DOI: 10.5281/zenodo.15076255

CURRENT APPROACHES IN CARDIOVASCULAR SURGERY

EDITOR
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Current Approaches in Cardiovascular Surgery

EDITOR

Assoc. Prof. Dilek Atik, Ph.D.

Publisher
Platanus Publishing®

Editor in Chief
Assoc. Prof. Dilek Atik, Ph.D.

Cover & Interior Design
Platanus Publishing®

Editorial Coordinator
Arzu Betül Çuhacıoğlu

The First Edition
March, 2025

Publisher's Certificate No
45813

ISBN
978-625-6634-95-4

Platanus Publishing®
Address: Natoyolu Cad. Fahri Korutürk Mah. 157/B, 06480, Mamak, Ankara, Turkey.
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CONTENTS

CHAPTER 1

Deep Venous Thrombosis: Symptoms, Diagnosis, and Treatment Methods

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1. DEEP VENOUS SYSTEM ANATOMY

The anatomy of the lower extremity veins is highly diverse. The veins of the lower extremity are divided into three groups: superficial, deep, and perforating veins. These systems consist of two main systems: the superficial venous system and the deep venous system. The perforating venous system connects these two systems. The veins of the lower extremity are classified into three separate groups:

A. Superficial venous system

B. Deep venous system

C. Perforating venous system

Superficial veins run above the muscular fascia, just under the skin. Deep veins accompany the arteries, running between the deep fascia and muscle tissues. Perforating veins pass through the deep fascia and connect the superficial and deep venous systems. The deep veins are the main drainage system of the lower extremity.

For the anatomy of the venous system in the lower extremity, new terminology was created in 2002 at a conference held in Rome by the presidents of the International Union of Phlebology and the International Federation of Anatomical Associations (Caggiati et al., 2002).

The deep venous system is examined in four sections from the foot upwards:

Foot Section: The digitalis plantaris vein and the intrametatarsal vein together form the arcus plantaris vein. The v. plantaris medialis branches from this arch and forms a plexus with the internal plantar veins at the level of the calcaneus, creating two posterior tibial veins. In the dorsal foot, submalleolar perforators form the anterior tibial veins (these veins contain approximately 8-19 valves) (Caggiati, Phillips, Lametschwandtner, & Allegra, 2006; Ceulen et al., 2010).

Calf Section: Moving upwards, the two fibular veins on the lateral side of the foot grow as the soleus vein joins them. At the knee level, the peroneal veins join with the posterior tibial vein, and this structure forms the popliteal vein, which joins the anterior tibial veins above the knee to form the popliteal vein (these veins contain approximately 8-11 valves) (Caggiati et al., 2006; Ceulen et al., 2010).

Thigh Section: As the popliteal vein (PV) ascends, it reaches the level of the adductor canal, where it becomes the femoral vein (FV). The PV can become compressed between the two heads of the gastrocnemius muscle (medial and lateral), which may lead to deep venous thrombosis in the lower extremity (Uhl & Gillot, 2015).

The PV passes through the hiatus tendineus (adductorius) into the adductor canal (Hunter's canal) along with the femoral artery and nerve (88% of cases). It may vary in its structure as unitrunkal (3%) or bitrunkal (9%). Here, it becomes the FV. In the distal thigh, the FV runs laterally to the femoral artery, but in the middle and proximal portions, it lies behind the femoral artery. The common femoral vein lies medially to the femoral artery.

Pelvic Section: The FV may have multiple branches at the level of the thigh. At the level of the femoral triangle, the great saphenous vein, lateral and medial circumflex veins, deep femoral vein, and the FV drain into it (typically containing 3-5 valves) (Caggiati et al., 2006; Ceulen et al., 2010). As the FV ascends, it is enclosed by the femoral sheath and follows the deep femoral artery, draining medial and lateral circumflex veins. In the distal portion, it connects with the PV and proximal inferior gluteal veins. It drains into the femoral triangle and becomes the external iliac vein after passing under the inguinal ligament (about 7-9 cm in length). The external iliac vein travels obliquely upwards, draining into the inferior epigastric vein and the circumflex iliac profunda vein. It joins the internal iliac vein anterior to the sacroiliac joint to form the common iliac vein.

On the right side, the external iliac vein lies medially to the external iliac artery, moving posteriorly as it ascends. On the left side, it lies medially to the artery throughout its course. At this level, the iliac vein generally contains one, sometimes two, valves. The left iliac vein is often compressed by the right iliac artery and the sacrospinal spine. For this reason, deep venous thrombosis (DVT) is more common on the left side. In these cases, May-Thurner Syndrome should be considered.

The internal iliac vein begins in the sciatic canal and travels medially to the artery. At the anterior side of the sacroiliac joint, the iliac vein joins with the external iliac vein to form the common iliac vein. The common iliac veins converge at the level of the fifth lumbar vertebra to form the inferior vena cava (IVC). The IVC then drains into the right atrium, and thus, a thrombus in the lower extremity may cause pulmonary embolism (PE) through the bloodstream (Ouriel, Green, Greenberg, & Clair, 2000).

2. DEEP VENOUS SYSTEM PHYSIOLOGY

The structural walls of veins contain fewer smooth muscle and elastic fibers compared to arteries. Gravity and hydrostatic pressure affect the functions of the superficial and deep veins, creating a retrograde (proximal to distal) flow. Additionally, diaphragmatic movements, intrathoracic negative pressure, postural vasoconstriction, the tone of the venous wall, the drawing force of the right heart chambers, and the pulsation effects of the accompanying arteries all support venous return. The musculovenous pump and the valves within the veins prevent the backflow of blood (Ceulen et al., 2010). Venous valves are present in all veins of the body, but their density is higher in the veins of the lower extremities. Both deep and superficial veins contain venous valves (Caggiati et al., 2006).

The number and density of valves decrease from distal to proximal, and the majority of them are bicuspid in structure. In the iliofemoral venous system, the number of valves is lower. Miles and colleagues, in their autopsy study, found that there are no valves in the inferior vena cava, but valves are present in the right iliofemoral venous system and the left iliofemoral venous system (Miles, Flowers, Parsons, & Benitone, 1973). The near absence of valves in the common iliac veins may be a possible reason for the reduced risk of postthrombotic syndrome after effective thrombolysis. In deep veins, the thrombus typically originates from the venous valve area. Thrombus accumulation usually occurs in the venous wall rather than the valves. The structure of venous valves, unlike the venous wall, exhibits antithrombotic properties. Endothelial protein C receptor activity and thrombomodulin are significantly more concentrated in valves compared to the vessel wall. Additionally, von Willebrand factor is found more densely in the vessel wall. Thanks to this feature of the valves, it is thought that early resolution in deep vein thrombosis and the preservation of venous valve function may be supported (Caggiati et al., 2006; Miles et al., 1973).

3. EPIDEMIOLOGY OF DEEP VENOUS THROMBOSIS

The DVT can clinically present as completely asymptomatic (less than 50% of patients show symptoms), but when symptoms do occur, there is a high likelihood of pulmonary embolism (PE) with an acute onset of severe respiratory distress. Due to the asymptomatic cases, the true incidence of the disease and the frequency of complications are not precisely known. Therefore, it is assumed that the actual incidence is much higher (Geerts et al., 2005; Rollins, Lloyd, & Buchbinder, 1988). The incidence of venous thromboembolism (VTE) is more than 1 per 1000; in the United States, more than 200,000 new cases are reported

annually. Of these cases, 30% die within thirty days, with one-fifth of these deaths resulting from sudden death due to PE. Risk factors for VTE include advanced age in men, recent surgery, trauma, immobilization, malignancy, central venous catheter/transvenous pacemaker placement, and previous thrombophlebitis. In women, additional risk factors include pregnancy, oral contraceptives, and hormone replacement therapy. Compared to the general population, the risk of developing DVT increases 13-fold due to trauma, 5-fold due to malignancy, 2-3 times with oral contraceptive use, and 8-fold with hospitalizations. In cases of acquired or inherited thrombophilia, the risk is also significantly higher (Fowkes, Price, & Fowkes, 2003).

The incidence of VTE increases with age, reaching 1% in individuals over 85 years old. The female/male risk ratio is found to be 1/2, with women being at higher risk at younger ages and men at higher risk in older ages. PE has a high mortality rate. The prognosis of the disease shows that 30% of patients who develop PE die within the first 30 days, and equally, 30% of patients are lost within the following 8 years due to recurrent attacks or chronic complications such as pulmonary hypertension (Gerotziafas & Samama, 2004).

4. PATHOPHYSIOLOGY OF DEEP VENOUS THROMBOSIS

The basic mechanisms that lead to venous thromboembolism were outlined by Virchow. The presence of just one of the three fundamental factors—slowed blood flow (stasis), damage to the vessel wall (endothelial injury), and hypercoagulability—can be a sufficient risk factor (Cooper & Groce, 2001). External pressures caused by aneurysms, tumors, and compression of the left common iliac vein by the left common iliac artery lead to slowed venous flow and venous stasis (May-Thurner syndrome – iliac vein compression syndrome).

