Medical University - Pleven

Faculty of Medicine

Department of Cardiology, Pulmonology and Endocrinology

Dr. Nikolay Sergeev Ivanov

Characteristics and interventional treatment of patients with vertebral artery stenosis

Dissertation work

for the acquisition of an educational and scientific degree "Doctor"

Field of higher education: 7. Health care and sports

Professional direction: 7.1 Medicine

Doctoral program: "Cardiology"

Scientific supervisor - prof. Dr. Plamen Marinov Gatsov, Ph.D.

Pleven 2024

The dissertation is written on 127 pages, of which literature review – 38, purpose, tasks and methods – 24, results – 26, conclusions, contributions, list of publications related to the dissertation – 4, bibliography – 12. The bibliography includes 145 literary sources, of which 10 – in Cyrillic and 134 – in Latin.

The dissertation contains 47 figures - 27 of them in overview and methods, 20 in results and 17 tables – 14 of them in results, 3 in overview and methods.

The doctoral student was enrolled in part-time doctoral studies on 19.11.2018 at the Department of "Cardiology, Pulmonology and Endocrinology" (order No. 2953/19.11.2018 of the Rector of MU Pleven).

The dissertation work was discussed and accepted for official defence at a meeting of the extended departmental council of the department "Cardiology, pulmonology and endocrinology", on November 28, 2024

Scientific jury:

1. Prof. Snezhana Tomova Tisheva, MD
2. Assoc. Konstantin Dimitrov Gospodinov, d.m.
3. Assoc. Ivan Hristev Manukov, d.m.
4. Assoc. Plamen Krasimirov Krastev, d.m.
5. Assoc. Svetlin Nedkov Tsonev, d.m.

The official defence of the dissertation will take place on .... at .... o'clock,

In ....

The defence materials are published on the website of the MU -www.mu-pleven.bg

CONTENTS

ABBREVIATIONS USED

BP	Blood pressure
AV	Aortic valve
AH	Arterial hypertension
VA	Vertebral angiography
VBS	Vertebro-basilar system
VBVI	Vertebrobasilar vascular insufficiency
RV	Right camera
RCA	Right coronary artery
RA	Right atrium
ECG	Electrocardiography
EchoCG	Echocardiography
DM	Diabetes mellitus
CN	Cranial nerve
MV	Mitral valve
MR	Magnetic resonance
CAD	Coronary artery disease
BSP	Blood sugar profile
CT	Computed tomography
CTA	Computed tomography angiography
LV	Left camera
LCA	Left coronary artery
LA	Left atrium
IVS	Interventricular septum

ODT	Optimal drug therapy
CBC	Complete blood count
AF	Atrial fibrillation
SCAG	Selective coronary angiography
HR	Heart rate
TIA	Transient ischemic attack
TTE	Transthoracic echocardiography
USE	Ultrasound examination
EF	Ejection fraction
AHA	American heart association
AICA	Anterior inferior cerebellar artery
AL	Amplatz left
AP	Anterior-posterior
AR	Amplatz right
BMI	Body mass index
BMS	Bare metal stent
DES	Drug eluting stent
EBU	Extra backup
IVC	Inferior vena cava
JL	Judkins left
JR	Judkins right
MRA	Magnetic resonance angiography
MRI	Nuclear magnetic resonance
NO	Nitric oxide
PICA	Posterior inferior cerebellar artery

1. INTRODUCTION

The vertebro-basilar system (VBS) plays an essential role in the blood supply of vital structures of the nervous system. As part of the circle of Willis, it contributes to the great compensatory capabilities of the cerebral circulation in some hemodynamic disorders. On the other hand, some pathological processes affecting the VBS can be fatal or lead to severe damage and functional deficits in the patient. The many varieties and abnormalities of the VBS are a frequent cause of hemodynamic disorders and vascular involvement from disease processes. 20% of ischemic strokes in VBS are caused by stenosis of the extra - or intracranial segments of the vertebral arteries. Atherosclerotic plaque is the basis of formation of vascular stenosis. A good knowledge of the varieties, as well as the anatomy, allows us to understand the pathophysiology and pathogenesis of these disorders, which, together with the characteristic clinical appearance, helps to make the diagnosis more quickly and accurately. This is the basis of starting the right treatment. Transcatheter selective angiography of the vertebral arteries has proven to be the method with the highest sensitivity and accuracy for the evaluation of extracranial segments of the vertebral arteries. It is also a safe and effective method of restoring normal circulation in the VBS.

2. PURPOSE

To investigate the possibilities of catheter selective angiography in the diagnosis of patients with a possible violation of the blood supply in the vertebro-basilar system, as well as the interventional methods of treatment in these patients.

3.TASKS

1. Through catheter selective vertebral angiography, to determine the anatomy of the extracranial arteries in patients with a clinical picture of VBS insufficiency.

2. To investigate the variations in the extracranial segments of the cerebral circulation in these patients.

3. To establish the most common pathological processes leading to hemodynamic disorders in the extracranial segments in patients with insufficiency in VBS.

4. To investigate the correlation between pathological processes in VBS and the coronary system.

5. To assess the possibilities of treatment with catheter methods in patients with circulatory disorders in the VBS.

4.METHODS

For the purposes of the dissertation, the following methods were used:

1. Anamnesis
2. Status
3. Laboratory studies
4. Electrocardiography (ECG)
5. Echocardiography (EchoCG)
6. Selective transcatheter angiography
7. Statistics

4.1 History

The anamnesis of all 74 participants in the study was taken from the data of the patients, their relatives, and the accompanying medical documentation. The doctor is informed about the patient's name, age, gender, education, profession and family status. Complaints reported by the patient are recorded in their own words, in chronological order of their appearance. If necessary, when he is not able to describe them precisely and clearly, the doctor asks the relatives accompanying the patient. Medical records are also reviewed in detail in chronological order. The history of past and accompanying diseases, operations, allergies is studied. Purposefully inquires about the condition of other organs and systems, as well as traumas experienced. A family history provides information about diseases in family members that are thought to be genetically transmitted, as well as the age and cause of death of parents or other close relatives. The social anamnesis points to harmful habits of the patient, such as alcohol, smoking, use of electronic cigarettes, drugs, opiates. Information is also required on lifestyle, nutrition, working conditions, living conditions.

4.2 Status

All patients are examined for their somatic status, starting with an assessment of whether the patient's age corresponds to the actual age. His general condition is determined, then the orientation to time, place and one's own personality. The skin and visible mucous membranes, head and neck areas are examined. The lungs are examined, respectively breathing by auscultation. Auscultation of the heart is performed with the patient lying down, at five auscultation points: fifth left intercostal space along the medioclavicular line, second right parasternal intercostal space, second left parasternal intercostal space, fifth left parasternal intercostal space and third left parasternal intercostal space. Auscultation determines the heart rhythm - regular or irregular, HR, the presence or absence of pathological noises. This is followed by measurement of BP on both arms in the axillary region. Measurements are taken in a sitting or lying position, after five minutes of rest. Abdominal status includes inspection, auscultation, determining peristalsis, superficial and deep palpation. The latter gives information about a pathological increase in the liver or spleen. The doctor conducts a bilateral succussio renalis. The physical status is completed with an examination of the extremities, including inspection and determination of peripheral vascular pulsations.

Patients who have anamnestic or physical data suspicious for hemodynamic disorders of VBS, as well as data from accompanying medical documentation for already proven disorders in VBS, are subject to consultation with a specialist neurologist, who takes a targeted neurological status, determining motor activity and coordination of the movements. The examination of motor activity includes the posture of the patient in a lying, sitting and standing position, gait, examination of the musculature, active movements, muscle strength, muscle tone, facial expressions, standing. Reflex activity was also examined by determining tendon reflexes of the four limbs, skin and mucosal reflexes, pathological reflexes, protective reflexes, grasping reflexes, and tonic reflexes. Romberg, Stewart-Holmes, Babinski-Weil, Unterberger tests are used to assess movement coordination. Romberg's test provokes milder forms of ataxia. The patient is in a standing position with arms stretched forward, legs close to each other with eyes open and closed. The test is negative when the patient does not stagger. When he wobbles in an indeterminate direction with eyes closed and eyes open, cerebellar Romberg is present. The test is positive when staggering only with closed eyes - the so-called sensory Romberg. When performing the Stewart-Holmes test, the patient maximally flexes the forearm to the shoulder. The doctor pulls the arm in the opposite direction, then suddenly releases it. Normally, the hand slightly deviates in the direction of folding and remains in this position. In hypotension, the arm flinches and may strike the patient's shoulder. In the Babinski-Weil test, the patient moves with eyes closed three steps forward and three steps back. With a unilateral cerebellar lesion, it begins to gradually deviate homolaterally to the side of the lesion. In Unterberger, the patient marches in place for about one minute with his eyes closed. Patients with brain damage deviate to 45 degrees homolateral to the damage.

4.3 Laboratory tests

Venous blood is taken from all patients for laboratory testing. The source is usually a vein in the forearm area. Blood is taken after disinfection of the puncture site and collected in vacutainers. From the collected blood and the separated serum, a complete blood count (CBC), hemostasis, biochemistry, in volume, according to the needs of each patient, are examined. In patients with DM and high blood sugar levels, a blood sugar profile (BSP) is additionally performed. In all patients, a lipid profile is examined, which is a major risk factor for the development of atherosclerosis, related to the formation of plaques and stenosis of the vertebral arteries.

The latter are a prerequisite for the occurrence of hemodynamic disorders of cerebrovascular blood circulation.

4.4 ECG

An ECG must be performed on all patients on the day of hospitalization, after catheter angiography, and on the day of discharge (Fig. 12). Electrocardiograms are performed on twelve-channel ECG machines recording the standard 12 leads. All ECGs are labelled with the patient's name, date and time and then made available for reading by a doctor. Emphasis in the reading of the electrocardiogram is the determination of the heart rhythm. It is the main instrumental method for establishing a diagnosis of “atrial fibrillation (AF)” in the patient in one of the three forms of the disease (episodic, persistent or permanent). AF predisposes to thrombus formation in the left atrium of the heart, leading to an increased risk of cerebral embolism.

