CHAPTER III

CARDIOVASCULAR DISEASES AND PREVENTION

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1. Cardiovascular Diseases

Cardiovascular diseases (CVDs) that consist of stroke, heart attack and other numerous cardiac and vascular conditions are the leading global cause of premature mortality and an important factor, which decreases quality of life (GBD 2017, Kumar et al. 2009). CVDs are actually a collection of diseases affecting the heart, blood vessels of the heart and the brain. In 2017, 18.8 million people died from CVDs worldwide (GBD 2017). According to the data of the Turkish Statistical Institute (TSI), CVDs was the leading cause of deaths in Turkey in 2016, accounting for 39.8% of all deaths (TSI 2016). According to the data reported by the Turkish Study of the Incidence of Chronic Diseases and Risk Factors (TKrHRF), the incidence of CVDs was found as 3.8% in men and 2.3% in women, but this rate raised up to 19.6% in men and 10.8% in women aged over 75 years (Unal and Ergor 2013). It is estimated that by 2030 annual medical costs associated with CVDs will rise to 1,044 USD (Mozaffarian et al. 2016) The consequences of these diseases are even worse in the developing countries (WHO 2004). According to the World Health Organization (WHO), over three quarters of deaths from CVDs occurs in low- and middle income countries (WHO 2017). Many types of CVDs occur as a complication of atherosclerosis.

1.1. Atherosclerosis

Atherosclerosis is a multifactorial chronic and inflammatory disease characterized by arterial stenosis and occlusion as a result of the disruption of the flexibility of the arteries (Yusuf et al. 2004, Khera & Kathiresan, 2017). It is a disease of arterial vasculature characterized by an imbalance and abnormal accumulation of inflammatory cells, matrix deposits and lipids in the walls of the medium and large arteries (Mota et al. 2017). Atherosclerosis is especially prevalent in the developed countries, but its incidence is rapidly increasing also among the populations in the developing countries (Herrington et al. 2016). Atherosclerosis begins in
the early periods of life (most commonly the second decade), but does not manifest until thrombotic complications such as coronary syndromes and stroke (Charakida et al. 2006). It is a complex pathological process occurring in the walls of the vessels over years. In this complex process, deposits (plaques) in the medium and large arteries cause the inner surface of the vessels to become irregular and the lumen of vessels narrows. Eventually the deposit (plaque) can rupture, leading to formation of a blood clot. When this clot occurs in a coronary artery, it can cause a heart attack, and if it occurs in the brain, a stroke may occur. In a heart attack, blood supply is interrupted due to the diseases of the vessels supplying the heart, which in turn lacks oxygen and nutrients to fuel its muscular contractions and pumping function. In a stroke, the same type of condition occurs in the brain, and lack of oxygen disrupts its normal functioning. Heart attacks and strokes are acute life threatening events mainly caused by a blockage, which prevent blood flow to parts of the heart or brain. Schematic illustration of atherosclerosis is given in Figure 1.

![Atherosclerosis](https://example.com/atherosclerosis.png)

**Figure 1.** Schematic illustration of the development process of atherosclerosis. ©2008 TRIALSIGHT MEDIA

Atherosclerotic lesions most commonly occur within arteries, but these lesions are especially seen at vessels curves and bifurcations where smooth blood flow is disrupted by shear forces produced by blood flow (Winkel et al. 2015). Vascular endothelium, monocytes/macrophages, smooth muscle cells, some growth factors and cytokines are involved in the atherosclerotic process. It is now widely recognized that a systemic inflammatory process is involved in atherogenesis, causing vascular damage. Therefore, people with autoimmune diseases characterized by chronic systemic inflammation such as rheumatoid arthritis (RA) are at an increased risk of developing CVD.
1.2. Risk factors of CVDs

In general, risk factors of CVDs include but are not limited with smoking, hypertension, dyslipidemia, diabetes mellitus, obesity, sedentary lifestyle and dietary factors (Capewell et al. 2010). The WHO reported that the incidence of CVDs can be reduced by half by the control of hypertension, obesity, cholesterol and smoking (WHO 2016). For a more accurate classification, risk factors of CVDs can be divided into two groups as modifiable and non-modifiable factors (Figure 2). Modifiable risk factors can be further divided into two groups as behavioral risk factors (tobacco use, unhealthy diet, sedentary life etc.) and physical risk factors (hypertension, high cholesterol, diabetes mellitus, obesity etc). On the other hand, several studies have shown the elevation of certain analytical parameters as physical risk factors of CVDs. These parameters include hsCRP, lipoprotein (a), fibrinogens, glycated hemoglobin and ceruloplasmin (Kumar et al. 2008). In addition, high homocysteine levels are associated with a higher risk of CVDs and stroke.