Hypercoagulability can result from genetic factors such as Factor V Leiden mutation, antithrombin III deficiency, protein C and S deficiencies, or acquired causes like cancer, sepsis, and estrogen therapies. Thromboembolism typically accumulates in the calf veins where the flow shape changes and turbulence occurs, and in the inner sections of venous valves (valve sinuses). The thrombus accumulation in the valve sinuses creates a nidus. During muscular contractility, on one hand, the veins are emptied and the thrombus is removed; on the other hand, the fibrinolytic system attempts to dissolve the formed nidus. When thrombus accumulates, it obstructs the blood flow in the vessel, and with the addition of erythrocytes and fibrin, the thrombus moves upward toward the next valve or vein. At this stage, the thrombus is still soft but grows progressively. If this thrombus is not lysed by the fibrinolytic system, it eventually leads to

complete occlusion and hardening over time. However, the most feared outcome, especially in the acute phase, is the embolization of the soft thrombus or its fragments to the pulmonary artery. PE typically develops due to thrombosis of the deep veins in the lower extremities (most commonly in the region from the iliac vein to the popliteal vein) (Naidich, 1999).

4.1 Genetic and Acquired Risk Factors in Deep Venous Thrombosis

Both genetic and acquired factors play a significant role in the development of VTE. Acquired risk factors for venous thromboembolism include:

Strong (odds ratio>10): Hip and leg fractures, hip or knee prosthesis surgeries, major surgeries, major trauma, spinal cord injuries.

Moderate (odds ratio=2-9): Arthroscopic knee surgery, central venous catheter, chemotherapy, congestive heart or lung failure, hormone replacement therapy, malignancy, oral contraceptives, stroke, pregnancy/postpartum period, history of VTE, thrombophilia.

Weak (odds ratio<2): Prolonged immobility (e.g., bed rest for 3 days, flights longer than 8 hours), laparoscopic surgery, obesity, pregnancy/prepartum, varicose veins, etc. (Cooper & Groce, 2001; Moheimani & Jackson, 2011; Naidich, 1999).

Similarly, genetic risk factors for the development of VTE are categorized as:

Strong: Antithrombin, protein C, protein S deficiencies, elevated Factor VIII.

Moderate: Factor V Leiden mutation, prothrombin 20110A, blood groups other than O.

Weak: Methylenetetrahydrofolate reductase (MTHFR) mutation, homozygous Factor XIII 34 allele, etc. (Anderson & Spencer, 2003; Ho, 2010; Moheimani & Jackson, 2011).

Notably, heterozygous Factor Leiden polymorphism increases the risk 3-8 times, while homozygous cases significantly increase the risk 20-80 times (Olaf & Cooney, 2017).

5. CLINICAL EVALUATION OF DEEP VENOUS THROMBOSIS

Approximately 60-70% of symptomatic VTE patients develop DVT. In symptomatic cases, pain, swelling, tenderness along the vein tract, erythema, or cyanosis may be observed. DVT typically begins in the calf region and progresses

to the femoral veins and other proximal veins. These signs can also appear in other conditions, so DVT must be differentiated from cellulitis, superficial phlebitis, ruptured Baker's cyst, knee joint issues, muscle abscesses, intramuscular hematomas, other musculoskeletal problems, and post-phlebitic syndrome. Asymptomatic cases usually begin in the deep veins below the popliteal trifurcation (distal DVT) and resolve spontaneously (Tromboembolizm, 2002). In untreated symptomatic cases (proximal DVT), 50% will develop symptomatic PE within 3 months. Post-thrombotic syndrome (PTS) is the most important complication of DVT. In 20-50% of patients, PTS can lead to lifelong leg pain, swelling, heaviness, edema, and stasis ulcers (Moheimani & Jackson, 2011). PTS develops in about 20% of patients within 2 years after DVT (Kearon, 2003).

5.1 Physical Examination

The most common symptom of DVT is pressure tenderness in the medial aspect of the calf. Specific physical examination findings in certain areas, as described by some clinicians, are important in diagnosing DVT (Shafer & Duboff, 1971; Wells, Owen, Doucette, Fergusson, & Tran, 2006):

Homans' sign: Pain in the calf with dorsiflexion of the foot.

Tschmarke's sign: Pain with calf squeezing.

Payr's sign: Pain with compression of the Achilles tendon.

Neageli-Natis sign: Pain in the leg during coughing or cramping in the calf during walking.

Löwenberg sign: Pain in the calf when a blood pressure cuff is inflated above systemic pressure in the thigh.

Diagnosing DVT based on clinical signs is not a reliable method. Clinical signs and symptoms only confirm DVT in about 25% of cases. To make an accurate diagnosis, clinical correlation with tests such as D-dimer or venous Doppler ultrasound (US), computed tomography (CT)-venography, or magnetic resonance imaging (MRI) is required (Ho, Hankey, Lee, & Eikelboom, 2005).

6. DIAGNOSTIC TESTS SUPPORTING THE DIAGNOSIS OF DEEP VENOUS THROMBOSIS

6.1 D-dimer

The level of D-dimer, a fibrin degradation product, is important in the diagnosis of DVT. Studies have shown that values below 0.5 μg practically rule out VTE in the absence of clinical symptoms and risk factors (Oger et al., 1998). However, the test can be positive in cases of surgical interventions, kidney disease, trauma, malignancies, severe infections, systemic lupus erythematosus, and pregnancy (Goldhaber et al., 1993).

6.2 Diagnostic Imaging

Venous Compression Ultrasound (US)

Various types of US (conventional, duplex, and color Doppler) can be used for DVT diagnosis. The inability to compress the proximal vein with mild pressure is helpful in confirming DVT. This method is called venous compression ultrasound. The diagnosis of proximal DVT is made if a segment of the vein in the popliteal or higher regions cannot be compressed (Cockett & Thomas, 1965). It is a non-invasive, widely available, inexpensive, and repeatable method. The sensitivity of compression US for proximal DVT diagnosis is 95%, with specificity of 96%. However, in isolated calf vein thrombosis, these values are reduced to 60% and 70%, respectively (Çepni & Tecimel). For detecting thrombus in the pelvic iliac and cava veins, conventional CT phlebography is more beneficial. It helps differentiate fresh thrombus from chronic thrombus remnants and identify external compressions on vessels (Lee & Levine, 2003; Lensing et al., 1992).

Contrast venography remains the gold standard for DVT diagnosis (Lee & Levine, 2003). However, it has drawbacks such as being invasive, costly compared to US, and requiring experienced personnel for interpretation. Recent advancements have reduced the need for venography by combining clinical probability with non-invasive tests to obtain reliable and safe results (Lensing et al., 1992; Tapson et al., 1999). Screening with venography is not performed in asymptomatic cases. MR imaging is more expensive than CT and has not been proven effective for DVT ("Prevention and treatment of venous thromboembolism. International Consensus Statement (guidelines according to scientific evidence)," 2006).

7. TREATMENT OF DEEP VENOUS THROMBOSIS

7.1 Anticoagulation Therapy for Deep Venous Thrombosis

In the acute and subacute phases of DVT, medical or surgical treatments aimed at dissolving the thrombus have the potential to relieve acute symptoms and reduce the risk of developing PTS. Thrombus resolution eliminates venous obstruction and can also restore the function of venous valves damaged by the clot. Early thrombolysis can prevent venous dilation and stasis that might develop later due to obstruction, thus preventing PTS (Kakkos et al., 2021; Kearon et al., 2008).

The goal of treatment in the acute phase is to prevent PE. Therefore, parenteral anticoagulation (unfractionated or low-molecular-weight heparin [LMWH]) should be initiated first. Standard anticoagulation therapy (strong recommendation [I], evidence level C) consists of at least 5 days of LMWH followed by coumadinization with a vitamin K antagonist (VKA), maintaining the INR in the range of 2-3, after which LMWH is discontinued. Due to the requirement for subcutaneous LMWH injections and the drug-food interactions of oral VKAs, more effective drugs have been developed. Dabigatran is a direct thrombin inhibitor, and rivaroxaban, apixaban, and edoxaban are factor Xa inhibitors, which are now preferred (Bozkurt et al., 2021).

In the next phase, the decision for medical or surgical treatment depends on whether the DVT is symptomatic acute, subacute, or chronic (recurrent) and the location of the thrombus (proximal-iliac, caval level) (strong recommendation [IIa] - evidence level A) (Bozkurt et al., 2021; Schulman et al., 1995).

The following conditions contraindicate thrombolytic therapy (Bozkurt et al., 2021):

Active bleeding diathesis

Active/recent gastrointestinal bleeding

Active/recent intracranial hemorrhage or cerebrovascular events/transient ischemic attacks (<3 months)

Recent brain/spinal surgery within the last three months

Severe liver failure

Renal failure (GFR<60 ml/min)

Indications for thrombolytic treatment in acute DVT (Bozkurt et al., 2021):

Acute presentation (<14 days)

Life expectancy >1 year

Low risk of bleeding

Phlegmasia cerulea dolens

Extensive proximal ± distal DVT

In thrombolytic therapy, fibrinogen levels should be closely monitored, and if they fall below 1 mg/dL, thrombolytic treatment should be discontinued (Enden et al., 2012).