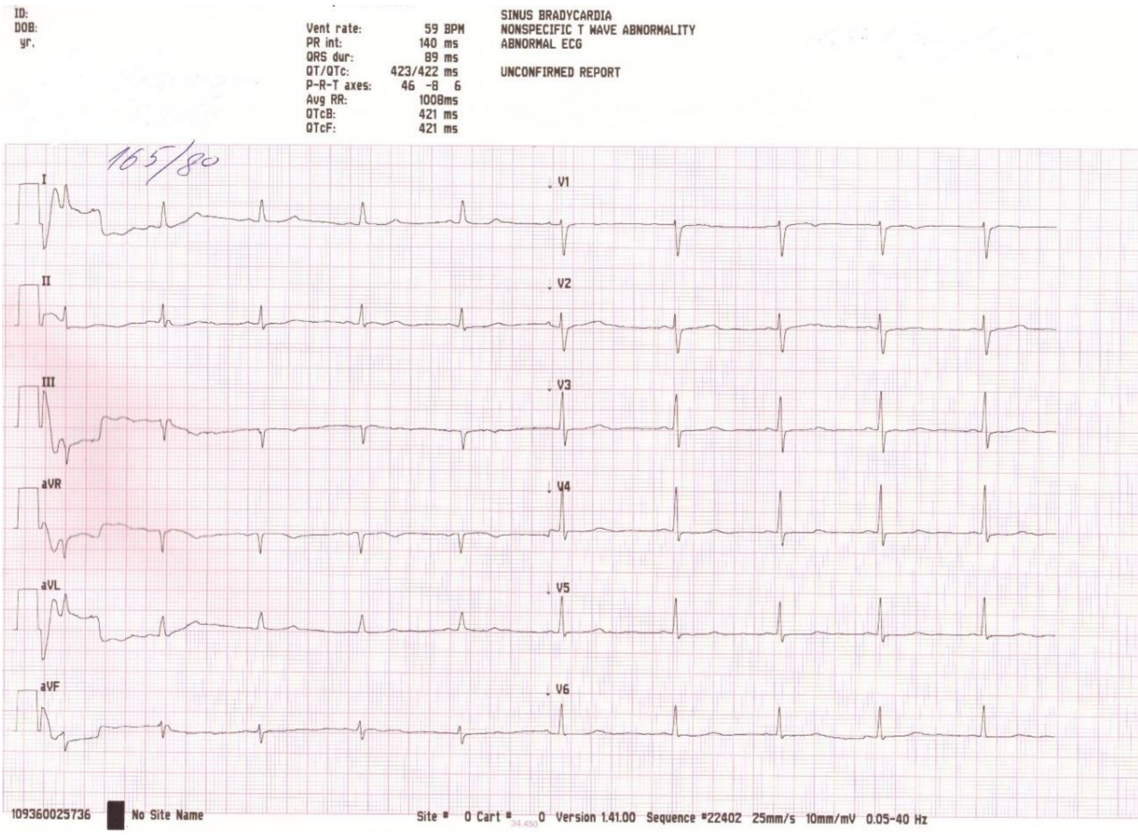

Figure 12: ECG of a patient.

4.5 EchoCG

Transthoracic echocardiography (TTE) was performed on all patients with upcoming catheter angiography. The study is performed according to a protocol including 69 items. After being brought into the EchoKG room, the patient is undressed from the waist up and placed in a supine position on a couch. The patient's data is entered into the software of the device, which includes: name, family name, age, height, weight. Based on the entered height and weight, the device automatically calculates the body mass index (body mass index - BMI), which is relevant to the subsequent measurements. The examination starts with a parasternal long-axis position. The left ventricle (LV) and the left atrium (LV) are examined. In M-mode, the thicknesses of the interventricular septum (IVS), the posterior wall of the LV (PWLV), the dimensions of the LV, the ejection fraction (EF) according to the Tychholz method are measured, and the pericardium is examined. The kinetics of IVS and PWLV are also evaluated. Structurally, the mitral valve (MV), the LV outlet and the aortic valve (AC) are assessed. LV outflow tract size and LA size are measured. The aortic, mitral and tricuspid valves are additionally assessed with colour Doppler from the same position. The examination continues for the parasternal short-axis position at the level of the aortic valve, mitral valve, papillary muscles, cardiac apex. Colour Doppler is again used. In this position, the pulmonary valve is also evaluated with colour Doppler and CW (continuous wave) Doppler. The next position is apical in four cavities. A structural analysis of the LV, LA, right ventricle (RV), right atrium (RA) and pericardium is performed. LV kinetic is assessed. The EF of LV is measured by Simpson's method. The volumes of LV and LA, basal and medial size of RV, transverse and longitudinal dimensions of LA and RA are measured. The valvular apparatus is again assessed using colour Doppler, PW (pulse wave) and CW Doppler. LV is also assessed with tissue Doppler laterally and medially. With PW-Doppler through the MV, the velocities of E and A (if the patient is in sinus rhythm) waves are measured, as well as their ratio – E/A. From the apical 2-cavity position, LV kinetics were again assessed, Sipson's EF is measured, and also LA volume indexed to the patient's BMI. In the apical position 5 cavity section, the outflow tract of the LV and AV is assessed with the help of colour and CW-Doppler. The examination continues in the subcostal position along the long and short axis, in which the LV, RV, LA, RA, IVS and MPP are again examined. Using a colour Doppler, the diameter of the inferior vena cava (IVC) is measured, inspiratory collapse is assessed. The aortic arch is viewed from a suprasternal position.

Conducted according to the algorithm described above, TTE is an instrumental method for diagnosing patients with a structurally altered heart, kinetic disorders, valve dysfunctions, LV systolic dysfunction, presence of thrombotic masses in any of the heart cavities, and the presence of vegetations on the valves. These conditions create a prerequisite for thrombus formation and cerebral embolization (Fig. 13).

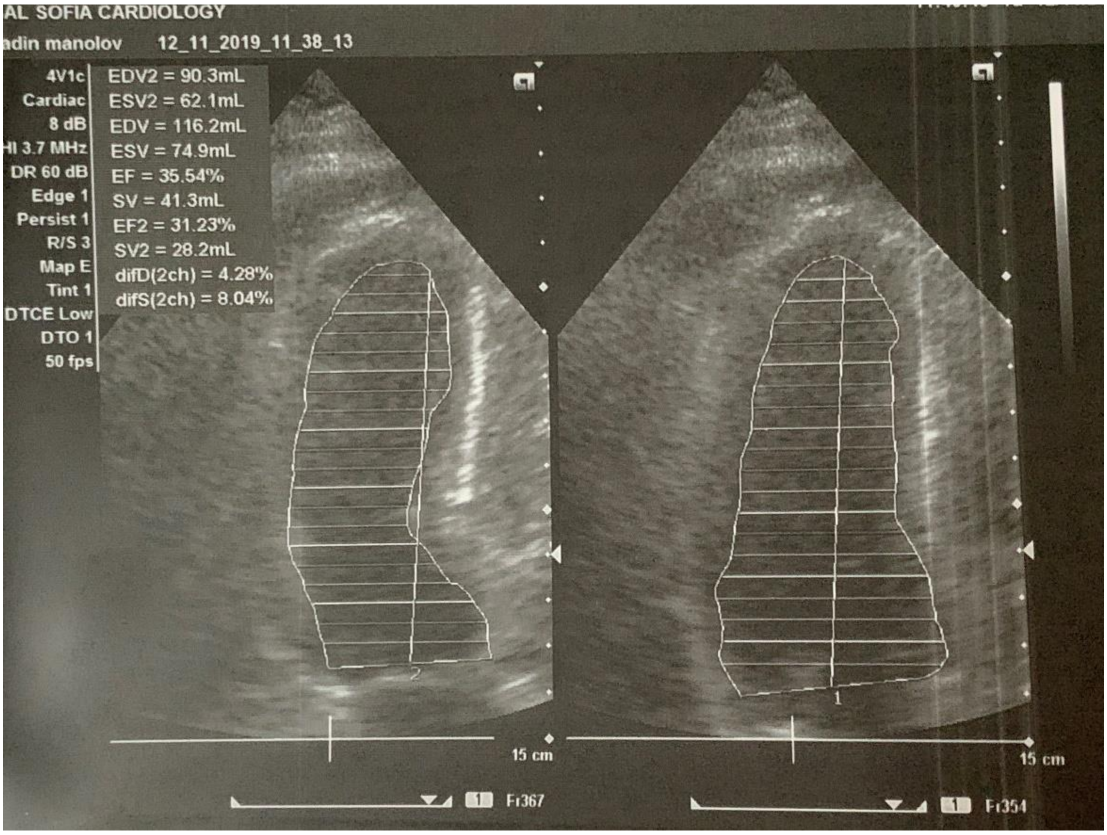

Figure 13: Transthoracic echocardiography.

4.6 Selective transcatheter angiography

4.6.1 Diagnostic selective transcatheter angiography

Angiography was performed in all 74 study patients. The anamnesis, clinical and neurological status, complaints and symptoms, data from the performed laboratory and instrumental tests (ECG, TTE) determine the volume of the angiographic examination. In 74 of the patients, selective coronary angiography (SCAG) was performed in the presence of clinical suspicion of the presence of coronary artery disease (CAD). Pathological changes of the coronary arteries can lead to life-threatening conditions, and their timely diagnosis and treatment is an important point in the patient's treatment. Also, in our work we study the correlation between the prevalence of atherosclerosis in two vascular basins – that of the coronary arteries and that of the extracranial segments of the cerebral arteries. For this reason, we consider it necessary to perform coronary angiography in all patients undergoing

cerebral angiography.

The main indication for performing an angiography of the cerebral arteries is clinical suspicion of ischemia in the area of the VBS. It includes the extracranial segments of the four main arteries supplying blood to the brain: left and right vertebral arteries, left and right common carotid artery, left and right internal carotid artery, truncus brachiocephalicus and both (left and right) subclavian arteries. Imaging of the subclavian arteries is important because anatomically the two vertebral arteries separate from the proximal segments of the left and right subclavian arteries except for anatomic variations in the separation. Contrast imaging of the initial segments of the truncus and the two subclavian arteries up to the level of separation of the vertebral arteries is an important and necessary condition for the diagnosis of vascular stenosis or occlusions located in these segments that would cause hemodynamic disturbances in VBS. Such are a significant reduction or complete cessation of blood flow to the vertebral arteries. Stenosis can become a source of peripheral embolization in the VBS basin. High-grade stenosis or occlusions of the subclavian arteries, located in the area between the ostium of the left subclavian artery and the ostium of the left vertebral artery on the left, or in the area between the truncus brachiocephalicus and the ostium of the right vertebral artery on the right, lead to the appearance of complete or incomplete "Steal" syndrome (in translation: "syndrome of the subclavian thief"). In these patients, the affected vertebral artery is disconnected from the cerebral blood supply, becoming a collateral and connection between the VBS and the subclavian artery. The result is ischemia in the VBS area due to redirection of blood flow to the affected limb.

All patient angiograms are performed in an angiography room equipped with an angiograph. The patient is positioned in a supine position. Vascular access is through the right radial artery or the right femoral artery. In about 5% of patients, the examination was performed through the left radial artery, due to the impossibility of performing it through the right.

For right radial access, the right arm is fixed to the angiographic table on which the patient is positioned. The puncture site in the area of the right wrist and right radial artery is disinfected with Braunol skin solution, after which the patient is covered with a disposable sterile sheet for angiographic examination. The area of the upcoming puncture is anesthetized with local anaesthesia applied subcutaneously, including 2 ml of 2% injection solution (20 mg/ml) of Lidocaine. Puncture of the radial artery i performed using the Seldinger method with a needle positioned in a 22G flexible cannula. The needle is directed at an acute angle to the radial artery (Fig. 14).

