 0,004). Univariate analysis also found a significance in perioperative dialysis mortality prevalence with diabetes (OR 2,94; CI 95 % (1,27-6,8); P = 0,02).	
Arnaoutakis et al. 2022	3 307 patients overall. 102 out of 761 AKI patients had diabetes. 251 out of 2 546 non-AKI patients had diabetes	Diabetes had a significant post-operative AKI association (AKI: 102/761 (15,7 %); non-AKI; 251/2 546 (11,2 %); P < 0,001). Multivariate analysis showed similar results (OR 1,58; CI 95 % (1,05-2,39); P = 0,03).	
Chen et al. 2021	432 patients. Diabetics: non-CRRT 11/369 (3,0 %); CRRT 9/63 (14,3 %)	Diabetes was a significant factor for CRRT (non-CRRT 11/369 (3,0 %); CRRT 9/63 (14,3 %); P = 0,000). Multivariate analysis also indicated that diabetes was a significant risk factor for CRRT (OR 6,868; CI 95 % (2,182-21,621); P = 0,001). However, diabetic patients with CRRT had no statistical difference in survival rate (non-survivor 6/29 (20,7 %); survivor 3/34 (8,8 %); P = 0,180).	

Molecular and histological changes			
Zhang et al. 2023	A total of nine ascending aorta samples were collected consisting of six ATAAD and three heart transplant donor samples	A cell proportion analysis found that ATAAD group had a considerably higher proportion of macrophages (24,51 % vs 13,69 %) and a significantly lower proportion of endothelial cells (5,72 % vs 8,51 %), mesenchymal cells (2,38 % vs 4,70 %) and fibroblasts (10,92 % vs 16,13 %). A macrophage transcriptome analysis showed an increased expression of chemokines CCL2 (C-C Motif Chemokine Ligand 2), CCL20, S100A8 (S100 Calcium Binding Protein A8) and S100A9 in ATAAD tissues. The aortic dissection group showed a significant breakage of elastic and collagen fibres in the aortic wall tissue, along with a thickening of the intima, possibly indicating an ongoing inflammatory response and an increase in secretory units. HE- staining revealed that smooth muscle cells in the media of aortic dissection tissue had lost their regular arrangement order and complete cell morphology. The expression levels of MMP9, MMP2, CD163, and CD68 were higher in aortic dissection tissue.	
Golledge et al. 2008	No specific sample size in given for the aortic samples	Resting monocytes exhibited a slight increase in MMP-9 secretion, but no changes in MMP-2 and interleukin 6 after being incubated with glycated monomer collagen. Activated monocytes showed no change in MMP secretion when exposed to glycated monomer collagen, but a significant decrease in MMPs and interleukin 6 secretion was observed when exposed to glycated collagen lattices. Activated monocytes and human peripheral blood monocytes exposed to glycated collagen lattices exhibited a marked reduction in MMP-9 secretion, along with a decrease in MMP-2 (for peripheral blood monocytes) and interleukin 6 (for monocytes) secretion. Cross-linked collagen lattices had similar effects as glycated collagen lattices on activated monocytes and peripheral blood monocytes, reducing MMP-9 and MMP-2 secretion markedly.	