7.2 Interventional Treatment for Deep Venous Thrombosis

Interventional treatment is suitable for patients with high-risk iliofemoral and caval DVTs due to the likelihood of developing PE and future PTS. The CaVenT study evaluates the breakdown of thrombus using various techniques (thrombolysis, mechanical aspiration, maceration) in situ (Comerota, 2010).

In patients with iliofemoral DVT, interventional treatment (catheter-directed thrombolysis) (strong recommendation [IIa] - evidence level B) is usually performed with ultrasound guidance through the popliteal vein. If the popliteal vein is thrombotic, intervention can be performed via the femoral vein (Bozkurt et al., 2021). After determining the thrombus location and length using venography, a multi-lumen catheter is used endovascularly. High-dose thrombolytics are given with direct thrombolysis to clear the thrombus, preserving venous valve function and preventing venous obstruction (Mewissen et al., 1999).

Reolytic devices perform mechanical thrombectomy (AngioJet, Boston Scientific, Watertown MA USA) by directing a high-speed saline jet backward through a catheter, creating a low-pressure vortex and performing maceration and aspiration with a vacuum system (Bernoulli principle). This process, commonly used with catheter-directed thrombolysis (pharmacomechanical thrombolysis), allows for aspiration of thrombus fragments (Kearon et al., 2008).

Ultrasonic-assisted thrombolysis (UAT) works by infusing plasminogen activators while simultaneously administering a pulsatile infusion of thrombolytic agents through the EkoSonic device (EKOS endowave, Bothell, Washington, USA). The ultrasonic waves spread through fibrin, thinning and

softening fibrin fibers without causing distal embolization. Routine vena cava filters are not recommended during catheter-based thrombolysis, but if a free-floating thrombus is present in the vena cava, temporary or permanent filters are recommended (Midulla et al., 2021).

Groups recommended for filter use (Bozkurt et al., 2021):

Patients with proximal DVT and high risk (those with contraindications to anticoagulation)

Patients with recurrent VTE despite anticoagulation therapy

Patients with pulmonary hypertension due to recurrent VTE, before endarterectomy

After embolectomy due to acute massive PE

Patients with acute trauma and hip fractures

Patients who experience bleeding complications while on anticoagulation therapy

After thrombolysis, venography is performed. If ongoing stenosis is identified, balloon dilatation and stent implantation may be used to assist venous drainage. Balloon dilatation is generally sufficient for arterial occlusions in the lower extremities; however, due to the high elastic "recoil" properties of venous lesions, balloon dilatation alone may not be enough and can cause early restenosis. Routine venous stenting is recommended after balloon dilatation in iliac vein occlusions (Taha, Lane, Shalhoub, & Davies, 2019).

7.3 Surgical Treatment for Deep Venous Thrombosis

Venous thrombectomy is a method applied to patients with proximal DVT. It is important to select patients for thrombectomy who have an iliofemoral presentation of the thrombus, symptoms lasting less than 7 days, a life expectancy of at least 1 year, and no bleeding tendencies. In surgical treatment, the procedure is initially performed under general anesthesia, with leg elevation, and elastic bandages are applied while the foot is in a dorsiflexed position. After making a surgical incision, the main femoral vein, saphenofemoral junction, and deep femoral veins are explored. Once the veins are safely exposed, a longitudinal incision is made in the main femoral vein. Intrainguinal thrombus is cleared. If the thrombus is located in distal regions, a distal posterior vein approach (cut-down) is performed, and the thrombus is removed using the Fogarty catheter with

a double catheter technique. Recently, endovascular interventions have been taking place in DVT cases and have shown more successful results than surgical interventions (SİNCİ, 2000).

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CHAPTER 2

Aortic Dissection: Diagnosis and Treatment Methods

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[1]

DEFINITION

Aortic dissection is an aortic wall disease that causes a tear (dissection) in the intima layer for any reason. This separates this layer from the media layer and forms a false lumen within the aorta. This condition can result in high mortality and morbidity, requiring emergency intervention, and can lead to aortic wall rupture or organ malperfusion.

HISTORY

Dr. Frank Nicholls described the findings from the autopsy performed after the sudden death of King George II of England in 1760 as follows: "…a certain amount of coagulated blood was found in the pericardium, about one liter…; the entire heart was compressed in such a way as to prevent the auricle from pushing blood into the vessels; as a result, the ventricles were found to be completely devoid of blood…; and in the body of the aorta, a transverse fissure about one and a half inches in length was found on the inner side, through which blood had passed shortly before from beneath the outer shell, forming a swollen ecchymosis." With this description, aortic dissection was first described in written documentation as having a pathological meaning. (1) The term aortic dissection was first used by Maunoir in 1802. In 1819, René Laennec, the inventor of the stethoscope, was the first person to use the term "dissecting aneurysm" (2). In 1922, Davy and Gates made the first diagnostic approach to aortic dissection based on the symptoms and examination findings of a 55-year-old male patient (3). In 1934, Shennan published the first significant scientific study containing clinical and pathological information on the subject (4). In 1954, DeBakey, Cooley, and Creech performed the first successful surgical resection to treat aortic dissection (5), and in 1982, they published a series of 527 patients over 20 years. (6) Furthermore, all developments in the diagnosis and treatment of aortic aneurysms have also significantly contributed to aortic dissection surgery. In 1996, establishing the International Registry of Acute Aortic Dissection (IRAD) led to the creation of a data pool that, with contributions from numerous international centers, became a guide in defining modern diagnosis and treatment (7). In 1999, two studies published in the New England Journal of Medicine revealed the results of using endovascular stent-grafts in the surgery of Type B aortic dissection, opening a new era in this field (8,9).

EPIDEMIOLOGY

The incidence of aortic dissection is estimated to be between 5 and 30 per million; however, it is difficult to determine the true incidence of the disease due

to the presence of patients who die without receiving a diagnosis (10,11). Studies conducted in large autopsy series have found the frequency of aortic dissection to be between 0.1% and 0.8%, and Hirst's autopsy series concluded that 40% of the patients had received an antemortem diagnosis (12,13). The incidence peaks in the 6th and 7th decades of life, while it occurs in younger patients with predisposing factors. It is observed to be approximately twice as common in males compared to females (14). Mortality has been reported to increase by 2% per hour during the first 12 hours following the onset of symptoms. It has been reported that the two-week mortality rate for patients who did not receive a diagnosis is 75%, while approximately 33% of untreated patients die within the first 24 hours, and 50% die within 48 hours (15).

PATHOPHYSIOLOGY

Many theories have been proposed regarding the pathogenesis of aortic dissection. Initially, it was thought that cystic medial degeneration, which results from the loss of function of the elastic layer and smooth muscle tissue in the media layer of the aorta, causing aortic aneurysm, was also the cause of aortic dissection. However, this theory was reconsidered after it was found that only a small number of patients with aortic dissection showed pathological cystic medial degeneration. Later studies revealed a close relationship between intramural hematoma and dissection (16). In intramural hematoma, the layer from the vasa vasorum to the media layer creates tension in the aortic wall, thus predisposing to intimal damage. Evidence also shows that the vasa vasorum becomes hyperplastic and develops chronic obstructive disease (17). It is thought that this condition leads to chronic medial ischemia and degeneration of the aortic wall.

ETIOLOGY

The etiology of aortic dissection includes any factor that can cause weakness in the aortic wall. Conditions such as connective tissue diseases and vasculitis directly cause aortic wall defects, while conditions like hypertension and hypervolemia can lead to dissection due to external mechanical pressure. Procedures like cardiac catheterization, cardiac surgery, cannulation, and intra-aortic balloon pump application can also cause aortic dissection iatrogenically.

Hypertension is one of the most important and common predisposing factors associated with aortic dissection. According to the data from the International Registry of Acute Aortic Dissection (IRAD), 72% of patients with aortic dissection have hypertension (10,14). While hypertension mechanically creates a load on the aortic wall, it also leads to calcification, fibrosis, and thickening of

the wall's internal structure. The fibrosis of elastic structures and the loss of smooth muscle cells result in reduced compliance. Additionally, the thickening of the intima leads to impaired nutrition of the aortic wall, thereby increasing the trauma sensitivity of the intimal tissue (18,19,20).

Genetic and connective tissue disorders, such as Marfan Syndrome, Ehlers-Danlos Syndrome, Loeys-Dietz Syndrome, Turner Syndrome, and Noonan Syndrome, can also lead to aortic dissection, especially by causing cystic medial degeneration in the media layer. Marfan Syndrome is the most commonly associated with aortic dissection among these diseases. In autosomal dominant Marfan syndrome, the failure of the fibrillin-1 glycoprotein, which plays an important role in the durability of connective tissue, results in cystic medial degeneration and aortic aneurysm in the aortic tissue (21). Additionally, mutations in TGF-beta receptor 1 (TGFBR1) and TGFBR2 lead to an increase in the bioavailability of TGF-B, which disrupts smooth muscle development and the structural integrity of the extracellular matrix (22,23,24). While Marfan syndrome has been diagnosed in 3% of patients with aortic dissection, it has been reported that this rate increases to 50% in patients under the age of 40 (25,26,27).