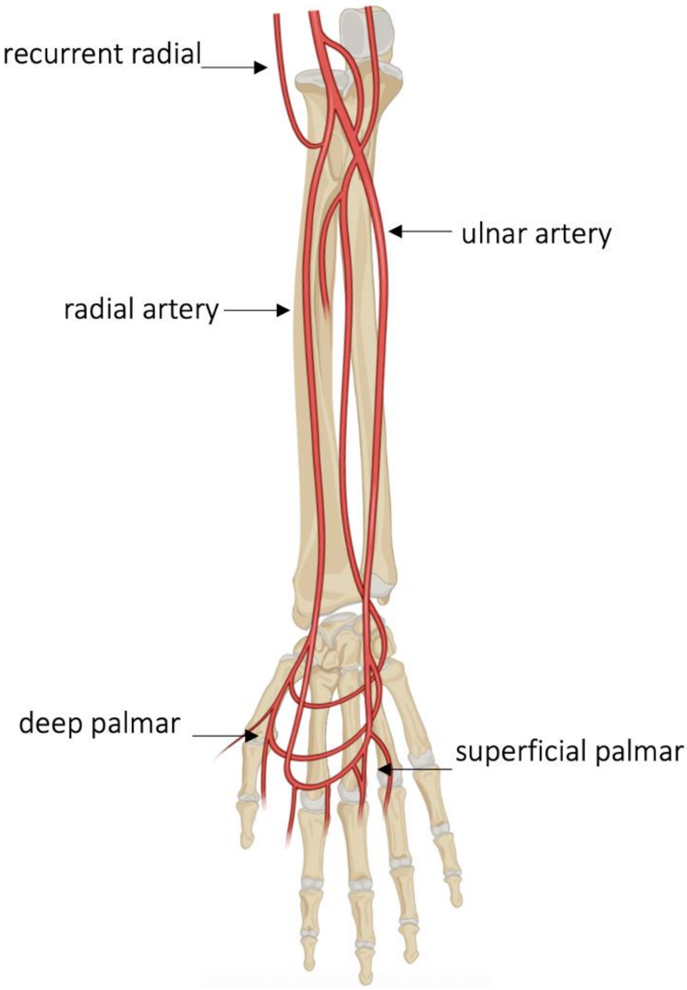

Figure 14: Anatomy of the arteries of the hand and forearm

After penetrating the lumen of the artery, the posterior wall of the vessel is punctured with additional pressure, after which the metal needle is removed. The cannula is gently withdrawn until a pulsating blood flow appears. The operator fixes the cannula with his left hand and with his right hand places a guide in the lumen of the radial artery. There should not be any resistance when passing with the driver. If this occurs, the puncture is repeated, stabbing more proximally. After positioning the introducer, the cannula is removed and replaced with a 6Fr radial catheter equipped with an introducer. Once the introducer is placed in the lumen of the artery, the introducer and guidewire are withdrawn together. The patency of the introducer is checked to ensure that we are in the true lumen of the vessel, then the patient is medicated through the introducer with 2.5mg Verapamil and 5000U Heparin. The introducer is washed with clean, sterile saline. Next is the placement of a 0.035" guide with a J-shape at the tip. With smooth passage of the guide, the use of fluoroscopy is not necessary. The appearance of resistance requires replacing the guide with a hydrophilic one or a coronary 0.014" guide.

After the guide reaches the area of the ascending aorta under fluoroscopy, a diagnostic 5Fr catheter is advanced. Tiger type is used for right radial access, and when access is through the left radial artery left and right Judkins catheters are used.

The factors that prevent radial arterial access are most often severe, insurmountable vascular spasm, pronounced tortuosity, highly tortuous artery, presence of accessory radial artery, "high" separation of radial and ulnar arteries from the brachial artery. In those cases, where catheter access is not feasible or the patient reports pain in the arm, alternate vascular access, such as the left radial or femoral, is attempted. For femoral vascular access, field preparation includes disinfection with Braunol's skin solution. Local anaesthesia is applied with Lidocaine 2% 10ml solution.

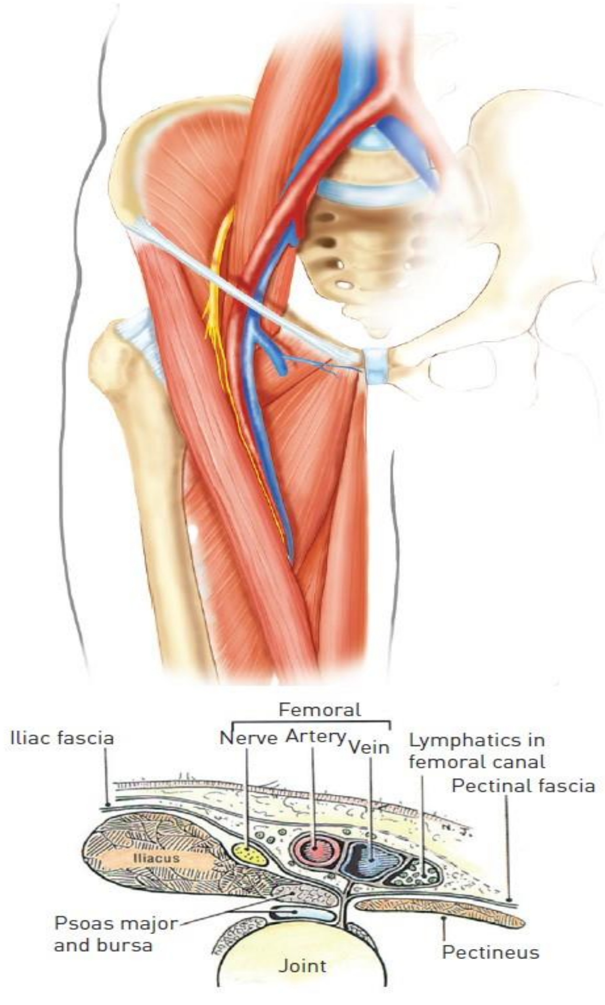

Figure 15: Anatomy of the femoral triangle.

The right common femoral artery is cannulated (Fig. 15). The latter extends between the external iliac artery proximally and the bifurcation of the femoral artery distally. In close proximity medial to the femoral artery is the femoral vein, and lateral to it is the femoral nerve. The inguinal ligament line connecting the anterior superior iliac spine to the pubic symphysis is used as a guide for the puncture level. The puncture site is usually made 1-2 cm away under this line of thought. The femoral artery is of sufficiently large calibre and is palpable in most patients. The puncture is made retrograde, with a needle directed at an angle of 30-45 degrees. Upon reaching the wall of the artery, the needle begins to pulse along with the vessel. Additional pressure follows, ensuring puncture of the anterior wall of the artery. It is desirable to avoid puncturing the posterior wall as well, due to creating a risk of hematoma. An indication of the tip of the needle entering the lumen of the vessel is the appearance of pulsating blood flow. Then the direction of the needle changes, with the end we are holding pointing towards the surface of the skin. A 6Fr or 7Fr femoral scalpel guide is placed through the needle. During insertion of the guide, no resistance or pain should be felt by the patient. After the guide is placed, the needle is withdrawn. An introducer is strung along the guide along with a dilator, where no resistance should be felt either. After cannulation of the artery with the introducer, the dilator and guidewire are removed together. The introducer is heparinized with 5000U Heparin, then washed with pure sterile saline. Providing femoral vascular access is performed without the use of fluoroscopy, except in cases where resistance is encountered when attempting to introduce the guidewire or the guidewire itself, as well as the appearance of pain. If necessary, resort to a second puncture. After securing femoral access, proceed with placement of a 0.035-inch J-guide. Going through it should also be without resistance. In case of obstruction in the passage through the iliac artery, an angiography is performed through the introducer, which clarifies what the problem is. In these cases, the J-guide can be replaced with a hydrophilic guide or a coronary 0.014” guide. The target that the guide must reach is the ascending aorta. The diagnostic 5Fr catheter is then placed. Left and right Judkins catheters are used.

Catheter angiography begins with an examination of the coronary arteries of the heart. After introducing the catheter into the ascending aorta along a guide, the latter is removed, the catheter is vented and connected to a closed system through which the contrast material is injected. The system is connected to a hemodynamic station in the angiography room. It provides real-time monitoring of the invasive pressure curve as well as its values. It also provides a monitor ECG image of the patient with heart rate tracking.

Navigation of the diagnostic catheter is performed by the operator using fluoroscopy without image magnification. The position of the tube is anterior-posterior (AP). From this position, the left coronary artery (LCA) is cannulated (Fig. 16). After positioning the catheter in the trunk of the LCA, four angiograms are performed in four standard projections: caudal view, left oblique caudal view, left oblique cranial view and right oblique cranial view. All fluorographs are taken at one magnification. If necessary, additional projections are made to visualize hard-to-see segments of the coronary arteries.

Figure 16: Catheter angiography of the LCA.

After clarifying the anatomy and status of the LCA, we proceed to the examination of the right coronary artery (RCA) (Fig. 17). The projection is left oblique, no magnification. The same diagnostic catheter – Tiger – is used. With selective cannulation of the vessel, two or three fluorography images are taken in projections: left oblique, left oblique cranial, right oblique. All are captured at one zoom.

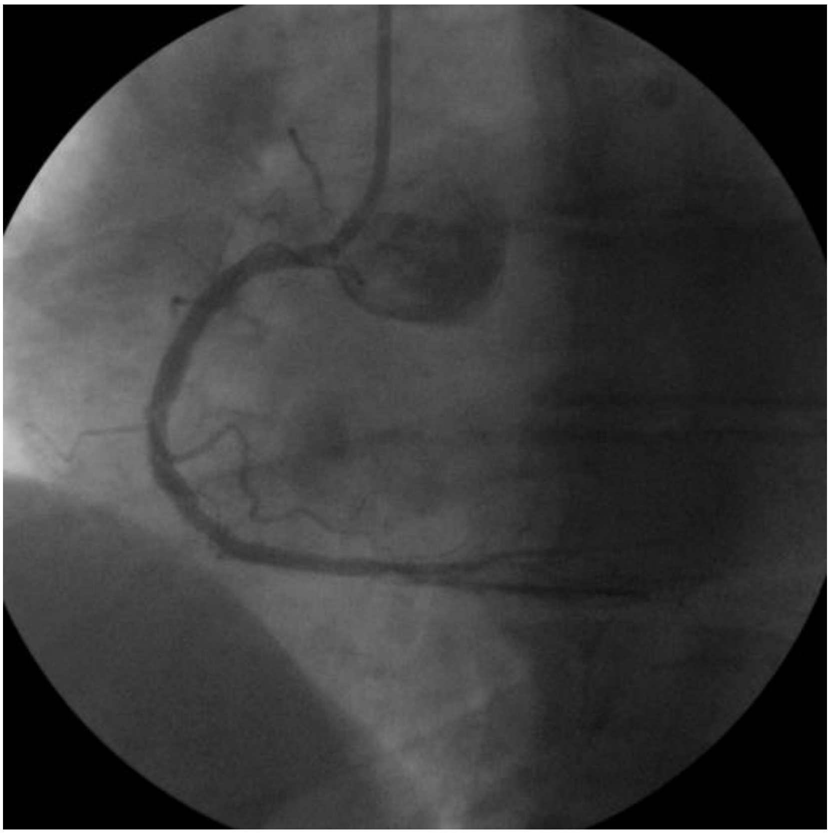

Figure 17: Catheter angiography of RCA.

Variations in the separation of the ostiums of the LCA and RCA, as well as the anatomical features of the aortic arch or truncus brachiocephalicus sometimes present difficulties in performing selective angiography. Other diagnostic 5Fr catheters are also used in these cases. Such for LCA are: Judkins left (JL) catheter with the size of the curve of the tip usually 3.0-3.5-4.0-4.5 cm.; leading 6Fr catheter type Extra Back Up (EBU) 3.0-3.5-4.0.; more rarely Amplatz Left (AL) 1.0-2.0 catheter. Alternative catheters for RCA are: Judkins Right 3.0-3.5-4.0; Amplatz Right (AR) 1.0-2.0; right EBU 3.0-3.5 catheter; Multipurpose catheter; Amplatz Left (AL) 1.0-2.0 catheter.