![Figure 2. Risk factors of cardiovascular diseases.](image)

1.3. How to prevent risk factors of CVDs

Most CVDs can be prevented by addressing behavioral risk factors. Lifestyle changes can be an important preventive measure in order to overcome the risk of developing CVDs. These changes may include at least 30 minutes of brisk walking 3-4 times a week, >4 servings/day of fresh fruits and vegetables etc. Grains and green leafy vegetables should be included in the diet. Tobacco use should be stopped and harmful alcohol consumption should be avoided. Being dependent on natural food instead of supplements could reduce the risk of future CVDs. People who are at a high risk of developing CVD due to modifiable physical risk factors such as hypertension, diabetes mellitus and hyperlipidemia need early
recognition of their conditions and management with appropriate medical therapy.

1. Symptoms of CVDs

Mostly a heart attack or stroke may be the underlying cause of CVDs. According to the data published by WHO, 85% of CVDs in 2016 resulted from a heart attack or stroke. These conditions are equal in men and women. The WHO estimates that 23.6 million people will die from CDV conditions by 2030 and mostly because of heart attack and stroke. Heart attack symptoms include (WHO 2017):

- Pain in the center of the chest
- Pain in the arms, left shoulder, jaw or back
- Shortness of breath, vomiting, cold sweat and becoming pale may also be observed.

Symptoms of a stroke are as follows (WHO 2017):

- Sudden onset of weakness and/or numbness in the face, arm. The weakness is mostly unilateral.
- Difficulty in speech, confusion
- Difficulty in vision
- Difficulty in walking and dizziness
- Fainting

2. Coronary Artery Disease

Also known as coronary heart disease or atherosclerotic heart disease, coronary artery disease (CAD) results from the inflammatory accumulation of macrophage white blood cells within the walls of the arteries supplying the myocardium. The lifetime risk of developing CAD after 40 years of age is 48% for men and 32% for women. Table 1 shows the major prognostic risk factors of coronary artery disease (Hachamovitch et al. 2003).
**Table 1. Major prognostic risk parameters of coronary artery disease**

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Echocardiography</th>
<th>Laboratory markers</th>
<th>Stress Perfusion Scintigraphy</th>
<th>Exercise ECG</th>
<th>Coronary anatomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Diabetes mellitus, Hypertension, Current smoking, Prior MI, PVD, Severity of angina</td>
<td>LVEF &lt; 50% Wall motion abnormality &gt; 3</td>
<td>Total cholesterol hs, CRP hs, Troponin</td>
<td>Reversible perfusion defect &gt; 10%LV</td>
<td>Exercise duration, Duke treadmill score</td>
<td>Left main disease 3-vessel disease especially proximal LAD Syntax score &gt; 32</td>
</tr>
</tbody>
</table>


CAD results from atherosclerosis of the coronaries or arteriosclerosis. In this process, the intima layer of the artery is damaged. Cholesterol begins to accumulate in the walls of the artery. One or several plaques adhere to the arterial endothelium, causing narrowing of the artery diameter, arterial occlusion and the formation of thrombosis. Mainly involved coronary arteries are the left coronary artery, left descending coronary artery, circumflex artery and right coronary artery (Figure 3).

2.1. Symptoms of CAD

The signs and symptoms of CAD are recognized at the advanced stage of the disease and most people do not show signs of the disease for years as the disease progresses and finally a sudden heart attack occurs. CAD is the most common cause of sudden death. The major symptom of CAD is chest pain, known as angina pectoris.

2.1.1. Angina Pectoris

Angina pectoris, which is one of the cardinal symptoms of CAD, was described for the first time by William Heberden in 1772 (Chapelle 1960). Almost half of CAD patients present with angina pectoris. Angina pectoris results from myocardial ischemia, which is caused by an impaired balance between the requirement and supply of myocardial O₂. Increased heart rate, contractility and wall tension increase the demand for oxygen. Coronary blood flow is provided by the pressure difference between diastolic blood pressure and end-diastolic blood pressure. Coronary occlusion or any other cause reducing coronary perfusion gradient will
result in myocardial ischemia. Angina pectoris manifests as a sensation of pressure in the chest, pain in the arm (usually one side), jaw and the other forms of discomfort. ‘Discomfort’ term is preferred over ‘pain’, because this sensation varies widely among individuals in intensity and character. People mostly do not perceive angina as pain unless it becomes severe.