Congenital anomalies, such as bicuspid aortic valve, aortic coarctation, and aortic hypoplasia, can also be causes of aortic dissection. Notably, the bicuspid aortic valve is an important predisposing factor independent of the aortic stenosis it creates. The incidence of bicuspid aortic valve in all aortic dissection cases is 7-15% (28,29,30). The aberrant right subclavian artery is another congenital vascular disease predisposing to aortic dissection (31). The right aortic arch is also prone to aortic dissection due to its fragility (32).

Pregnancy, especially in the third trimester, is a risk factor for aortic dissection (33). In approximately half of the aortic dissection cases in women under 40 years of age, TAAD (Thoracic Aortic Aneurysm and Dissection) has been identified either during pregnancy or in the postpartum period (34,35). Women with Marfan syndrome who develop aortic root dilation are at significant risk for aortic dissection during pregnancy. Peripartum aortic dissection can also lead to the first diagnosis of Marfan syndrome.

Blunt trauma tends to cause localized tears, hematomas, or obvious aortic transection. It rarely leads to classic dissection. On the other hand, iatrogenic trauma is associated with true aortic dissection and accounts for 5% of cases. Procedures such as cardiac catheterization and intra-aortic balloon pump can cause aortic dissection due to direct trauma to the aortic intima. Cardiac surgery,

although more common in aortic valve surgery, carries a very low risk of acute aortic dissection, ranging from 0.12% to 0.16% (36,37).

Among inflammatory diseases, giant cell arteritis is associated with aortic dissection and an autoimmune mechanism is considered responsible (38). It is generally accepted that inflammatory processes in the aortic tunica media do not play a significant role in developing aortic dissection. However, inflammatory diseases that cause widespread medial necrosis can rarely lead to proximal aortic dissection cases. The spirochete Treponema pallidum, which causes syphilis, was the leading cause of aortic aneurysm before the widespread availability of antibiotics and was responsible for 5-10% of all cardiovascular deaths. However, the transverse scar bands observed in syphilis act as a barrier against the progression of dissection (39). Due to the decreasing incidence of syphilis today, it is unlikely to establish a link between syphilis and dissection. In Crawford's case series involving aortic dissections, aortitis was found in 1.3% of cases.

Cocaine use can lead to aortic dissection due to the release of catecholamines, which cause hypertension and connective tissue damage. In cases of severe chest pain associated with substance use, aortic dissection should be considered in the differential diagnosis (40).

AORTIC ANATOMY

The aorta is the main vascular structure that extends from the aortic annulus to the iliac bifurcation. The term "aortic root" refers to the starting section of the aorta, the complex that forms the left ventricular outflow tract of the heart. This complex structure includes the ventriculo-aortic junction, aortic valve leaflets, the sinuses of Valsalva, and the sinotubular junction. The aortic root continues as the ascending aorta. Then, the section of the aortic arch is bounded by the innominate artery and the left subclavian artery. The descending thoracic aorta extends to the diaphragmatic hiatus. The section from the hiatus to the iliac bifurcation is called the abdominal aorta (41,42).

The anatomical position of the aortic leaflets alone is insufficient for the aortic valve to function correctly with complete coaptation. This function is based on the anatomical relationships between the aortic annulus and the aortic cusps, and to explain this, the concept of the functional aortic annulus has been defined. The functional aortic annulus is the anatomical ring in the shape of a crown, which is bounded by the sinotubular junction, the ventriculo-aortic junction, and the entry points of each of the aortic valve leaflets. The proper coaptation of the valve is achieved through the coordinated function of all these structures.

The tissue of the ventriculo-aortic junction consists of fibrous tissue in the region extending to the membranous part of the septum. At the same time, the remaining segment is composed of ventricular myocardium (43,44).

From a surgical perspective, the ventriculo-aortic junction refers to the line corresponding to the plane where the prosthetic valve is implanted (45). The connection points of the three leaflets are the commissures. The sections of the aortic wall, limited proximally by the ventriculo-aortic junction and distally by the sinotubular junction, are called the sinuses of Valsalva. Three sinuses of Valsalva segments are determined according to the corresponding coronary artery (left, right, and non-coronary). The left and right coronary ostia originate from the corresponding sinus of the Valsalva segment. The region between the right and non-coronary sinus segments is anatomically closely related to the cardiac conduction system that runs through the membranous septum and is near the septal leaflet of the tricuspid valve.

The plane connecting each commissure's upper edges is the sinotubular junction (STJ). The STJ forms the boundary where the aortic root ends and the ascending aorta begins. In cases of dilation occurring in this region for any reason, aortic insufficiency may arise due to less coaptation of the leaflets (46). The ascending aorta extends from the STJ level to the origin of the innominate artery, and distal to this level, the aortic arch begins.

CLASSIFICATION

Aortic dissections can be classified in two different ways: clinically and anatomically.

Clinical Classification

Aortic dissection can be classified into three categories: acute, subacute, and chronic, based on the time elapsed from the onset of symptoms to the diagnosis (47). The first two weeks after the onset of symptoms are considered the acute phase. This is when the aortic wall's fragility is highest due to dissection and inflammation, and the rupture risk is also the highest. It has been reported that 74% of deaths occur within the first two weeks in patients with aortic dissection who do not receive treatment (12). The period between two weeks and eight weeks is considered the subacute phase. Chronic dissections refer to cases that occur more than eight weeks after the onset of the first symptoms. The mortality rate significantly decreases if the patient remains hemodynamically stable during this phase.

Anatomical Classification

The DeBakey and Stanford classifications are the most widely accepted among anatomical classifications.

DeBakey Classification:

DeBakey Type 1 dissections: These involve a dissection that extends from the proximal aorta to the iliac arteries, affecting the entire aorta.

DeBakey Type 2 dissections: These involve a dissection limited to the ascending aorta.

DeBakey Type 3a dissections: These involve dissections limited to the descending aorta, from the distal left subclavian artery to the aortic hiatus.

DeBakey Type 3b dissections: These involve dissections extending from the distal left subclavian artery to the iliac arteries (48).

Stanford Classification:

Stanford Type A: Dissections involving the ascending aorta, regardless of distal involvement, are classified as Type A.

Stanford Type B: All dissections that may involve the aortic arch but do not include the ascending aorta (53).

Non A-Non B: This term is used for dissection types where the proximal part of the dissection flap begins at the aortic arch (49).

Svensson Classification:

Because intramural hematoma and aortic ulcers can create dissection findings and clinical manifestations, a new classification has been proposed by Svensson and colleagues (50):

Class I: Classic aortic dissection with an intimal flap between the true and false lumen.

Class II: Medial separation with the formation of intramural hematoma or hemorrhage.

Class III: Hidden or discrete dissections without hematoma formation, with eccentric bulging at the tear point.

Class IV: Aortic ulceration and surrounding hematoma, usually due to plaque rupture that develops subadventitially.

Class V: Iatrogenic and traumatic dissections.

ESVS, EACTS New Classification:

Finally, in 2020, the European Vascular Surgery Society (SVS) and the European Association for Cardio-Thoracic Surgery (EACTS) proposed an entirely new classification schema that defines aortic dissection anatomy in more detail. According to this schema, the proximal region where the intimal flap of the dissection begins, and the distal region where it extends are anatomically defined (Figure 2). According to this classification, Type A is used for dissection with an entry tear in zone 0, and the distal zone it extends to is added as a subscript. For example, a dissection starting in zone 0 and ending in zone 9 is A9. In Type B dissections, the number of the zones where the dissection begins and ends is added to the B symbol. For example, a dissection starting in zone 3 and ending in zone 9 is defined as B39. If the dissection begins in zone 0 but the location of the entry tear cannot be defined, it is considered "Undefined" and is indicated by the symbol I. The distal extension zone number is added (e.g., I9) (51).

CLINIC

Symptoms

Aortic dissection can present a wide range of clinical scenarios due to the nature and function of the aorta itself. Symptoms can occur when the dissection flap occludes the origin of side branches (Dynamic Obstruction), or they can arise when the flap progresses within the side branch itself (Static Obstruction) (52).

The most commonly encountered symptom (90%) is chest pain that often radiates to the neck and jaw but usually extends to the back and abdomen. Chest pain is typically accompanied by excessive sweating, a fear of death, or anxiety (10).

Cerebral malperfusion can lead to symptoms such as stroke, paralysis, or syncope (9%). Sometimes, syncope may occur not due to a cerebrovascular event but due to cardiac causes, such as cardiac tamponade, acute aortic insufficiency, or left ventricular outflow obstruction, or as a result of cerebral hypoperfusion caused by trauma to aortic baroreceptors. Focal neurological deficits are seen in 17% of cases. Acute paraplegia occurs in 1-3% of cases. Approximately 50% of

neurological symptoms are transient. In about 30% of these cases, the absence of chest pain delays diagnosis (53,54,55).