In patients with femoral vascular access, coronary angiography typically also begins with examination of the LCA. It starts with using a diagnostic 5Fr JL catheter in size 3.5 or 4.0. X-ray tube position is AP, no magnification. After cannulation of the LCA, the standard four projections are performed, analogous to the radial access. Anatomical anomalies require the use of alternative catheters: leading 6Fr catheter type Extra Back Up (EBU) 3.0-3.5-4.0.; more rarely Amplatz Left (AL) 1.0-2.0 catheter. LCA is searched in left oblique projection without magnification. JR 3.0-3.5-4.0 catheter is used, which can be replaced with AR 1.0-2.0, AL 1.0-2.0, right guide 6Fr EBU catheter, Multipurpose catheter in case of anomalous separation of the RCA ostium. After cannulation of the artery, the fluorography described for the radial access is recorded.

After performing selective coronary angiography, proceed to angiography of the cerebral arteries, left subclavian artery, truncus brachiocephalicus and right subclavian artery. The object of the study is: the extracranial segments of the carotid arteries, including the two common carotid arteries (left and right), the extracranial segments of the two internal (left and right) carotid arteries; the extracranial segments of the left and right vertebral arteries; the proximal segments of the left and right subclavian arteries.

In radial vascular access, diagnosis of the cerebral and subclavian arteries begins with the use of the diagnostic 5Fr Tiger catheter. The x-ray tube is positioned in a left oblique position without magnification, allowing better visualization of the aortic arch and ostiums of the target vessels. The catheter is positioned in the arch of the aorta, aiming after applied pressure to bend into the inferior wall of the arch so that its tip points cranially. A slight clockwise or counter clockwise rotation provides control over the catheter tip. In this way, the left subclavian artery is cannulated first. The catheter is positioned in its proximal segment, before or at the level of the ostium of the left vertebral artery. Usually, two fluorographs are made without magnification, in projections: left slant and the perpendicular to it – right slant. The patient's head is positioned in a neutral position, without support, which provides the straightening of the neck necessary for good visualization of the vessels. In this way, the ostium and proximal segment of the subclavian artery are visualized. Good imaging of the left vertebral artery is also often provided despite nonselective injection of contrast material (Fig. 18). If the latter is poorly visualized, it is switched to its selective cannulation and injection of contrast into the ostium of the vessel.

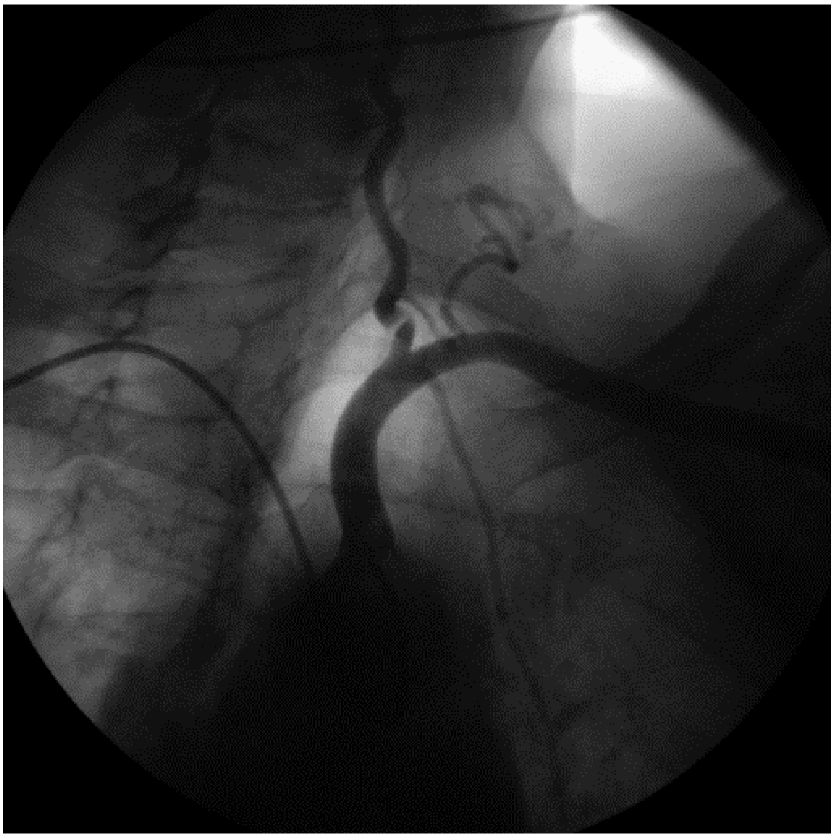

Figure 18: Catheter angiography of the left subclavian and left vertebral arteries

The four segments of the vertebral artery are traced. Subsequently, the catheter is removed from the subclavian artery and selectively placed in the left common carotid artery in a left oblique view without magnification. Two or more fluorography images are taken depicting the left common carotid artery, the bulbus, and the left external and internal carotid arteries in their extracranial segments. It is important that the bifurcation is well imaged, as it is a predilection site for stenosis to form. The left carotid artery system is imaged sequentially in right oblique projection, left oblique projection, and if necessary, additional AP or left and right oblique views are taken with angulation until the vessels are fully visualized (Fig. 19).

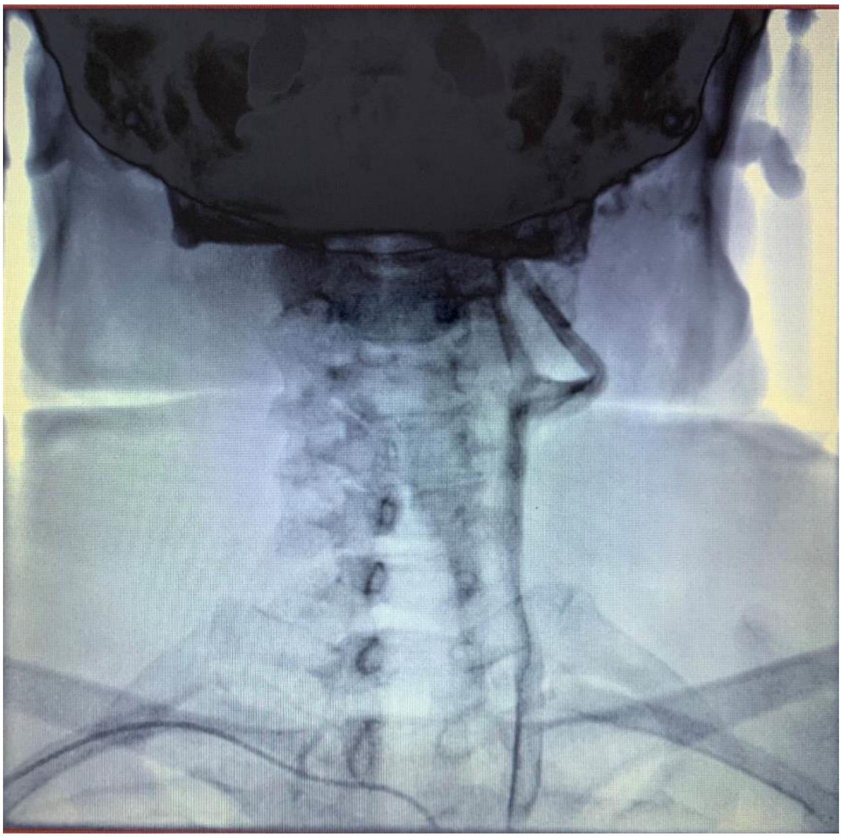

Figure 19: Catheter angiography of the left carotid artery.

Cerebral angiography continues with catheter placement in the brachiocephalic trunk, which divides into the right common carotid artery and right subclavian artery. The right vertebral artery separates from the latter. The search for the truncus is performed in a left oblique projection without magnification. Cannulation of the ostium of the right common carotid artery provides good visualization of the vessel, the bulbus with the bifurcation, and the extracranial segments of the right internal and external carotid arteries (Fig. 20). Similar to the left carotid artery, imaging is performed in a minimum of two perpendicular projections, usually left oblique and right oblique without magnification. If necessary, additional projections with angulation or AP projection are performed.

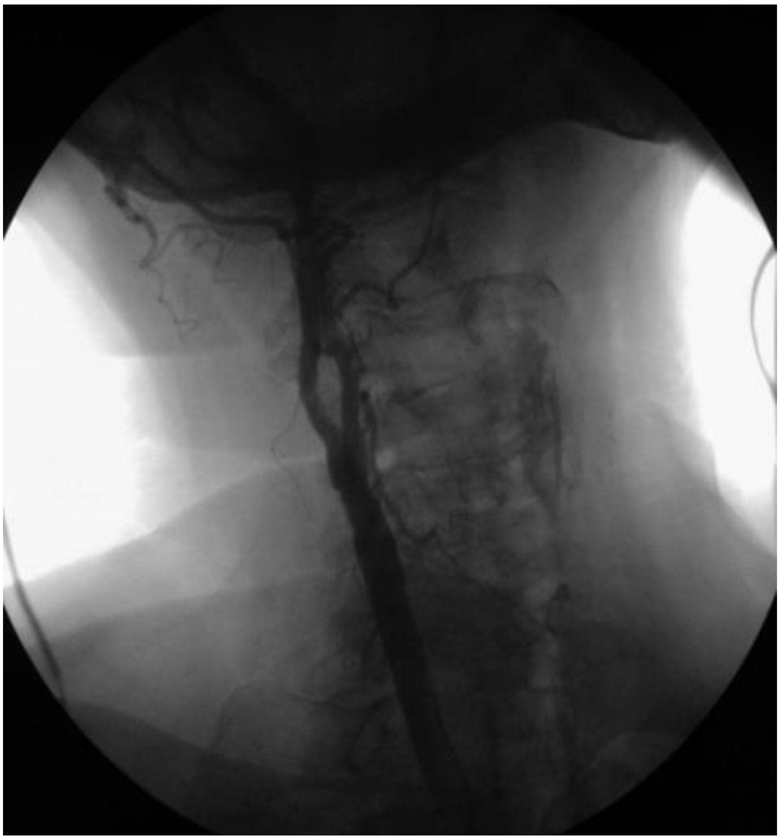

Figure 20: Catheter angiography of the right carotid artery.

The search for the right subclavian artery and right vertebral artery is in the AP projection without magnification. When the catheter reaches the proximal segment of the subclavian artery, fluorography is performed in the AP to clarify the proximal segment of the vessel. If the vertebral artery is also well visualized from this position, additional projections such as left oblique or right oblique with or without angulation are made, aiming to depict the four segments of the vessel. In the event that non-selective injection of contrast is not sufficiently informative for the vertebral artery, selective cannulation with the catheter is resorted to (Fig. 21). The latter is done by gently pulling the catheter, and the direction of the tip should coincide with the direction of the ostium of the vessel.