Angina is divided into two subtypes as stable and unstable angina. The occurrence of stable angina is predictable. Stable angina occurs upon physical exertion or feeling considerable stress. Typically, the frequency of stable angina does not change and it does not become worse over time. On the contrary, unstable angina occurs at rest or on stress exertion. The frequency and severity of pain increase. An attack of unstable angina is an emergency and requires seeking medical aid. When left untreated; unstable angina leads to heart attack, heart failure or arrhythmias that can become life threatening conditions.

2.2. Diagnosis and treatment of CAD

The diagnosis of CAD is established through electrocardiogram (ECG), echocardiogram, exercise stress test, nuclear stress test, cardiac catheterization and angiogram, and cardiac CT scan. Treatment of CAD has three approaches including lifestyle changes, medical therapy and surgical therapy.

Lifestyle changes include quitting smoking, a healthy diet, regular exercise, weight loss and reducing stress. Medical therapy included administration of cholesterol modifying drugs, aspirin, beta-blockers, calcium channel blockers, ranolazine, nitroglycerin, angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARB). Surgical procedures aim to restore and/or improve coronary blood flow and include percutaneous coronary revascularization and coronary artery bypass grafting. Coronary artery bypass grafting (CABG) can be applied as cabg with heart lung pump, cabg in beating heart, aortic no tuch cabg, full arterialized cabg and minimally invasive cabg.

3. Hypertension

Hypertension is a chronic elevation of blood pressure that causes end-organ damage and leads to morbidity and mortality in the long term. It is a health condition occurring as a result of repeatedly elevated systolic blood pressure above 140 mmHg and diastolic blood pressure above 90 mmHg. Systolic blood pressure is the pressure in the arteries as the heart pumps blood into the arteries, while diastolic blood pressure is the pressure that results from a relation of arteries after contraction (Cunha and Marks
Systolic hypertension is a predictor of coronary and cerebrovascular risk especially in elderly patients. Treatment of systolic hypertension is effective in control of the risk and reducing morbidity in these patients. The pathogenesis of hypertension is a multifactorial and complex process. The kidney both contributes and is affected by hypertension (Hall JE et al. 2012). In hypertension, the extent of the target organs (heart, brain and kidneys) determines outcome.

Hypertension is a major health problem worldwide because of its high prevalence and association with cardiovascular diseases. Globally, hypertension causes 7.1 million premature deaths (Whitworth 2003). It has been estimated that 1.56 billion people will have hypertension by 2025 (Kearney et al. 2005). Hypertension is a common risk factor for many diseases including CVDs, cerebrovascular diseases and kidney disease, and is a major risk factor of premature mortality and morbidity worldwide (Lim et al. 2013, Hay et al. 2017). Efficient management of hypertension has resulted in significant reduction of the incidences of coronary artery disease and stroke in developed countries. However, it remains a great concern to resolve in many regions of the world due to the increasing incidence of hypertension related diseases such as stroke, end-stage renal disease and heart failure (WHO 2004 hypertension report). Studies have reported that an individual who is normotensive at age 55 years has a 90% lifetime risk of developing hypertension within the rest of his/her life (Chobanian et al. 2003). Stages of hypertension is shown in Figure 4.
Figure 4. Staging of hypertension according to the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Bethesda (MD): National Heart, Lung, and Blood Institute (US) (JNC 2004).

3.1. Types of Hypertension

There are mainly two types of hypertension: primary (essential) and secondary hypertension. In primary hypertension, blood pressure increases, but the reason for this is not known and can cause cardiac, cerebral and renal damage. It is associated with some risk factors including ageing, genetic, and environmental factors (Weber et al. 2014, Messerli et al. 2007). Patients with primary hypertension have difficulty in memory and attention (Lande et al. 2017). The other type, secondary hypertension accounts for about 5% of all hypertension cases. The cause can be determined in this type of hypertension. Secondary hypertension is generally resulted from chronic renal disease, renal dysfunction, adrenal gland tumor etc. (Weber et al. 2014).