Acute myocardial infarction findings may be seen in 10% of cases due to coronary artery malperfusion. Visceral malperfusion (15%) can lead to mesenteric ischemia and related symptoms such as abdominal pain, nausea, diarrhea, or renal malperfusion, resulting in oliguria or anuria. Acute peripheral vascular disease symptoms, such as ischemia, may be the primary reason for seeking medical attention due to the loss of pulses in the extremities. Patients with peripheral malperfusion have approximately twice the rate of renal and mesenteric ischemia and mortality. (56,57,58)

Unfortunately, due to these varied clinical presentations, 30% of patients are initially misdiagnosed with another condition. (59)

Physical Examination

Many patients with aortic dissection have chronic hypertension. Hypertension accompanied by tachycardia is usually the first finding. On the other hand, the presence of hypotension along with tachycardia can indicate pericardial tamponade, myocardial infarction, or severe aortic insufficiency, all of which are associated with a poor prognosis. The possibility of pseudohypotension due to subclavian artery obstruction should be considered. (60)

In 20% of patients with aortic dissection, a loss of peripheral pulses in the extremities is observed. Therefore, a thorough peripheral pulse examination should be performed on all patients. The presence of permanent or temporary pulse loss and motor and sensory deficits in the extremities can provide insight into the location of the dissection. (61)

In cardiac examination, a newly developed diastolic murmur may indicate aortic insufficiency. Among the causes of aortic insufficiency are the loss of leaflet support mechanisms, dilation of the aortic annulus, aneurysmal enlargement of the sinotubular junction, and the dissection flap prolapsing into the ventricle during diastole, which prevents the coaptation of the leaflets. (62,63) Pulsus paradoxus and increased central venous pressure should raise suspicion for pericardial tamponade. A reduction in breath sounds on the left side during lung examination should be a clue for hemothorax.

A detailed neurological examination is important to assess cerebral or spinal malperfusion. Loss of consciousness, ischemia-induced paresis, and other neurological findings have been reported in up to 40% of cases of proximal aortic

dissection. (64) Although rare, physical examination findings may include vocal cord paralysis (due to pressure on the left recurrent laryngeal nerve), hemoptysis (due to tracheobronchial compression), hematemesis (due to esophageal perforation), superior vena cava syndrome, Horner's syndrome (due to compression of the upper cervical sympathetic ganglion), and dyspnea (due to compression of the pulmonary artery).

DIAGNOSIS

As with any disease, the most important step in aortic dissection is considering the possibility based on the patient's history and clinical findings and establishing a preliminary diagnosis. This becomes even more crucial when considering the high mortality and morbidity rates associated with the disease. Diagnostic tests such as echocardiography, computed tomography, magnetic resonance imaging, and angiography are used to reach a definitive diagnosis.

Electrocardiogram (ECG)

An electrocardiogram (ECG) should be routinely performed in all patients with chest pain or suspected cardiovascular disease. In patients with aortic dissection, ECG findings may suggest acute myocardial infarction due to coronary malperfusion. Signs of left ventricular hypertrophy due to aortic insufficiency may also be observed. However, these findings do not provide specific data for diagnosing aortic dissection.

Echocardiography (ECHO)

Transthoracic echocardiography (TTE) is commonly used as an initial method for diagnosing aortic dissection through two-dimensional ultrasonographic imaging. It is used to evaluate the aortic valve, aortic root, and ascending aorta and assess valvular and ventricular function and pericardial effusion. Transesophageal echocardiography (TEE) provides superior results compared to TTE. It has a specificity and sensitivity of over 95%. However, it is an invasive procedure and carries a small risk of complications such as esophageal perforation, respiratory distress, aspiration, and hemodynamic instability. (65)

Echocardiography can be considered advantageous compared to other diagnostic methods due to its noninvasive nature (minimal invasion in TEE), low cost, no use of contrast agents, absence of radiation, and the ability for intraoperative evaluation. Its disadvantages, however, include being operator-dependent and requiring experience.

Computerized Tomography (CT)

After the invention of computerized tomography, Gomes et al. were the first to define an aortic aneurysm using CT in 1977, thus utilizing this technique in aortic pathologies. (66,67) In 1979, Harris et al. were the first to define aortic dissection using CT. (68)

Contrast-enhanced CT is the most commonly used noninvasive imaging technique for visualizing the thoracic aorta. CT allows for the rapid and accurate detection of aortic anatomy and pathology. It identifies calcifications, penetrating ulcers, dissection, pseudoaneurysms, and mural thrombus.

Numerous software options are available, enabling 3D imaging and measurements. ECG-gated CT, synchronized with an electrocardiogram, helps prevent motion-related artifacts, especially in the proximal aorta.

The main disadvantage of CT in aortic dissections is its requirement for contrast agents, which can potentially cause acute kidney failure. In contrast-free CT scans, while the aortic diameter can be assessed, obtaining information about other changes is challenging.

Magnetic Resonance Imaging (MRI)

MRI was first used in diagnosing aortic dissections by Herfkens et al. in 1983 (69). Its advantages include being noninvasive, not involving radiation, and often providing sufficient imaging without the need for contrast agents. Contrast-enhanced MR angiography using gadolinium provides more accuracy in determining aortic measurements but cannot be used in patients with kidney disease.

MRI imaging may be insufficient if the blood flow velocity in the true and false lumens is equal in aortic dissection. In these cases, MRI synchronized with ECG can be performed, allowing differentiation by the cessation of flow in the false lumen during diastole. In chronic dissections, it is more difficult to obtain the flap appearance than in acute dissections due to the formation of a thrombus within the false lumen. (70)

MRI provides high-quality imaging, but the scanning time is longer. During this time, it becomes more difficult to intervene in case of any problems that may arise with the patient. Additionally, MRI is not available in every center, and its cost is high. For these reasons, it has not become a routine tool in clinical practice.

Angiography

The presence of two separate lumens or an intimal flap in angiography confirms the diagnosis of aortic dissection. (71) However, it is not used routinely due to its invasive nature, potential to cause rupture as part of the procedure, and the availability of many noninvasive alternatives.

Treatment

Medical Treatment

Patients diagnosed with aortic dissection should be promptly monitored. The primary goal of medical treatment is to prevent the progression or rupture of the dissection. To achieve this, it is essential to reduce fluctuations in blood pressure over time (anti-impulse therapy). (72) Therefore, close rhythm and blood pressure monitoring is required. The initial target for systolic blood pressure should be 120-130 mmHg, and the mean arterial pressure (MAP) target should be 60-75 mmHg. The target heart rate should be 60-80 beats per minute. Beta-blockers are ideal for this purpose due to their negative inotropic and negative chronotropic effects and their antihypertensive properties. (73) In practice, Metoprolol and esmolol are commonly used. Esmolol is cardioselective and has a short half-life, making it safe even in patients with bronchospastic conditions. The initial dose is 0.1-0.5 mg/kg via slow infusion over 1-5 minutes. After that, an intravenous infusion of 0.025-0.2 mg/kg/min can be continued. On the other hand, Metoprolol can be administered intravenously, starting with 5 mg, followed by slow infusion up to a total dose of 15 mg. Subsequently, an infusion rate of 2-5 mg/h can be used for further management. Heart failure, advanced AV block, severe bradycardia, and severe bronchospastic disease are contraindications for the use of beta-blockers. Calcium channel blockers are limited to situations where beta-blockers cannot be used. (74) Nitroprusside, with its vasodilatory and negative inotropic properties, is a treatment option in the presence of severe hypertension (HT). However, it is not recommended to use nitroprusside without beta-blockers, as it may increase the fluctuations in blood pressure over time due to reflex tachycardia. Pain causes catecholamine discharge, so pain management is crucial to minimize sympathetic activity. Opioid analgesics can be used as pain relievers. Blood products and fluid replacement should be administered in cases of hypotension and shock.

Surgical Treatment

Type A aortic dissection, which involves rupture or intramural hematoma in the ascending aorta, is an indication for emergency surgical intervention due to the poor prognosis observed in cases that progress without surgery, as previously explained.

The goal of surgical treatment is to prevent aortic rupture and direct blood flow into the true lumen, thereby preventing the progression of the dissection. Pericardial tamponade is relieved. Additionally, aortic insufficiency caused either by the primary progression of the dissection or by the dilation of the ascending aorta or prolapse of the dissection flap is also addressed and resolved after surgical intervention.

Aortic dissection presents various scenarios depending on the anatomical location of the tear. Therefore, the surgical treatment involves different combinations tailored to the specific case.