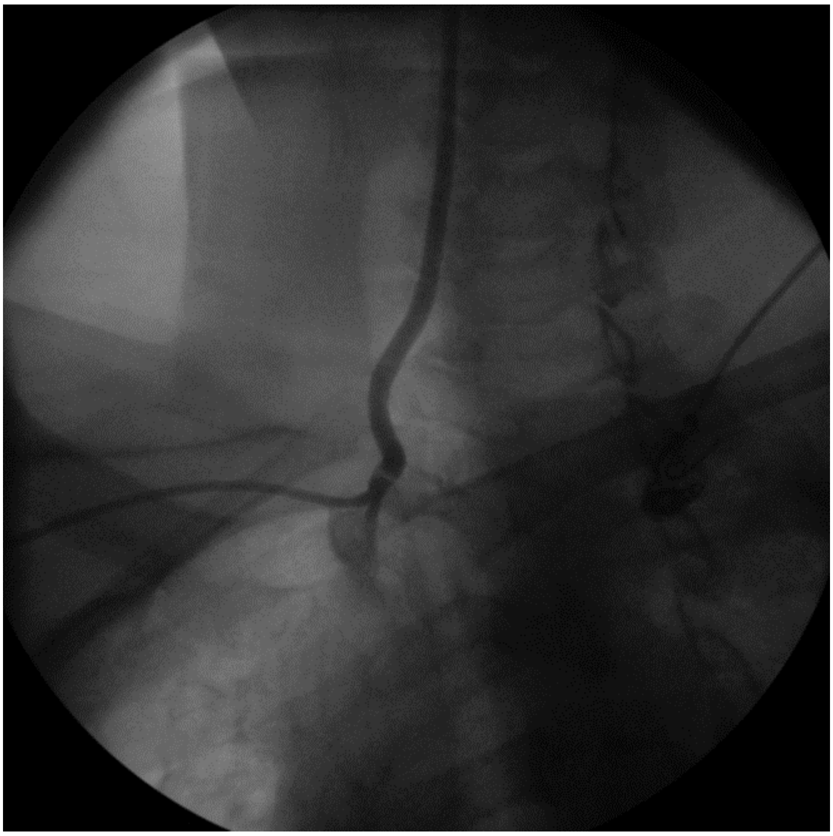

Figure 21: Catheter angiography of the right vertebral artery

Most often, lesions of the vertebral arteries are located ostially or along the course of the first segment (V1). Therefore, they should be examined carefully and in at least two different projections.

In some patients, the Tiger catheter does not allow full-volume angiography to be performed. These are patients with tortuous and elongated vessels, or anatomical vascular variations. In these cases, other types of diagnostic or guiding catheters are used. For the left arteries, these are: JL 3.5-4.0-4.5; Vertebral Catheter; Simmons 1.0-2.0 Catheter. In the right arteries: JR 3.0-3.5; Vertebral Catheter; Simmons Catheter. In cases with anomalies in the separation from an atypical location of one of the cerebral arteries, selective cannulation with one of the listed catheters is attempted. If this is not possible, aortography is performed with a Pigtail 5Fr catheter and an automatic contrast injector. The examination is in a left oblique projection without magnification. The amount of contrast that is injected is 35-40ml. at a speed of 12ml/sec. Aortography provides information about the outlet of the great cerebral arteries and allows subsequent selective angiography of the anomalous vessel.

When arterial course changes obstruct access with a particular catheter, a 0.035" J-guide, hydrophilic 0.035" or 0.020" J-guide, or coronary 0.014" guidewire are used to facilitate access distally into the test artery and the used catheter is placed on it.

If catheter angiography cannot be performed in the volume described above, then an alternative femoral access is used. It is believed that the anatomy is more favourable for conducting the study. The most commonly used diagnostic catheter for examining the cerebral and subclavian arteries is the 5Fr JR catheter size 3.0-3.5-4.0. Also used: JL, Vertebral Catheter, Multipurpose Catheter. It is appropriate to position the catheter with a hydrophilic 0.035" J-guide or a standard 0.035" J-guide.

Catheter angiography of the cerebral arteries and the subclavian arteries aims to prove or reject hemodynamically significant changes in the course of the vessels, such as stenosis and occlusions caused by atherosclerosis, aneurysms, dissections, kinking, coiling, hypoplasias, aplasias, dynamic stenosis. When the patient has clinical and anamnestic evidence of dynamic stenosis of the vertebral or carotid arteries, this type of lesion is subject to additional investigation. The suspected dynamic stenosis lesion is necessarily examined in the best imaging projection, recording four fluorography: one in neutral head position, one with head rotated to the left, one with the head rotated to the right, and one with head rotation from left to right or vice versa (fig. 22). Most often, dynamic stenosis are located in the upper segments of the arteries, at the level of C1-C2, or the point of entry into the cranial cavity.

Figure 22: Dynamic left vertebral artery stenosis in neutral head position and rotation

4.6.2 Interventional treatment

About 25% of ischemic strokes are located in the vertebrobasilar circulation. 20-25% of them are due to atherosclerosis, which leads to the formation of hemodynamically significant stenosis along the course of the vertebral arteries. Most often, stenosis affect the ostium of the vessel and the first segment (V1) (Fig. 23). Less commonly, they involve some of the remaining segments (V2-V4) or the basilar artery intracranially. Patients with significant vertebral artery stenosis were considered symptomatic if they experienced an ischemic stroke in the VBS pool, a transient ischemic attack (TIA), or reported a clinical manifestation of the disease in the past 6 months. The most common symptoms are vertigo, dizziness, unilateral limb weakness, dysarthria, headache, nausea, vomiting. Abnormalities in neurological status also prompt further investigations and a search for vascular damage. Stenosis ≥50% localized along the course of the extracranial segments of the vertebral artery, diagnosed in symptomatic patients, is considered significant. These patients are subject to interventional treatment. Of the 74 catheter angiograms performed, in 11 of the patients we diagnosed significant narrowing of the vertebral arteries associated with clinical presentation or deviations in neurological status. In two patients, hemodynamically significant disorders of the subclavian arteries were visualized – one complete occlusion in a proximal segment and one high-grade stenosis also in a proximal segment of the artery (Fig. 24). These patients were considered suitable for interventional treatment (2,5,7-10,14,15,38-41,45-49).

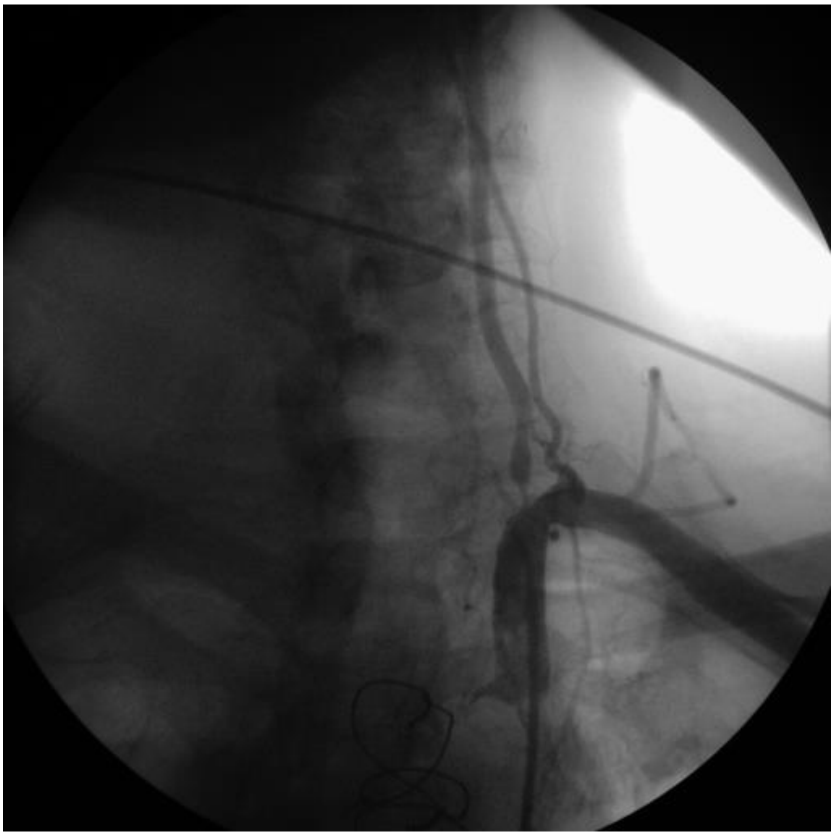

Figure 23: Ostial stenosis of the left vertebral artery.

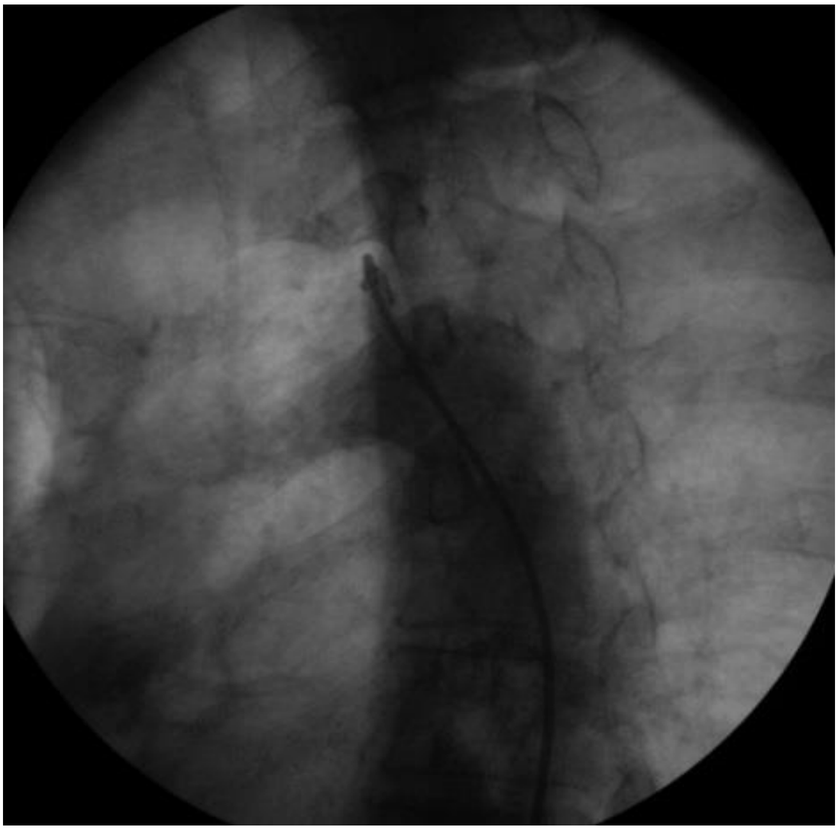

Figure 24: Left subclavian artery occlusion

4.6.2.1 Interventional treatment of the vertebral artery

Angioplasties of the vertebral arteries were performed through the femoral approach in 10 patients and through the radial approach in 1 patient. Patients are fully heparinized with intra-arterial injection of Heparin. The working projections are AP, left oblique or right oblique, and cranial or caudal angulation can be added, without magnification. 6Fr guiding catheters are used, which are threaded over an exchangeable 0.035" J-guide or a hydrophilic one. The ostium of the vessel is cannulated in cases where ostial stenosis is not registered. In case of ostial involvement of the artery, the guiding catheter is positioned as close as possible to the ostium with the tip directed towards the vascular lumen. An embolic protective device is not used during the procedure, due to the high risk of dissection or vascular spasm, complicating and making the intervention difficult. The small calibre of the vertebral arteries compared to that of the carotid arteries, the tortuous first segment in most cases, the angle of separation of the artery relative to the subclavian artery and the tendency to spasm are unfavourable factors leading to a high risk of using a protective device. A coronary 0.014" guidewire is selectively placed in the vertebral artery, the tip of which is positioned distally intracranially. Severe stenosis are predilated with a simple “semicompliant” balloon. A “Non-compliant” balloon is used in marked calcinosis, usually affecting the ostium of the vessel. Balloon predilatation is also performed when direct stent passage through the stenosis is not feasible. The balloons used are 2.0-2.5mm in diameter, expanded to 8-14atm. Stent implantation follows. Drug-free stents (BMS) were used in 4 patients. 7 patients were stented with drug-eluting stents (DES). Sizes are from 2.0-4.0mm for BMS and from 3.5-4.0mm for DES. The lengths are selected to completely cover the stenosis, with the proximal and distal ends of the stent covering 2-3 mm of healthy vessel area. Expansion is at 8-16 atm. Stents, which are placed ostially, prolapse 1-2 mm into the lumen of the subclavian artery, after which balloon postdilatation, is necessarily performed, i.e. called “flair” aiming for proximal optimization of the stent (Fig. 25).