Dua et al. 2010	16 hyperglycaemic mice and 16 normal glycaemic mice	In hyperglycaemic mice, plasminogen activator inhibitor-1 (PAI-1) expression was found to be increased both systemically and within the aortic wall. Plasma PAI-1 levels were significantly higher in diabetic abdominal aortic aneurysm (AAA) mice compared to AAA mice, both at baseline and after elastase infusion. Following elastase infusion, PAI-1 expression increased at post-operative day in both groups, but subsequent plasma levels returned to near baseline. Aortic PAI-1 gene expression was also increased in diabetic-AAA mice prior to elastase infusion. However, hyperglycaemia led to a reduction in aortic macrophage and MMP-9 expression. Immunohistochemical analysis showed that diabetic-AAA mice had a lower number of MAC-2 and MMP-9-stained cells per cross sectional area compared to AAA mice at 14 days post-operation. In diabetic-AAA mice, PAP complexes were consistently lower compared to AAA mice at all time points following elastase infusion of AAA.	
Åstrand et al. 2007	39 diabetes type 1 patients and 46 healthy controls	Intima-media thickness in the abdominal aorta was larger by 22 % in diabetic patients (P < 0,001). A 20 % reduction in aortic wall stress was also observed (P < 0,001).	
Croccia et al. 2013	18 patients. 7 patients had diabetes which was controlled with oral therapy	Among diabetic patients, the absolute diameter change at level D was 3.7 ± 3 mm (P = 0,05) with a percentage change of $10,4 \pm 6.8$ % (P = 0,03). In contrast, nondiabetic patients showed an absolute diameter change of $0,9 \pm 0,7$ mm, and a percentage change of $2,9 \pm 2$ %. Percentage area change of $21,5 \pm 12.8$ % among diabetic patients and $8,5 \pm 6.4$ % (P = 0,04) among nondiabetic patients.	

<p>Zheng et al. 2022</p>	<p>552 patients. Different HbA1c levels were: HbA1c \geq 6,5 accounted for 8,7 %, HbA1c < 5,7 accounted for 41,67 %, and 6,5 > HbA1c \geq 5,7 accounted for 49,64 %.</p>	<p>A notable decrease in mRNA expression of GluT1 in patients with aortic dissection ($P < 0,0001$). A significant reduction in GluT1 levels in thoracic aortic smooth muscle cells of aortic dissection patients compared to individuals without the condition ($P < 0,01$).</p>	
<p>Zheng et al. 2022</p>	<p>14 mice in the insulin resistance group, 14 mice in normal group</p>	<p>The insulin resistance group of mice showed a higher number of smooth muscle cells with a disordered arrangement and thinner basement membranes when compared to the control group. Additionally, the extracellular matrix was found to be increased, while the elastic fibre layer exhibited smaller, fragmented fibres with reduced thickness. Furthermore, the density of collagen fibres was observed to be higher in the insulin resistance group. In the insulin resistance group, the protein expression of osteopontin, MMP2, and MMP9 was found to be significantly higher $P < 0,05$, $P < 0,01$, $P < 0,001$, respectively, while that of transgelin and alpha smooth muscle actin was significantly lower $P < 0,01$, $P < 0,01$, respectively.</p>	

Neurologic dysfunction			
Eusanio et al. 2013	473 patients of which 22 had diabetes. 8 diabetic patients had a central cannulation and 14 had femoral cannulation.	Multivariate analysis found diabetes to be an independent predictor of permanent neurologic dysfunction (OR 6,6; P = 0,007).	
Haldenwang et al. 2012	122 patients of which 16 had diabetes	Univariate analysis did not find a statistical correlation between diabetes and postoperative temporary neurologic dysfunction (P = 0,088). Multivariate analysis, on the other hand, found diabetes to be a risk factor for temporary neurologic dysfunction (OR 3,95, CI 95 % (1,18–13,24); P = 0,026).	
Dumfarth et al. 2020	338 patients of which 26 had diabetes	They did not find diabetes to be a risk factor for new postoperative neurologic injuries (OR 1,196; CI 95 % (0,429-3,335); P = 0,732), nor did they find any statistical significance between diabetes and preoperative neurologic dysfunction (with preoperative neurologic dysfunction: 5/50 (10 %); without preoperative neurologic dysfunction: 21/288 (7,3 %); P = 0,507).	
Helder et al. 2020	25 462 patients. 13 741 and 11 721 of ascending aorta only and any arch procedure, respectively.	No correlation between permanent postoperative stroke and diabetes neither in the univariate nor the multivariate analysis (univariate: OR 1,00; CI 95 % (0,86-1,17); multivariate: OR 1,03; CI 95 % (0,87-1,21)). The same trend continues in the updated database between the years 2014-2016: (univariate: OR 1,11; CI 95 % (0,86-1,43); multivariate: OR 1,14; CI 95 % (0,86-1,50).	No specific mention is made about the number of diabetic patients

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