If the aortic root is unaffected by dissection, a supracoronary graft interposition can be performed at the sinotubular junction level, preserving the coronary buttons. In the case of commissural separation or aortic insufficiency, the insufficiency can be corrected with resuspension sutures. (75,76) Aortic valve replacement can be done alongside the supracoronary graft interposition if there is an independent pathology in the aortic valve. The Bentall and Cabrol procedures may be performed if the aortic root is involved. In cases where the aortic valve is normal, but the aortic root and ascending aorta need replacement, valve-sparing root replacement techniques (such as David and Feindel) can be applied. (77,78)

Homograft conduits and the use of pulmonary autografts are also among the options. Distally, replacing the ascending aorta to the greatest extent possible is the most suitable approach. Selective cerebral perfusion techniques or total hypothermic circulatory arrest with hemiarcus or total arcus replacement should be planned according to the extent of the dissection. If there are pathologies in the descending aorta, additional techniques such as the elephant trunk and frozen elephant trunk can be used. (79,80)

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CHAPTER 3

Karotis Arter Stenozu

Servet Turgut[1]

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1. GİRİŞ VE GENEL BİLGİLER

Serebral iskemi, dokulara yeterli oksijenin iletilememesi sonucunda oluşur. Bu durum, arterlerin stenoz/oklüzyonuna bağlı oksijen taşıma kapasitesinin azalmasıyla oluşabilir (Zétola & Rundek, 2022). Karotis stenozu, tüm iskemik inme olaylarının yaklaşık %7'sinden sorumludur (Dharmakidari, Bhattacharya, & Chaturvedi, 2017). Amerikan Kalp Derneği (AHA) verilerine göre, 2013 yılında inme, dünyadaki ölüm nedenleri arasından ikinci sıradaydı (6.5 milyon). Sadece Amerika Birleşik Devletleri'nde, inme, ulusal sağlık harcamalarının %1.7'sini teşkil ediyor ve 2030 yılına kadar inme üzerindeki toplam yıllık maliyetin %129 artması bekleniyor. Orta/şiddetli karotis arter stenozunun yaygınlığı özellikle 50 yaşın üzerinde ve yaşla birlikte artar ayrıca bu durum erkekleri kadınlardan daha fazla etkiler (Saxena, Ng, & Lim, 2019).

Karotis stenozuna bağlı oluşan serebral iskemi riski birkaç faktöre bağlıdır. Genel olarak, yakın zamanda karotis stenozu nedeniyle semptom yaşayan hastalarda (semptomatik karotis stenozu), karotis stenozuna bağlı semptomları hiç yaşamamış hastalara nazaran inme riski daha yüksektir (asemptomatik karotis stenozu). İnme riski zamanla değişkendir ve en yüksek risk, olayın meydana geldiği ilk haftalarda görülür. Yineleme riski, hemisferik inme geçiren hastalarda, geçici iskemik atak (TIA) geçiren veya oküler olay (amaurosis fugax veya retinal iskemi) geçiren hastalara kıyasla daha yüksektir. Sadece mevcut olay ve ilk semptomların başlamasından bu yana geçen süre değil, aynı taraftaki karotis stenozunun derecesi, gelecekteki inme riskini belirlemek için diğer bir önemli risk faktörüdür. İnme riski ciddi karotis stenozu olan hastalarda daha yüksektir. İnme riski için bilinen diğer risk faktörleri arasında ileri yaş, düzensiz ve ülserli plak yüzey morfolojisi, anjiyografik kollateral akımın yokluğu, azalmış beyin reaktivitesi, hipertansiyon ve koroner kalp hastalığı bulunmaktadır (Müller & Bonati, 2021). Karotis arter stenozu, semptomatik veya asemptomatik olarak görülebilir ve bu iki durum arasındaki ayrım, yönetim sürecini önemli ölçüde değiştirebilir. Akut nörolojik iskemi, geçici iskemik atak (TIA) ve inme sendromlarını kapsar. Karotis arter stenozundan kaynaklanan iskemi ve sonuç olarak ortaya çıkan semptomlar genellikle anterior dolaşım (orta serebral arter veya anterior serebral arteri içeren) veya retinal arter kaynaklıdır. Karotis arter stenozu genellikle posterior dolaşımda nörolojik semptomlara yol açmaz, çünkü İnternal Karotis Arter (ICA)'den gelen emboliler, Willis poligonunun anatomisi ve hemodinamik özellikleri nedeniyle öncelikli olarak anterior dolaşıma girer. Bu nedenle, karotis arter stenozu genellikle vertigo veya serebellar disfonksiyon gibi semptomlar için ayırıcı bir tanı olarak düşünülmez. Ayrıca, yüz ve boyunu

besleyen bir arter olan eksternal karotis arter darlığı genellikle soruna yol açmaz ve inme için bir risk faktörü olarak kabul edilmez (Arasu, Arasu, & Muller, 2021).

Karotis arter stenozlarının derecelendirmesinde esas olarak NASCET (North America Symptomatic Carotid Endarterectomy Trial) ve ECST (European Carotid Surgery Trial) yöntemleri kullanılmaktadır (Kürşat, 2021).

Grade 0: plak içermeyen normal damar

Grade 1: %0-29 stenoz

Grade 2: %30-69 stenoz

Grade 3: %70-99 stenoz

Grade 4: %100 oklüzyon

1.1. Semptomatik Karotis Arter Stenozu

Semptomatik karotis arter stenozu, önceki altı ay içinde meydana gelmiş ve hemodinamik olarak anlamlı bir ICA darlığına (yani stenoz >50%) bağlı bir nörolojik iskemi epizodu ile ilişkilidir. Semptomatik karotis arter stenozunun bulguları genellikle ani ve hızlı başlayan duyu veya motor fonksiyon kaybı, disfazi veya tek taraflı görme kaybıdır (retinal arter dahil olduğunda). Önemli bir nokta, görme ile ilgili bulguların ipsilateral, serebral bulguların ise kontralateral olacağıdır (Dodick, Meissner, Meyer, & Cloft, 2004).

1.2. Asemptomatik Karotis Arter Stenozu

Asemptomatik karotis arter stenozu, önceki altı ay içinde nörolojik iskemi epizoduna neden olmamış, ancak hemodinamik olarak anlamlı bir stenozun varlığıdır. Çoğu durumda, asemptomatik hastalık, karotis üfürümünün dinlenmesi sonucu, aksiyal görüntüleme sırasında insidental bir bulgu olarak veya semptomatik hastalığı değerlendirirken kontralateral tarafta gerçekleştirilen karotis arter doppler ultrasonografi sonrasında tespit edilir (Arasu, Arasu, & Muller, 2021).

2. KAROTİS ARTER STENOZUNDA TANI YÖNTEMLERİ

2.1. Karotis Arter Renkli Doppler Ultrasonografi

Karotis arter hastalığı için ilk tercih edilen değerlendirme yöntemidir. Bu yöntem, stenoz derecesini doğruluğu kanıtlanmış, ucuz ve non-invaziv şekilde değerlendiren bir yöntemdir (Wardlaw, Chappell, Best, Wartolowska, & Berry, 2006). Renkli doppler ultrasonografi, karotis ve vertebral arterler hakkında son

derece önemli bilgiler verir. Ayrıca, artmış kardiyovasküler risk açısından önemli bir belirleyici olan intima-media kalınlığını ve aterosklerotik plakların yerleşimini, uzunluğunu, yapısını ve içeriğini net bir şekilde gösterir (Mintz & Hobson, 2000). Duyarlılığı %92.6, özgüllüğü ise %97'dir (Anzidei et al., 2012). Temel dezavantajı, doğruluğun ultrasonografın deneyimine ve yeteneklerine dayanmasıdır (Criswell, Langsfeld, Tullis, & Marek, 1998).

2.2. Bilgisayarlı Tomografi Anjiyografi (BTA)

En yaygın kullanılan ikinci tanı metodudur. Kullanımı, hem hastalığı tanımlamada hem de tedavi sonrası takip dönemlerinde son derece uygundur (Anzidei et al., 2012). Radyasyon maruziyeti ve iyotlu kontrast kullanımı gibi riskleri vardır. Şiddetli plak kalsifikasyonunun varlığı, darlık derecesinin abartılmasına yol açabilir (Tendera et al., 2011).

2.3. Manyetik Rezonans Anjiyografi (MRA)

Ciddi karotis stenozu için doppler ultrasonografiden daha iyi sonuçlar verir. Bununla birlikte, kontrastla iyileştirilmiş MRA, stenoz derecesini olduğundan fazla gösterebilir (Ismail et al., 2023). Vasküler anatomiyi üç boyutlu olarak detaylı şekilde vermesi, arkus aortadan intrakraniyal bölgeye kadar kesintisiz bir görüntü sağlama yeteneği, radyasyon içermemesi gibi önemli avantajlara da sahiptir. Bu nedenle tedavi öncesi dönemde tercih edilen bir görüntüleme yöntemidir. Dezavantajları arasında inceleme süresinin uzun olması, metalik klips, kalp pili ve protez varlığında kullanılamaması yer alır. Ayrıca, teknik kaynaklı venöz kontaminasyon, solunum artefaktları gibi bazı olumsuz etkileri de mevcuttur (Kürşat, 2021).