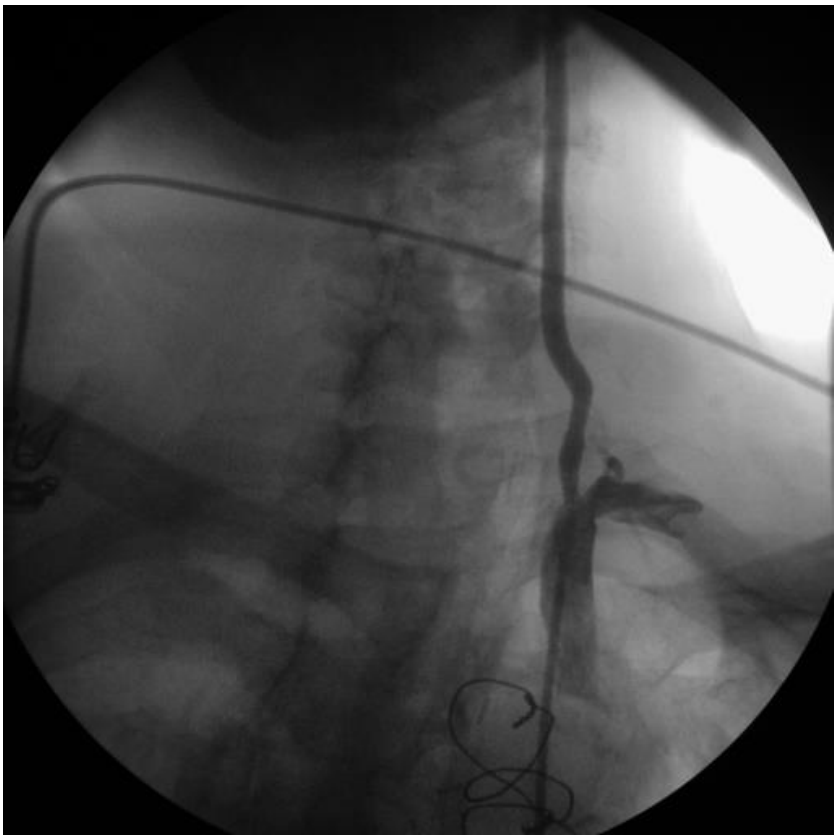

Figure 25: Final result after stenting the ostium of the left vertebral artery.

4.6.2.2 Interventional treatment of the subclavian artery

Interventional treatment of the subclavian artery was performed in two patients. One has a registered total occlusion of the left subclavian artery, the other with a significant 70% ostial stenosis. The interventions were performed through a right femoral access with a femoral 6Fr catheter and a 6Fr JR 3.5 guiding catheter positioned in the subclavian artery. Patients were fully heparinized with Heparin. The working projections are left oblique or right oblique. The target lesion was traversed in both cases with a coronary 0.014" guidewire, which was placed distally in a segment of the brachial artery. In the patient with 70% stenosis, balloon predilatation was performed with 4.0/10mm and 5.0/10mm balloons. Follow-up stenting with a peripheral stent (BMS) placed over a dilatation balloon. Stent size is 7.0/18mm, inflated to 8atm. The proximal end of the stent protrudes 2-3 mm into the arch of the aorta. Post-dilatation (“flair”) with the stent balloon to 8atm. An optimal immediate angiographic result was achieved with preserved blood flow also in the left vertebral artery. In the patient with the occluded artery, balloon predilatation was performed with a 4.0/10mm coronary balloon and a 5.0/10mm peripheral balloon inflated to 12 atm. Stenting was undertaken with one BMS 7.0/60mm to 8atm. The stent is placed immediately after the ostium of the subclavian artery to the ostium of the left vertebral artery. Placement of a second 0.014" guidewire in the vertebral artery was deemed unnecessary due to the right angle of separation of the vertebral artery relative to the subclavian. Switched to postdilation with a 6/12mm balloon to 12atm. A very good angiographic result was achieved with the restoration of blood flow in the subclavian artery and the left vertebral artery, which led to the elimination of the "steal" syndrome in the patient, which was depicted during the angiographic diagnosis. This, in turn, led to a significant improvement in the blood supply to the brain through the basin of the left vertebral artery (Fig. 26).

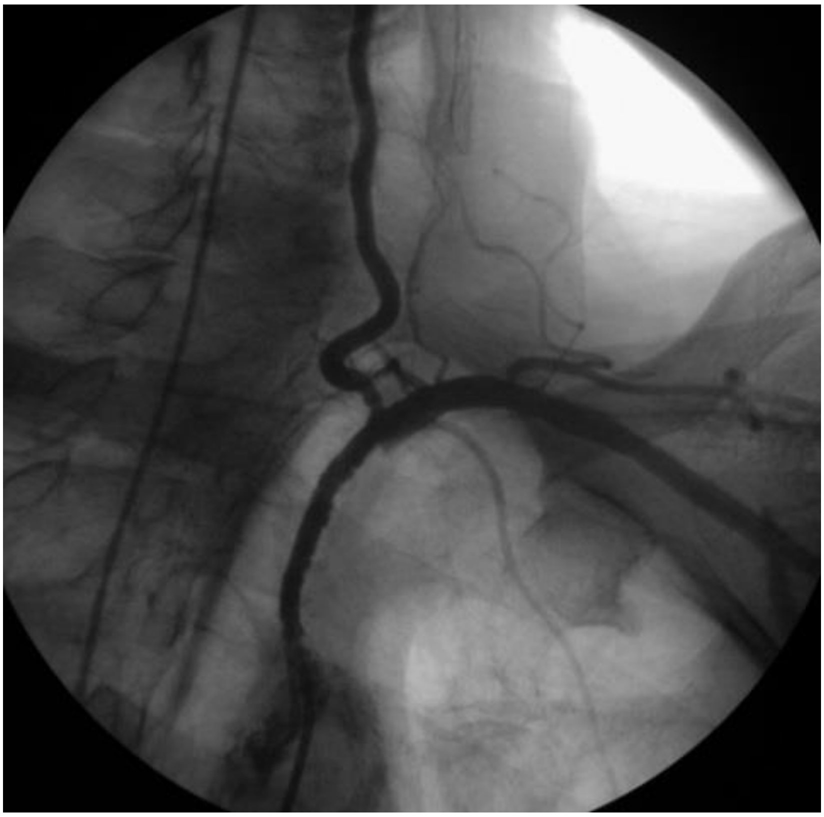

Figure 26: Final result after stenting of the left subclavian artery with restoration of blood flow in the left vertebral artery.

After completion of the invasive examination or intervention, local hemostasis of the puncture site is started (Fig. 27). In all patients with radial access, the radial artery is removed at the end of the procedure. A hemostatic band (bracelet) is placed at the puncture site, which provides compression by inflating a balloon. After the third hour of applying the bandage, gradual decompression begins in 15 minutes. In the absence of bleeding, the bracelet is removed.

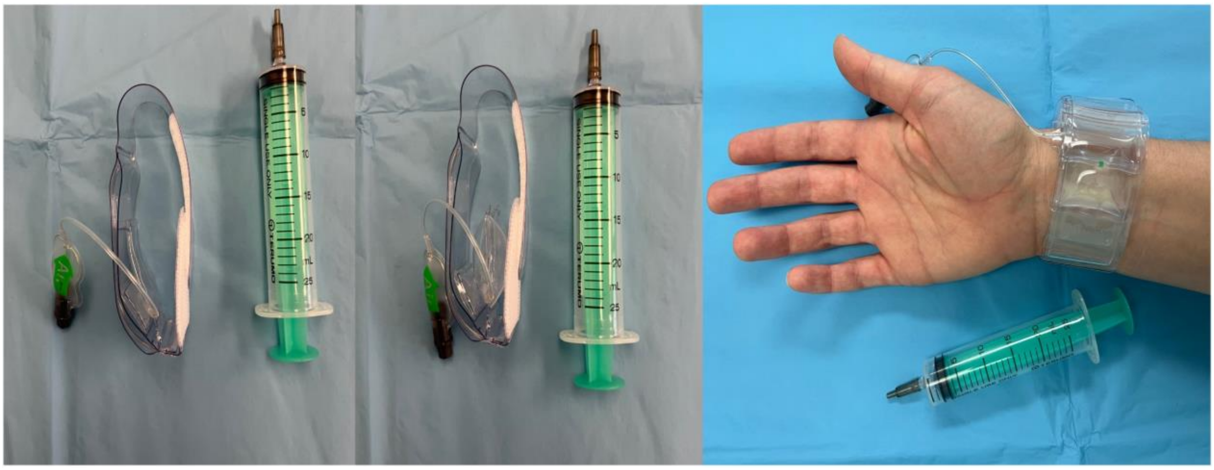

Figure 27: Haemostasis set in a radial vascular access patient.

Patients with femoral access are taken out of the angiography room, leaving the catheter in the femoral artery. At the third hour, control hemostasis is examined and, with normal indicators, the deceleration is removed. After its removal, decompression is carried out - manually or by means of a femstop. In the absence of active bleeding, a compression bandage is applied, and weight is applied to the puncture site. At the sixth hour, the compression bandage is removed, and the patient's leg remains immobile for another six hours.

5.RESULTS

5.1 CLINICAL CONTINGENT

A prospective (June 2020 - December 2022) clinical-epidemiological study was conducted covering 74 patients with clinical and instrumental data, suspicious for hemodynamic disorders along the course of the extracranial segments of the vertebral arteries, as well as the proximal segments of the subclavian arteries, of which 44 (59, 5%) males and 30 (40.5%) females (Fig. 1). The relative share of males is significantly greater than that of females ($p=0.021$). The average age of the studied contingent was 69.24±8.99 years, ranging from 42 to 88.

Figure1: Frequency distribution of the studied contingent by gender

From fig. 2 it is clear that the largest number of males (19) are from the 60-69 age group, followed by 70-79 with 10, and the least (2) - 40-49. For females, the largest number (15) are from the age group 70-79, followed by 60-69 with 12, and the least (0) - 40-49.