3.2. Risk factors of hypertension

The risk factors that can lead to hypertension include smoking, stress, excessive salt intake, obesity and alcohol. With tobacco exposure, the number of intracranial arterial segments increases with atherosclerotic plaques, leading to hypertension (Gać P et al. 2017). Increased stress activates the sympathetic nervous system, increasing blood pressure
Sympathetic system is also activated by salt intake because increased plasma volume and cardiac output due to salt intake. In people with essential hypertension, the most significant cause is obesity. Excessive alcohol intake causes hypertension through oxidative stress, vascular injury, decreased production of nitric oxide and impaired baroreceptors (Husain et al. 2014).

3.3. Complications of hypertension

Cardiac consequences of hypertension include CAD and left ventricular hypertrophy. CAD is associated with hypertension, which accelerates the disease, leading to myocardial ischemia and myocardial infarction. The incidence of myocardial incidence is higher in hypertensive patients. There are two major factors contributing to myocardial ischemia: (1) increased oxygen demand due to pressure and (2) decreased oxygen supply due to atheromatous lesions. Another complication of hypertension is heart failure that results from chronic pressure overload. Aortic aneurysms and dissections, which cause serious mortality due to hypertension, may also develop. Treatment of aortic aneurysm dissection is usually surgical.

3.4. Treatment of hypertension

Lifestyle changes are the first step to control hypertension. These changes include sodium restriction, weight loss, decreasing alcohol intake and regular exercise. Medical therapy is indicated when lifestyle changes fail or hypertension is already at an advanced stage. All anti-hypertensive drugs exert their actions by decreasing cardiac output or peripheral vascular resistance or both. The most commonly used antihypertensive drugs are as follows:

- Diuretics
- Beta-blockers
- Calcium channel blockers
- Angiotensin converting enzyme inhibitors
- Angiotensin II receptor blockers
- α1-Adrenergic blockers
- Direct vasodilators
- Central adrenergic inhibitors
- Natriuretic peptides

5. Heart valve disease (Valvular heart disease)

Heart valve disease (HVD) is a group of the cardiac pathologies seen in one or more of the four valves of the heart, which progresses by ageing and leads to serious health problems if left untreated. The exact incidence of heart valve disease is unknown. Its prevalence in the USA has been
Common forms of HVD are given in Figure 5. The most significant forms of HVD include aortic stenosis, aortic regurgitation (chronic and acute), mitral stenosis and mitral regurgitation (chronic and acute), and will be discussed below.

Figure 5. Common forms of heart valve disease

5.1. Aortic valve stenosis

Aortic stenosis (AS) is the most common valve disease characterized by progressive thickening, calcification and fibrosis of valvular leaflets, leading to valve obstruction (Pawade et al. 2015). AS is a public health problem and the most common form of HVD in Western countries as reported by a study, which has evaluated the effects of this valvular pathology in 185 countries (Yadgir et al. 2020). Its rate of prevalence is similar between men and women. Light alcohol consumption has been found to be associated with a low risk of AS, while smoking, hypertension, diabetes mellitus, renal insufficiency, obesity and metabolic syndrome seem to be involved in the development of AS (Larsson et al. 2017). Patients typically become symptomatic when the aortic valve area is severely reduced and show symptoms such as angina, dyspnea and fainting, usually upon exercise. AS is the second most common fatal heart disease following coronary artery disease. Three major causes of AS are atherosclerosis, congenitally malformed valves and rheumatic heart disease. Most people with AS do not show symptoms until the amount of restricted blood flow becomes significantly reduced. The main symptoms of AS include: angina, shortness of breath, dizziness, edematous ankles and/or feet and significantly decreased ability to perform daily activities.

The diagnosis of AS starts with physical examination. The classic crescendo-decrescendo murmur is heard especially at the right upper sternal border. In severe AS, the physical findings of systolic heart failure
becomes more prominent. After physical examination, the patient is evaluated with a transthoracic echocardiogram. Alternative diagnoses are ruled out with this examination. Echocardiographic examination also can detect associated aortic regurgitation, which can complicate the management of AS. (Nishimura et al. 2014). When non-invasive assessments of the aortic valve fail, the first invasive method to be attempted is catheterization. The management of AS included medical therapy and surgery. Medical management of patients with mild-to-moderate AS include ACE inhibitors, beta-blockers and aldosterone receptor antagonists. In addition, comorbidity in these patients such as hypertension should also be managed properly. Aortic balloon valvuloplasty is preferred in children, while surgical intervention may include mechanical/bioprosthetic valve replacement.