2.4. Dijital Subtraksiyon Anjiyografi (DSA)

Darlığın derecesinin doğrulaması için kullanılan altın standart yöntemdir. Kontrast madde uygulanmadan önce ve sonra çekilen iki röntgen görüntüsünün birbirinden çıkarılmasıyla damarın yüksek kontrastlı bir şekilde gösterilmesi sağlanır. DSA'nın ayrıca serebral hiperperfüzyon fenomenini (HPP) öngörmede elverişli olduğu gösterilmiştir. Duyarlılık %75'e kadar yüksek, özgüllük ise %100'dür (Uno, Takai, Yagi, & Matsubara, 2020). HPP nadir görülür ancak morbidite ve mortaliteye yol açabilir ve watershed tipi serebral enfarktüse sebep olabilir (Müller & Bonati, 2021). DSA invaziv bir yöntemdir ve işlem sırasında %0.1-0.5 arasında inme riski görülür (Ismail et al., 2023).

3. TEDAVİ YÖNTEMLERİ

Semptomatik veya asemptomatik karotis stenozu olan hastalar, diyet, egzersiz, sigarayı bırakma ve kilo verme konularında yaşam tarzı önerileri almalıdırlar. Diyetler; meyve, sebze, tam tahıl, fındık ve baklagiller açısından zengin olmalı; düşük yağlı süt ürünleri ve deniz ürünleri açısından ılımlı olmalı; işlenmiş etler, şekerli içecekler, rafine tahıllar ve sodyum açısından düşük olmalıdır. Düzenli bir egzersiz, inme riskinde %25'lik bir azalmayla ilişkilendirilirken, obezite inme riskinde önemli artışlarla sebep olur. AHA'nın kardiyovasküler hastalıkları önlemek için önerdiği egzersiz yoğunluğu; haftada en az 150 dakika, orta düzeyde egzersiz yapabilmek için haftada beş kez 30 dakika veya haftada en az 75 dakika yoğun aktivite yapabilmek için haftada üç kez 25 dakika olarak belirlenmiştir (R. Naylor et al., 2023).

3.1. Medikal Tedavi

Medikal tedavi; arteriyel hipertansiyon, hiperkolesterolemi, diyabetin tedavisiyle birlikte antitrombotik ilaçlar olan aspirin ve klopidogrel kullanımını içerir (Mintz & Hobson, 2000). Antiplatelet kullanımı, asemptomatik hastalarda inme riskini azaltmadan ciddi kanama riskini artırabileceği gerekçesi nedeniyle tartışmalıdır. Antiplatelet tedavisinin kar-zarar dengesi asemptomatik hastalar için iyi analiz edilmelidir. Yüksek riskli plakları olan hastalara antiplatelet tedavisi önerilir (Hackam, 2021). Asemptomatik hastalarda tercih edilen ilk antiplatelet ilaç aspirin monoterapisidir. Klopidogrel, aspirin intoleransı olan hastalarda kullanılabilir (Uno, Takai, Yagi, & Matsubara, 2020). Başlangıç kolesterol düzeyine bakılmaksızın, semptomatik serebrovasküler hastalığı olan hastalarda statinlerin faydası kanıtlanmıştır. The İnme Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) çalışması, geçici iskemik atak (TIA) veya inme geçirmiş 4731 hastada yüksek dozda atorvastatin (günde 80 mg) ile plasebo arasındaki sonuçları değerlendirmiş, atorvastatin alan hastalarda, 5 yıllık fatal ve non-fatal inmede %26 oranında anlamlı bir risk azalması olduğu görülmüştür (Tendera et al., 2011). AHA'nın 2018 kılavuzları asemptomatik karotis arter hastalarında LDL-C'nin <1.8 mmol/L (70 mg/dL) olarak tutulmasını önermiştir (Hackam, 2021).

Kuzey Amerika'daki Semptomatik Karotis Endarterektomi Çalışması ve Asemptomatik Karotis Arter Hastalığı Çalışması'na katılan tüm hastaların akademik bir merkez tarafından yapılan incelemesinde, hastaların %84'ünde evre II veya daha ileri hipertansiyon (sistolik >160 veya diyastolik >90 mm Hg) saptanmıştır. Bu hastalarının %17'sinde renal arter hipertansiyonu tespit edilmiş ve bu oran, tedaviye dirençli hipertansiyonu olanlarda daha yaygın olarak

gözlenmiştir (%25). Bu bulgu, asemptomatik karotis arter stenozu hastalarında eşzamanlı renal arter stenozunun yüksek derecede varlığını göstermektedir. Bu durum özellik arz eder çünkü renin angiotensin sistemi üzerinde etkili olan ilaçlar, renal arter hipertansiyonunda kan basıncını etkili bir şekilde düşürebilir. Anjiyotensin dönüştürücü enzim inhibitörleri ve anjiyotensin reseptör blokerleri ayrıca aterosklerotik kardiyovasküler hastalığı olan hastalarda karotis arter aterosklerozunun ilerlemesini tersine çevirmeye ve vasküler olayları engellemeye yardımcı olabilir (Hackam, 2021). American Heart Association/American College of Cardiology 2017 hipertansiyon yönergeleri, hipertansiyonu ve kardiyovasküler hastalığı olan hastalarda hedeflenen kan basıncını <130/80 mm Hg olarak belirlemiştir (Whelton, P. K et al., 2018).

American Diabetes Association 2021 kılavuzlarına göre, çoğu tip 2 diyabet hastası için hedef hemoglobin A1c düzeyi <7.0% olmalıdır ve bu durum ciddi hipoglisemi gelişmeden sağlanmalıdır (American Diabetes Association, 2020). Kardiyovasküler faydası kanıtlanmış olan glukoz düşürücü tedaviler tercih edilir. Bunların arasında özellikle metformin, SGLT-2 (sodyum-glukoz ko transporter-2) inhibitörleri ve GLP-1 (glukagon benzeri peptid-1) reseptör agonistlerinin kullanımı faydalıdır. Bu tedavilerin kardiyovasküler olayları azaltmadaki rolüyle ilgili olarak American Heart Association/American College of Cardiology tarafından da yayınlanmış öneriler mevcuttur (Hackam, 2021).

3.2. Girişimsel ve Cerrahi Tedavi

3.2.1. Karotis Arter Stentleme (KAS)

KAS, daralmış olan arteryel segmenti ortadan kaldırmak için stentin endovasküler yolla yerleştirilmesi işlemidir. Karotis endarterektomi (KEA) ile karşılaştırıldığında perioperatif inme oranında önemli bir artışa yol açmaktadır. KEA'nın kontrendike olduğu durumlarda daha kullanışlıdır, örneğin genel anestezi riski yüksek olan veya daha önce bu bölgeye uygulanan cerrahi veya radyoterapi nedeniyle "hostile neck" durumunda olan hastalarda uygulanabilir (Arasu, Arasu, & Muller, 2021). Bu işlem lokal anestezi altında gerçekleştirilir. Periferik sinir hasarı riski olmadan yapılır ve ağrı daha azdır (Mintz & Hobson, 2000).

3.2.2. Karotis Endarterektomi (KEA)

Karotis endarterektomi (KEA), mortalite oranı ve perioperatif komplikasyon oranı düşük olan cerrahi bir tedavi yöntemidir. NASCET çalışmalarının sonuçları, ICA'nın %70'in üzerinde olan stenozlarında KEA'nın önemli vurgular. KEA, stenoz oranı %70-99 olan hastalarda kesinlikle endikedir ve yalnızca

perioperatif riskin <6% olduğu kurumlarda yapılmalıdır. KEA, iskemik olayın ardından mümkün olan en kısa süre içerisinde yapılmalıdır. Bu süre iki haftayı aşmamalıdır. Geleneksel olarak cerrahlar; TIA veya inme olayının sonrasında, ilk bir ay içinde operasyon yapmaktan kaçınmışlardır, çünkü algılanan periprosedürel komplikasyon riski daha yüksek olarak görülmüştür. Ancak yapılan randomize kontrollü çalışmaların analizlerinde, iskemik serebral olaydan sonraki ilk 2 hafta içinde operasyon geçiren hastalarda inme veya ölüm riskinin artmadığı gösterilmiştir. Sekonder inme önleme kılavuzları, bir TIA veya hafif inme ile başvuran hastalar için KEA'nın 2 hafta içerisinde yapılması gerektiğini önermişlerdir (Mintz & Hobson, 2000).

3.2.2.1 Anestezi Yöntemi

Karotis endarterektomi genel anestezi (GA), derin veya yüzeysel servikal blok ile bölgesel anestezi ve hatta sadece lokal anestezi (LA) altında gerçekleştirilebilir (Perler, 2013). Hem genel anestezinin hem de lokal anestezi yönteminin avantaj ve dezavantajları bulunmaktadır. Lokal anestezi altında cerrahi müdahale yapılırken nörolojik ve kardiyak komplikasyonlar daha hızlı şekilde tespit edilebilir ancak hasta uyumsuzluğu durumunda müdahale zorlaşabilir. Genel anestezi altında ise hastanın solunum yolu daha rahat kontrol altında tutulabilir ve hastadan kaynaklanan faktörler minimize edilmiş olur. Yapılan çalışmalar, ilk 30 gün içinde ölüm, inme ve diğer komplikasyonlar açısından lokal anestezi ve genel anestezi arasında anlamlı bir fark olmadığını göstermiştir (Rerkasem, Orrapin, Howard, Nantakool, & Rerkasem, 2021).