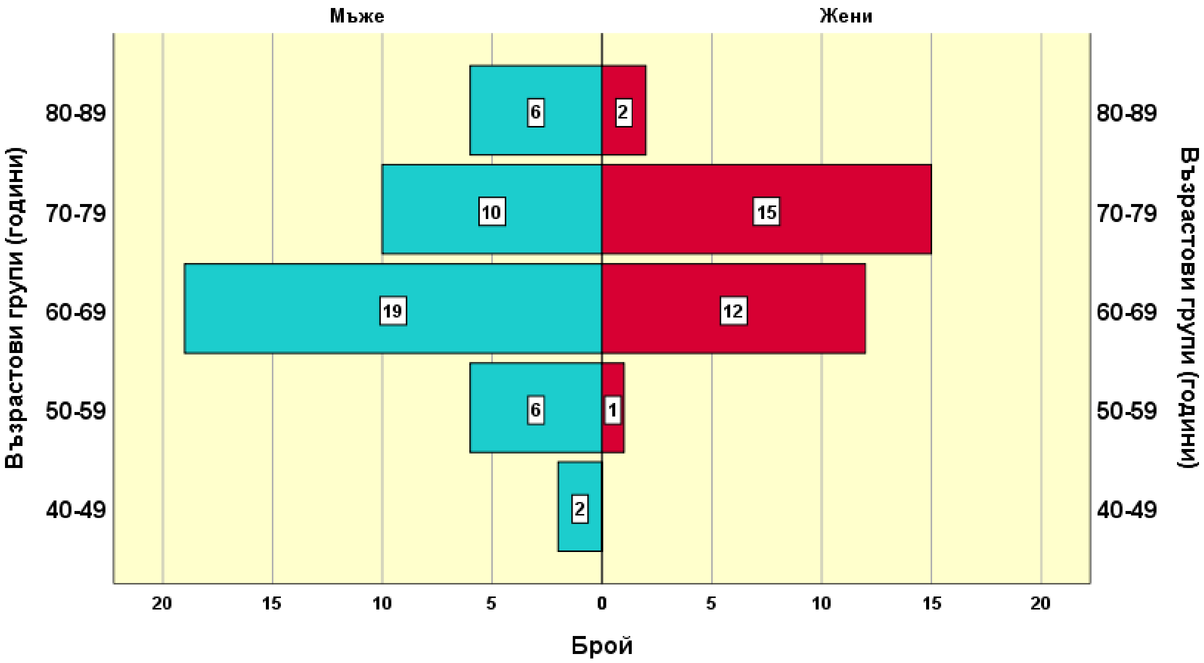

Figure2: Distribution of the studied contingent by gender and age groups

5.2 STATISTICAL METHODS

Data were entered and processed with the statistical packages IBM SPSS Statistics 25.0. and MedCalc Version 19.6.3., as well as Office Excel 2021. $p<0.05$ was accepted as a level of significance at which the null hypothesis is rejected.

The following methods were applied:

1. ***Descriptive analysis*** – the frequency distribution of the considered signs is presented in tabular form.
2. ***Graphical analysis*** – to visualize the obtained results.
3. ***Variational analysis*** – to assess central tendency and statistical dispersion.
4. ***Fisher's exact test, Fisher-Freeman-Halton exact test and a test χ^2*** **-** to test hypotheses about the presence of dependence between categorical variables.
5. ***Nonparametric Kolmogorov-Smirnov and Shapiro-Wilk test*** – to check the distribution for normality.

6. ***Student's t-test*** – to compare the arithmetic means of two independent samples.

7. ***Nonparametric Mann-Whitney test*** – to test hypotheses about a difference between two independent samples.

8. ***ROC curve*** – to determine threshold values for quantitative variables.

9. ***Multiple binary logistic regression analysis*** - for a quantitative assessment of the factors for the investigated event.

5.3 RESULTS

5.3.1 Descriptive statistics

We present the distribution of patients (number/%) by risk factors, taking dyslipidemia, smoking and atrial fibrillation (AF) as risk factors for the development of cerebrovascular disease.

In fig. 3 shows that from the studied risk factors:

- Dyslipidemia has the largest relative share (94.6%), followed by smoking with 56.6%;
- Atrial fibrillation has the lowest frequency in the studied sample - 24.7%.

Figure 3: Frequency distribution of risk factors

Of the 74 patients studied, information was available for 32 regarding the cardiovascular disease risk factor "smoking". The results obtained from these patients show that 56.3% were smokers and 43.8% were non-smokers (Fig. 4).

Figure 4: Frequency distribution of smoking patients (based on data from 32 people)

Regarding the accompanying diseases (Fig. 5), for which we consider arterial hypertension (AH), coronary artery disease (CAD), diabetes mellitus (DM) and heart failure (HF), it can be seen that

- In 72 out of a total of 74 patients (97.3%), arterial hypertension was observed, followed by CHD with 61.6%;
- With the smallest relative share is heart failure – 12.2%.

Figure 5: Frequency distribution of accompanying diseases

All patients in the study underwent angiography of the extracranial segments of the vertebral arteries, the common carotid arteries, the internal and external carotid arteries, and the proximal segments of the subclavian arteries. In 64 of the examined patients, stenosis of one of the above-listed arteries was diagnosed. From the frequency distribution of the established stenosis, it can be seen that carotid artery stenosis have the largest relative share (39.2%). This includes all narrowings, significant and insignificant, covering the two common carotid arteries, the two internal and the two external carotid arteries. The group of angiosignificant stenosis followed with 21.6%. Narrowings of the extracranial segments of the vertebral arteries, which are >50%, fall here. 16.2% is the proportion of angio-insignificant stenosis, which is interpreted as stenosis of the extracranial segmental vertebral arteries <50%. The narrowings of the subclavian artery are 8.1%, including all stenosis in the proximal segments of the two subclavian arteries. The least – only one or 1.4% is angiodynamic stenosis. Angiodynamic stenosis is defined as stenosis of the vertebral artery in the extracranial segment, which occurs during head rotation.

From fig. 7 it is clear that with regard to carotid stenosis and vertebral artery stenosis, men have a higher relative share. Women have a higher percentage of dynamic stenosis and subclavian artery stenosis.

The frequency distribution of established stenosis by age groups showed that the age group 60-69 years dominates in most of them, followed by 70-79 years.

The age group 40-49 years is least represented (with only one or 3.4%) in carotid artery stenosis (Fig. 8).

Figure 6: Frequency distribution of identified stenosis in the entire sample

Figure 7: Frequency distribution of detected stenosis by gender

Figure 8: Frequency distribution of detected stenosis by age group

We present distribution (number/%) of stenosis of the vertebral arteries by segments (V1, V2, V3, V4) - overall for the group, by gender and by age groups;
From table 1 it becomes clear that:

- Angiodynamic stenosis is located only in segment V3;
- Nine (75%) of the angio-insignificant stenosis were located in segment V1, two or 16.7% in segment V2, and one (8.3%) – in two of the segments - V1 and V4;
- 15 (93.8%) of the angiosignificant stenosis were located in segment V1, and one or 6.3% in segment V2;

Table1: Frequency distribution of stenosis by segments (V1,V2,V3,V4)

- total for the group

Segments	Frequency	Angiodynamic (n=1)	Angio non-significant (n=12)	Angio significant (n=16)
V1	n	0	9	15
	%	0	75,0	93,8
V2	n	0	2	1
	%	0	16,7	6,3
V3	n	1	0	0
	%	100,0	0	0
V1V4	n	0	1	0
	%	0	8,3	0
No data available	n	0	0	0
	%	0	0	0

On the table 2-4 shows the frequency distribution of the three groups of stenosis of the vertebral arteries (angiodynamic stenosis; angio non-significant stenosis; angio-significant stenosis) by gender and age groups:

- The only angiodynamic stenosis was found in a woman in the age group 60-69 years;
- Nine angio non-significant stenosis located in segment V1 were distributed in a 2:1 ratio for males, 77,8% in the 60-69 age group and one each (11,1%) in the 70-79 and 80-89 age groups ;
- The two angio non-significant stenosis located in the V2 segment were distributed in a 1:1 ratio between both sexes and in age groups 70-79 and 80-89 years;
- The only angio non-significant stenosis located simultaneously in two segments was found in a man in the age group 50-59 years;
- The 15 angiosignificant stenosis located in the V1 segment were distributed in a ratio of 4:1 for males, 46.7% in the age group 60-69 years, followed by 33.3% in the age group 70-79 years, 13.3% - 50 -59 years and 6.7% - 80-89 years;
- One angiosignificant stenosis located in segment V2 was in a man and in the age group of 70-79 years.

Table 2: Frequency distribution of angiodynamic stenosis by segments (V1,V2,V3,V4), gender and age groups

Segments	Frequency	Gender		Age group (years)				
		Males	Females	40-49	50-59	60-69	70-79	80-89
V1	n	0	1	0	0	1	0	0
	%	0	100,0	0	0	100,0	0	0
V2	n	0	0	0	0	0	0	0
	%	0	0	0	0	0	0	0
V3	n	0	0	0	0	0	0	0
	%	0	0	0	0	0	0	0
V1V4	n	0	0	0	0	0	0	0
	%	0	0	0	0	0	0	0

Table 3: Frequency distribution of angio non-significant stenosis by segments (V1,V2,V3,V4), gender and age groups

Segments	Frequency	Gender		Age group (years)				
		Males	Females	40-49	50-59	60-69	70-79	80-89
V1	n	6	3	0	0	7	1	1
	%	66,7	33,3	0	0	77,8	11,1	11,1
V2	n	1	1	0	0	0	1	1
	%	50,0	50,0	0	0	0	50,0	50,0
V3	n	0	0	0	0	0	0	0
	%	0	0	0	0	0	0	0
V1V4	n	1	0	0	1	0	0	0
	%	100,0	0	0	100,0	0	0	0

Table 4: Frequency distribution of angiosignificant stenosis by segments (V1,V2,V3,V4), gender and age groups

Segments	Frequency	Gender		Age group (years)				
		Males	Females	40-49	50-59	60-69	70-79	80-89
V1	n	12	3	0	2	7	5	1
	%	80,0	20,0	0	13,3	46,7	33,3	6,7
V2	n	0	1	0	0	0	1	0
	%	0	100,0	0	0	0	100,0	0
V3	n	0	0	0	0	0	0	0
	%	0	0	0	0	0	0	0
V1V4	n	0	0	0	0	0	0	0
	%	0	0	0	0	0	0	0

In the studied sample, 5 patients with occlusions of the vertebral arteries were found (Fig. 9).

The results of the table 5 show that all five occlusions were in male patients, with 4 or 80% of them in the 60-69 age group and only one (20%) in the 50-59 age group.

Figure 9: Frequency distribution of patients with vertebral artery occlusion

Table 5: Frequency distribution of patients with angioocclusion by gender and age groups

Frequency	Gender		Age group (years)				
	Males	Females	40-49	50-59	60-69	70-79	80-89
n	5	0	0	1	4	0	0
%	100.0	0	0	20.0	80.0	0	0

6 patients were found to have stenosis/occlusions of the subclavian arteries. 4 or 66.6% have insignificant stenosis. 1 (16.6%) had complete subclavian artery occlusion and 1 (16.6%) had subtotal occlusion. (Fig.10)

Figure 10: Frequency distribution of patients with subclavian artery stenosis

In the following figs. 11-12 and table. 6, the patients are divided according to clinical symptoms – overall for the group, by gender and by age groups. It can be seen that:

- The patients with vertigo have the largest relative share (28.8%), followed by those with weakness and dizziness with 6.8% each;
- Three of the studied symptoms - unstable gait, ataxia, headache - are represented by 3 cases each;
- Single cases of impaired vision, vomiting and nausea were also found, and there were no patients with diplopia;

- In the symptoms of vertigo, weakness, dizziness and impaired vision, male patients predominate, while in unsteady gait, ataxia, headache, vomiting and nausea, female patients;
- For the only symptom with statistical representation, the largest number of cases (9 or 42.9%) were from the 60-69 age group, followed by 70-79 years with 8 or 38.1%, and in the 40-49 age group there are no patients.