5.2. Aortic regurgitation

Aortic regurgitation is a disease characterized by inadequate closure of the valvular leaflets. AR occurs when part of the blood ejected from the left ventricle into the aorta during the systolic phase flows back to the left ventricle during the diastolic phase. The incidence of AR has been reported as 13% in men and 8.5% in women (Coffey et al. 2016). Based on the etiology, AR can be classified as acute and chronic AR and based on the severity as mild, moderate and severe AR. Because of this backflow, workload of the left ventricle increases. Patients with acute AR may remain asymptomatic for long years. However, if left unnoticed and untreated, this condition eventually may lead to congestive heart failure. In chronic AR, left ventricular hypertrophy enables the left ventricle to adapt to increased diastolic volume. Whereas in acute AR, there is no time for this adaption and the increase in the left ventricular diastolic volume results in the increased left ventricular diastolic pressure (Stout and Verrier 2009).

As AR worsens, symptoms begin to manifest. The symptoms of AR include fatigue, weakness, dyspnea, angina, and arrhythmias. Echocardiography plays a critical role both in diagnosis and management of AR. In evaluation of patients with AR, classifying the severity of the regurgitation is the first step. A loud diastolic murmur, a third heart sound and a widened pulse pressure are signs of severe AR, but are not specific (Tribouilloy et al. 2001). ECG, chest X-ray and echocardiography are adjuvant imaging modalities. Doppler echocardiography is the mainstay of the evaluation of AR. In the management, AR patients may have a high risk of developing endocarditis and should be administered antibiotic prophylaxis. Conservative treatment usually contains vasodilators mostly in mild-to-moderate AR, while surgical option includes valve replacement using either a mechanical or a biological prosthesis in patients with severe AR.
5.3. Mitral stenosis

Mitral stenosis (MS) is a valvular heart disease characterized by inability of the blood to flow from the left atrium to the left ventricle at the level of the mitral valve. MS is divided into two classes as pure MS and mixed MS. Pure MS accounts for about 25% of all heart valve diseases, while this rate is nearly 40% in mixed MS. Chronic rheumatic heart disease, rheumatic fever, hypoplasia of the left ventricular cavity and endocardial fibroelastosis are involved in the etiology of MS. Among these, the most common cause of MS is rheumatic fever (Gordon et al. 1992).

Symptoms of MS include dyspnea, cough, tachycardia, fatigue, hoarseness, edema in feet and embolic symptoms. The diagnosis of MS is established with physical examination, ECG, exercise tolerance test, chest X-ray and echocardiography. Medical treatment of MS includes treatment of complications such as atrial fibrillation and dyspnea. The used medications include beta-blockers, calcium channel blockers, long-acting nitrates, warfarin and heparin (Nishimura et al. 2014, ESC 2012). Surgical treatment options include balloon and mitral valve replacement.

5.4. Mitral regurgitation

Mitral regurgitation (MR) is a valvular disease caused by pathology of the valve that prevents normal closure (primary MS) or LV dysfunction, which affects proper closure of the mitral valve (secondary MR). Based on the disease onset MR can be acute or chronic in nature. Acute MR results from any disruption of normal valvular mechanism. Possible pathologies in acute MR are as follows:

- Growth of vegetations on the leaflets in case of endocarditis.
- Chordae rupture in patients with degenerative disease.
- Papillary muscle rupture because of an ST-elevation MI.

In chronic MR, anatomy of the mitral valve is normal, but its function is impaired due to left ventricular pathologies such as inability of the leaflets to meet properly due to dilatation of mitral annulus, and abnormal movement of the left ventricle following infarction or ischemia. MR (acute and chronic forms) affects approximately 5/10,000 people.

Symptoms of MR include dyspnea with exertion, fatigue, reduced exercise ability, tachycardia and swelling of the legs, abdomen and veins in the neck. Chest pain is less common. Before the treatment, severity of MR should be established. Imaging tools used to classify severity of MR include transoesophageal echocardiography and transthoracic echocardiography. In addition, ECG, exercise test and biochemical analysis are also performed. Medical treatment of primary MR consists of
vasodilators and inotropic agents. Whereas, in chronic MR classical heart failure treatment is applied with beta-blockers, ACE inhibitors, aldosterone antagonists and diuretics. In surgical treatment, valve repair is preferred over replacement as much as possible (Feldman et al. 2011).