3.2.2.2. Cerrahi Teknik

Skapula arkasına yerleştirilen bir rulo ve başın altına konulan dolgulu bir halka ile birlikte kullanılır; böylece boyunda aşırı ekstansiyon olmadan bir miktar ekstansiyon sağlanır. Cilt insizyonu için iki seçenekten biri kullanılabilir. Standart kesi, sternokleidomastoid kasının medial kenarına paralel uzunlamasına yapılan bir kesidir. Alternatif yöntemde ise genellikle çene açısının 1 ila 2 cm altına paralel şekilde, cilt katlantısını içerecek şekilde yapılan kesidir (Perle, 2013).

Eversiyon Karotis Arter Endarterektomisi için, standart oblik cilt kesisi yapılır ve sternokleidomastoid kasın medial kısmından; İnternal Karotis Arter, Ana Karotis Arter (ACA) ve Eksternal Karotis Arter diseksiyonu gerçekleştirilir. İCA, ACA'in bulbus kısmından transekte edilir ve İCA everte edilir. Adventisyal tabaka korunacak şekilde endarterektomi yapılır. Sonrasında, transekte edilmiş İCA, ACA'ya yeniden anastomoz edilir. Lüzum halinde İCA kısaltılabilir (Aslim,

E., 2010). Eversiyon karotis endarterektomisi ile geleneksel karotis arter endarterektomisi arasında perioperatif inme, ölüm ve lokal komplikasyonlar (hematom, kraniyal sinir yaralanması) açısından fark gözlenmemiştir (Cao, P., De Rango, P., & Zannetti, S., 2002).

3.2.2.3. Karotis Endarterektomi'de Karotis Sinüs Blokajı

KEA sonrası hemodinamik instabilite, postoperatif morbidite ve mortalite ile yakından ilişkilidir (Tang, Walsh, Gillard, Varty, Boyle, & Gaunt, 2007). Hemodinamik instabilitenin sonucu olarak miyokard enfarktüsü, yeni nörolojik olaylar veya hatta ölüm meydana gelebilir. Hipertansiyon hastaların %56'sında görülür ve bu durum yara hematomuna, hiperperfüzyon sendromuna, inmeye ve miyokard enfarktüsüne sebep olabilir. Hipotansiyonun hasta popülasyonunun %50'sinde geliştiği gözlenmiştir. Bu durum yeni endarterektomize edilen arter içerisindeki kan akışını azaltabilir ve trombüs oluşumuna ardından da inmeye sebep olabilir. Ayrıca, sistemik hipotansiyon, eşlik eden koroner arter hastalığı olan hastalarda koroner perfüzyonu azaltabilir ve miyokard enfarktüsüne yol açabilir. KEA sonrası hipotansiyon nedensel olarak, karotis arterin adventisyasında bulunan özelleşmiş nöronlar olan karotis sinüs baroreseptörlerinin değişikliğine bağlanmıştır. Bu reseptörler, kan basıncında küçük bir artış hissedildiğinde uyarılan özelleşmiş nöronlardır. Bu durum kompansatuar bradikardi ve ardından kan basıncında bir düşüşü tetikler (Tang et al., 2007). Karotis sinüs blokajının temel amacı, KEA sonrası hemodinamik instabiliteyi en aza indirgemek ve ameliyat sonrası dönemde görülebilen hipotansiyon, hipertansiyon veya aritmileri azaltmaktır. Ancak, bu yöntemin avantajlarına dair belirgin kanıtlar bulunmamaktadır (Kürşat, 2021).

3.2.2.4. Karotis Endarterektomi'de Şant Kullanımı

Karotis endarterektomi ameliyatı esnasında şant kullanımı tartışmalıdır. Bazı cerrahlar rutin olarak kullanımını savunurken, bazıları seçici şantlama veya hiç şantlama yöntemini tercih etmektedir. Bazı dezavantajlar oluşturabilir. Bunlar arasında plağın kalkması, hava embolisi, arteriyel diseksiyon ve akut arteriyel tıkanıklık yer alabilir. Şant kullanımını destekleyenler, şantın serebral kan akışının sürdürülmesindeki önemini vurgularlar ve bu sayede şantın operasyonun daha uzun sürede yapılabilmesine olanak sağladığını savunurlar (Aburahma, Mousa, & Stone, 2011).

3.2.2.5. Karotis Endarterektomi'de Protamin İle Nötralizasyon

KEA sırasında heparin, vasküler klemp uygulanmadan önce rutin olarak uygulanmaktadır. Ancak heparinin protamin ile nötralizasyonu halen tartışma

konusudur. Heparine bağlı komplikasyonlar genellikle hayati tehlikeye neden olmayacak kadar nadirdir. Son dönemde gerçekleştirilen kapsamlı meta-analizlerde, protaminin ölüm, inme ve miyokard enfarktüsü üzerinde etkisiz olduğu, bununla birlikte boyun bölgesinde gelişen hematom ve revizyonu önemli ölçüde azalttığı gösterilmiştir (Polat, Akay, Koksal, & Bozkurt, 2019).

3.2.2.6. Karotis Endarterektomi'de Arteriotominin Kapatılması

KEA sırasında damar kapatma için ideal cerrahi teknik halen tartışmalı bir konudur (Uno, Takai, Yagi, & Matsubara, 2020). Yapılan çalışmalarda sonuçlar incelendiğinde, yama kullanımının ve eversiyon endarterektominin, takipte restenoz oranını ve nörolojik olayları azalttığı gösterilmiştir. Safen ven, sığır perikardı, dakron, politetrafloroetilen (PTFE) ve polyester gibi çeşitli materyallerin kullanılabildiği bu yamaların sonuçları birbiri ile benzerdir (Kürşat, 2021). Hemostaz süresi, PTFE yama kullanılan vakalarda, venöz yama veya dakron yama kullanılan vakalara göre daha uzundur. Safen ven yama kullanılan vakalarda anevrizmatik genişleme eğilimi olduğu gösterilmiştir ve bu nedenle birçok cerrah son zamanlarda sentetik yama kullanmayı tercih etmiştir (Uno et al., 2020).

3.2.2.7. Karotis Endarterektomi'de Sinir Hasarı

KEA sırasında en fazla yaralanma riski bulunan sinirler, fasiyal (V. sinir) sinirin marjinal mandibular dalı, vagus (X. sinir) sinirin laringeal dalları ve hipoglossal (XII. sinir) sinirdir. Bu sinirler, karotis bifurkasyonuna yakınlığından dolayı risk altındadır. Çoğu kraniyal sinir yaralanması muhtemelen retraksiyona veya klemplemeye bağlıdır Ancak koter kullanımı veya hemostaz için ligasyon kullanımlarından da kaynaklanabilir. Hipoglossal sinir, KEA sırasında en sık yaralanan kraniyal sinirdir ve yüksek yerleşimli lezyonlara erişimi artırmak amacıyla kesinin üst kısmına yapılan retraksiyon esnasında yaralanabilir. Fasiyal sinirin marjinal mandibular dalı genellikle mandibular retraksiyon nedeniyle ikinci en sık yaralanan sinirdir ve cilt insizyonunun kranial uzantısı sırasında da yaralanabilir. Üst ve rekürren laringeal sinirler aynı zamanda karotis arterin posteriorundaki diseksiyonlar ve klemplenme sırasında yaralanabilir (Beasley & Gibbons, 2008).

3.2.2.8. Karotis Endarterektomi'de Serebral Monitorizasyon

KEA ve KAS sırasında serebral iskemi nedeni ile güvenilir ve etkin bir izlem ihtiyacı bulunmaktadır. Genel anestezi ile yapılmayan bilinç açık hastalarda

nörokognitif fonksiyonların doğrudan izlenmesi, serebral iskemiyi tespit etmede yüksek duyarlılık ve özgüllüğe sahiptir; ancak, genel sonuç üzerindeki olumlu etkisi henüz gösterilmemiştir. Genel anestezi altındaki hastalarda ise karotis işlemleri esnasında, serebral iskemiyi izlemek ve iskemiye erken müdahale etmek için; Elektroensefalografi, Somatosensoriyel ve Motor Uyarılmış Potansiyel, Serebral Oksimetri, Transkranial Doppler ve Karotis Güdük Basıncı gibi yöntemler kullanılmaktadır. Her bir modalitenin, KEA ve KAS sırasında serebral iskemiyi izleme açısından avantajları ve dezavantajları vardır ve şu anda hiçbiri diğerlerine karşı net bir şekilde üstünlük göstermemektedir. Bu nedenle, bu gibi yüksek riskli işlemlerde serebral iskemiyi daha iyi tespit etmek amacıyla farklı izleme modalitelerini birleştirmek, özellikle genel anestezi nedeniyle nörokognitif fonksiyonların doğrudan değerlendirilemediği hastalarda önemlidir ve önerilir (Li, Shalabi, Ji, & Meng, 2017).

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