6. Peripheral artery disease

Peripheral artery disease (PAD) is an acute/chronic disease occurring in the arteries that provide blood flow from the aorta toward the periphery in the body. PAD is narrowing of the peripheral arteries supplying the legs, arms, stomach and head. PAD is caused by atherosclerosis and most commonly affects arteries in the legs. PAD patients are at a very high risk of developing cardiac or cerebrovascular disease (Shammas 2007). Risk factors of PAD include:

- Hypertension
- Diabetes mellitus
- Hyperlipidemia
- Homocysteinemia
- Uric acid metabolism
- Hypercoagulation
- Smoking
- Obesity
- CAD

PAD has serious complications including critical limb ischemia, stroke and heart attack. Symptoms of PAD are painful activities such as climbing stairs, intermittent claudication, numbness and weakness of the legs, coldness in one leg compared to other, color change in legs, slower growth of toenails, ischemic ulcer, a weak pulse in the legs or feet and erectile dysfunction in men.

Findings on physical examinations include inability to receive pulses, heat differences between the extremities, muscle atrophies and ischemic color changes in the extremities. Management of PAD involves lifestyle changes, medical treatment (iloprost, clopidogrel, cilostazol, acetyl salic acid), intravascular interventions and surgical interventions (anatomic and/or extra-anatomic bypass procedures). The measures that should be taken to prevent PAD are:

- Quitting smoking
- Keeping blood glucose under control
- Regular exercise
Lowering cholesterol and blood pressure
● Low-saturated fat diet
● Weight loss for overweight or obese persons

6.1. Acute extremity ischemia (Acute limb ischemia)

Acute extremity ischemia (AEI) is a condition in which localized ischemia develops as a result of the occlusion of arterial structure by an embolic or thrombotic material. AEI is a sudden decrease in limb perfusion, which leads to a threat in the viability of the affected limb (Setghi et al. 2013). The most common complaint is sudden-onset pain and coldness in the affected extremity. Embolism, thrombosis, hypercoagulability states, arterial trauma, iatrogenic causes, aortic dissection, vasospasm, arteritides and thoracic outlet syndrome are involved in the etiology of AEI. Findings in the physical examination are shown in Figure 6.

Figure 6. Findings of acute extremity ischemia

Differential diagnosis of AEI involves critical chronic extremity ischemia, acute deep vein thrombosis, spinal cord or peripheral nerve compression. The diagnosis of AEI is established with medical history, physical examination, biochemical analysis (including lactate and thrombophilia screening), ECG, Doppler ultrasound scan and CT angiography (Van DH et al. 2018). Conservative management of AEI is carried out with a prolonged course of heparin and regular assessment of the patient, although AEI is a surgical emergency. Surgical treatment options of embolic-cause AEI are embolectomy with a Fogarty catheter, local intra-arterial thrombolysis and bypass surgery in the case of insufficient flow back, while thrombotic AEI is treated with local intra-arterial thrombolysis, angioplasty and bypass surgery (Fluck et al. 2020).
7. Venous disorders

Common venous system disorders include chronic venous insufficiency, deep vein thrombosis, excessive blood clotting, superficial venous thrombosis (phlebitis) and varicose. Venous disease is more common than PAD and affects about 30 million people only in the USA (Criqui and Aboyans 2015).

Symptoms of venous disorders involve burning, fatigue, itching, pain, swelling, throbbing, muscle cramping, pigmentation and ulcer depending on the type of the disease. CEAP classification is used for standardization of venous disorders. CEAP includes a description of the clinical class (C) based on the etiology (E), anatomical (A) distribution of the reflux or obstruction in the veins and underlying pathophysiology (reflux or obstruction) (P). CEAP classification of venous disorders is shown in Table 2 (Eklof et al. 2004).

**Table 2. CEAP classification of venous disorders**

<table>
<thead>
<tr>
<th>CEAP</th>
<th>Clinical Classification</th>
</tr>
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<tbody>
<tr>
<td>C0</td>
<td>No visible or palpable sign of venous disease</td>
</tr>
<tr>
<td>C1</td>
<td>Telangiectasies or reticular veins</td>
</tr>
<tr>
<td>C2</td>
<td>Varicose veins</td>
</tr>
<tr>
<td>C3</td>
<td>Edema</td>
</tr>
<tr>
<td>C4a</td>
<td>Pigmentation or eczema</td>
</tr>
<tr>
<td>C4b</td>
<td>Lipodermatosclerosis</td>
</tr>
<tr>
<td>C5</td>
<td>Healed venous ulcer</td>
</tr>
<tr>
<td>C6</td>
<td>Active venous ulcer</td>
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Age, gender, weight height, bowel habits, a history of deep venous thrombosis and genetics, sedentary life and occupation predispose to develop varicose veins (Pfisterer et al. 2014). Treatment of venous disorder includes several techniques such as compression therapy, endovenous laser ablation, radiofrequency ablation, endothermal heat-induced thrombosis.
Non-thermal treatment options are sclerotherapy, mechanochemical ablation, and cyanoacrylate.

8. Deep vein thrombosis (DVT)

DVT and its major complication pulmonary embolism, together known as venous thromboembolism (VTE) are one of the important causes of morbidity and mortality worldwide. VTE is the third most common cardiovascular pathology (Raskob 2014). In the USA, 900,000 new cases and 300,000 deaths are reported annually due to VTE (Heit 2017). DVT usually develops in the deep veins of the legs, leading to pain, edema, redness and abnormalities in gait. The development of DVT involves a complex cascade of events. When limb muscles do not contract properly and regularly, blood flow rate decreases in certain veins, increasing the risk for developing DVT (Bovill and van der Vliet 2011). Risk factors of DVT involve recent surgery, recent trauma to the leg, pregnancy, immobilization due to a condition such as a medical illness, hormonal medications including contraceptives and genetic factors.

Diagnosis of DVT is based on imaging studies including duplex ultrasonography, D-dimer blood test, contrast venography and magnetic resonance imaging. Medical treatment of DVT is applied with anticoagulants, thrombolitics. Compression therapy with stockings and compression devices. Thrombectomy is used as the surgical approach in the treatment of DVT. Interventional radiology procedures are also used for the treatment of DVT. Mechanical thrombectomy is used following interventional radiologic procedures in selected patients with acute DVT, while balloon angioplasty and stent placement can be used in patients with chronic DVT.

9. Cerebrovascular disease

Cerebrovascular disease is a group of conditions and disorders that affect blood vessels and blood supply to the brain. The most common cause of cerebrovascular disease is atherosclerosis. In addition, thrombosis and cerebral venous thrombosis may also cause cerebrovascular disease. Cerebrovascular disease is the fifth most common cause of mortality in the USA with 147,810 deaths in 2018 (CDC 2018). Common types of cerebrovascular diseases are shown in Figure 7.
Although symptoms of cerebrovascular disease vary depending on the site of the blockage, the common symptoms include a severe and sudden-onset headache, hemiplegia, confusion, hemiparesis and slurred speech. The most common cerebrovascular disease is by far stroke.

Stroke is a cerebrovascular disease characterized by sudden-onset neurologic deficit mostly due to brain infarction (ischemic stroke) and rarely because of intracerebral hemorrhage (Johnston et al. 2009). Stroke also significantly contributes to the development of cognitive decline and dementia (Viswanathan et al. 2009). Stroke causes significant morbidity and mortality as well as healthcare costs worldwide. There is also a considerable burden of post-stroke care (Rajsic et al. 2018).

Common factors leading to stroke are large artery atheroma and cardiac embolism sources in ischemic stroke, while small artery disease is involved both in ischemic and hemorrhagic stroke (Greenberg 2006).

Risk factors of stroke include age, race, waist-to-hip ratio, family history, smoking, alcohol consumption, hypertension, diabetes mellitus hyperlipidemia, atrial fibrillation, Western style diets (O'Donnell 2010) and obesity. Signs and symptoms of stroke are as follows (CDC 2020):

- Sudden numbness or weakness in the face, arms or legs (especially unilateral)
- Sudden difficulty in speaking and understanding, confusion
- Sudden problem in seeing by one eye or both eyes
- Sudden trouble in walking, dizziness, loss of balance, impaired gait
- Sudden-onset headache of unknown cause
Stroke prevention is achieved by modifying the risk factors. The best preventive measures to be taken against stroke are eating a healthy diet, avoiding smoking and alcohol abuse, and regular exercise.
References:


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