Figure 11: Frequency distribution of patients according to established symptoms (entire sample, data missing for one of the patients)

Figure 12: Frequency distribution of established symptoms by gender (data missing for one of the patients)

Table 6: Frequency distribution of established symptoms by age groups

Symptoms	Frequency	Age group (years)				
		40-49	50-59	60-69	70-79	80-89
Vertigo (n=21)	n	0	1	9	8	3
	%	0	4,8	42,9	38,1	14,3
Dizziness (n=5)	n	0	1	1	3	0
	%	0	20,0	20,0	60,0	0
Weakness (n=5)	n	1	0	3	1	0
	%	20,0	0.0	60,0	20,0	0
Headache (n=3)	n	0	1	0	2	0
	%	0	33,3	0,0	66,7	0
Ataxia (n=3)	n	0	0	2	1	0
	%	0	0	66,7	33,3	0
Unsteady gait (n=3)	n	0	0	0	3	0
	%	0	0	0	100,0	0
Nausea (n=1)	n	0	1	0	0	0
	%	0	100,0	0	0	0
Vomiting (n=1)	n	0	1	0	0	0
	%	0	100,0	0	0	0
Impaired vision (n=1)	n	0	0	0	0	1
	%	0	0	0	0	100,0
Diplopia (n=0)	n	0	0	0	0	0
	%	0	0	0	0	0

Table 7 and fig. 13 shows a distribution (number/%) according to the type of cerebro-vascular accidents experienced (cerebral stroke in the large hemispheres; cerebral stroke in VBS; TIA) - overall for the group and by gender and age groups. It becomes clear that from the considered indicators:

- With the largest relative share (40.5%) are IMI large hemispheres, followed by IMI VBS with 24.3%;
- The least (only one or 1.4%) were patients with TIA.

In fig. 14-15 it is seen that:

- In IMI large hemispheres men predominate, and in IMI VBS - women;
- The only TIA was in a male patient;
- IMI large hemispheres have representatives in all age groups, but they are the most (40%) in the group 60-69 years, followed by 70-79 with 33.3%;
- Patients with IMI VBS are the most in the age group 70-79 years, followed by those in 60-69 and 80-89, and in the youngest age groups they are completely absent;
- The TIA patient is in the age group of 60-69 years

Indicators	**Frequency**	**Total**	**Gender**		**Age group (years)**				
			Males	Females	40-49	50-59	60-69	70-79	80-89
IMI large hemispheres	n	30	17	13	1	5	12	10	2
	%	40,5	56,7	43,3	3,3	16,7	40,0	33,3	6,7
IMI VBS	n	18	8	10	0	0	6	9	3
	%	24,3	44,4	55,6	0	0	33,3	50,0	16,7
TIA	n	1	1	0	0	0	1	0	0
	%	1.4	100,0	0	0	0	100,0	0	0

Table 7: Frequency distribution of IMI large hemispheres, IMI VBS, TIA in total, by gender and age groups

Figure 13: Frequency distribution of large hemisphere IMI large hemispheres, IMI VBS and TIA, total

Figure 14: Frequency distribution of IMI large hemispheres, IMI VBS, TIA by gender

Figure 15: Frequency distribution of IMI large hemispheric, IMI VBS, TIA by age groups

From the distribution (number/%) of patients with interventions of the vertebral and subclavian arteries in general for the group, by gender and by age groups, given in table. 8 and fig. 16-17 it becomes clear that:

- The frequency distribution of intervention and stenting indicators completely matches, i.e. all intervened patients were stented, and there were no patients in whom only balloon angioplasty was performed.
- Interventions were performed in 13 or 17.6% of patients;
- The ratio between the two genders is 7:6 in favour of males;
- Most (42.6%) of patients with these procedures were in the 60-69 age group, followed by 70-79 with 38.5%;
- Single cases are observed in age groups 50-59 and 80-89 years, and in the interval 40-49 - they are completely absent.

Table 8: Frequency distribution of the intervened patients of the v.a. – total for the group, by gender and age groups

Indicator	Frequency	Total	Gender		Age group (years)				
			Males	Females	40-49	50-59	60-69	70-79	80-89
Intervention	n	13	7	6	0	1	6	5	1
	%	17,6	53,8	46,2	0	7,7	46,2	38,5	7,7
Stenting	n	13	7	6	0	1	6	5	1
	%	17,6	53,8	46,2	0	7,7	46,2	38,5	7,7

Figure 16: Frequency distribution of the interveners by gender

Figure 17: Frequency distribution of the interveners by age group (years)

In fig. 18 it can be seen that:

- Stented patients were 13 or 17.6%;
- For this purpose, DES stents were used in 7 or 9.5% of them and BMS stents in 6 or 8.1%.

Figure 18: Frequency distribution of stented patients, overall and by type of stent

Balloon pre- and post-dilations were in 7 or in 9.5% of patients (Fig. 19).

Figure 19: Frequency distribution of balloon dilatations

An analysis of the relationship between statistically representative stenosis and gender showed (table 9):

- Absence of such in angio-insignificant significant stenosis;
- Presence of borderline ($p<0.1$) statistically significant relationship between gender and carotid artery stenosis, expressed in a higher relative proportion of men.

No statistically significant correlation was found between the presence of statistically representative stenosis and age (Table 10).

No significant correlation of the vertigo symptom with gender and age was found (tables 11-12).

The analogous analysis of the dependence between the indicators IMI large hemispheres and IMI VBS with gender and age showed (tables 13-14):

- Lack of statistically significant dependence with gender;
- Presence of a statistically reliable relationship between IMI VBS and age, expressed in a significantly greater average age in patients with IMI VBS.

Table 9: Analysis of the relationship between statistically representative stenosis and gender

Indicator	Frequency	Males	Females	R
Angio non-significant stenosis (n=12)	n	8	4	0,749
	%	20,0	13,8	
Angiosignificant stenosis (n=16)	n	12	4	0,153
	%	30,0	13,8	
Carotid artery stenosis (n=29)	n	21	8	***0,080***
	%	52,5	28,6	

Table 10: Analysis of the relationship between statistically representative stenosis and age (years)

Indicator	No	Yes	R

	n	$\overline{X}$	SD	n	$\overline{X}$	SD	
Angio non-significant stenosis	56	69,34	9,25	12	68,67	8,24	0,817
Angiosignificant stenosis	52	69,29	9,01	16	69,00	9,35	0,912
Carotid artery stenosis	38	69,92	7,79	29	69,79	9,17	0,951

Table 11: Analysis of the relationship between the symptom of vertigo and gender

Indicator	Frequency	Males	Females	R
Vertigo (n=21)	n	11	10	0,434
	%	25,0	34,5	

Table 12: Analysis of the relationship between the symptom of vertigo and age (years)

Indicator	No			Yes			R
	n	$\overline{X}$	SD	n	$\overline{X}$	SD	
Vertigo	51	68,35	9,41	21	71,05	7,86	0,252

Table 13: Analysis of the relationship between IMI large hemispheres, IMI VBS and gender

Indicator	Frequency	Males	Females	R
IMI large hemispheres	n	17	13	0,808
	%	39,5	44,8	
IMI VBS	n	8	10	0,171
	%	19,0	34,5	

Table 14: Analysis of the relationship between IMI large hemispheres, IMI VBS and age

Indicator	No			Yes			R
	n	$\overline{X}$	SD	n	$\overline{X}$	SD	
IMI large hemispheres	41	70,78	7,73	30	67,60	9,75	0,130
IMI VBS	52	67,98	9,06	18	73,67	6,42	**0,017**

In fig. 20 it was seen that periprocedural complications were absent in 73 of the patients. In 1 patient, an insignificant complication was registered, resulting in a post-procedural headache, which was controlled by taking an analgesic.

Figure 20: Frequency distribution of patients by number of complications

6. DISCUSSION

Knowledge of the anatomy and dysontogenesis of the vertebral arteries is of key importance for making an accurate diagnosis, as well as for accurately performing diagnostic tests, such as selective transcatheter vertebral angiography. Anatomical variations are also taken into consideration when determining the therapeutic approach in patients with vertebral artery pathology. A large part of the anatomical variations is a variety of the norm and they are usually benign, but they can be a prerequisite for hemodynamic disorders along the course of the vessels, such as, for example, atherosclerotic plaques leading to the formation of stenosis. In our study, examining 74 patients, data were collected on abnormalities in the separation of the left and right vertebral arteries. Hypo- and aplasias were also noted as they are directly related to cerebral blood supply. In the available literature, anomalies of the right vertebral artery are more common and more heterogeneous. They are primarily related to the origin of the vessel, with the most common variants being anomalous separation from the bifurcation of the right subclavian artery and the right common carotid artery in 1-4% of cases. In 1-3%, it is separated by a separate ostium directly from the aortic arch, more often in the area between the left subclavian artery and the left common carotid artery. Variations in the origin of the left vertebral artery are primarily related to the direction and course of the vessel relative to the subclavian artery and less commonly to its site of origin. Most often, the ostium is directed upwards or backwards in 45-47% of cases. In 8% of patients, it separates from the aortic arch with a separate ostium.

In our cohort of patients, no abnormality was found in the origin of the right vertebral artery. There were 5 anomalous separations of the left vertebral artery. In 4 of them or 5.4%, the vessel originates with a separate ostium from the Ao arc, which is 2.6% less than the percentage in the literature reference. One is the case of early separation of the vertebral artery immediately after the ostium of the left subclavian artery. The absence of anomalies of the right vertebral artery and the preponderance of anomalies in the left vertebral artery is in complete contrast to the data described above.

Vertebral arteries with a diameter of less than 2 mm and delayed contrast filling during angiography are considered hypoplastic. According to literature data, the frequency of hypoplasia of the left artery reaches 45%, of the right artery up to 32%, and bilateral hypoplasia is observed in up to 25% of cases. In our patients, 3 hypoplasias were described, all three of which were on the right vertebral artery, which is also opposite to literature data. The percentage discrepancy is also large - 4.0% for the patients examined by us, compared to 32% for the population. Bilateral hypoplasia was also not recorded. Aplasia of the left vertebral artery was found in two patients or 2.7%. There were no cases with aplasia of the right artery. The available data on missing vertebral artery are scarce. In 2008 a study was published by Kohei Morimoto et al., according to which the incidence of aplasia was 4.6%. Patients were examined with MRI angiography. The discrepancy in the number of hypoplastic arteries can be explained by the different imaging methods that are used in clinical practice to image the vertebral arteries. Ultrasound diagnostics is widely advocated due to the fact that it is a fast, safe and inexpensive method that can be applied at the patient's bedside. A disadvantage of USE is that 10-20% of vertebral arteries or their segments cannot be imaged. The reason for this is anatomical features, anomalies, bone structures, small calibre of the artery, patients with a short neck and obesity. Methods such as magnetic resonance angiography and CT angiography are significantly more sensitive than USE. The sensitivity of CT angiography reaches 100%. This sensitivity decreases when evaluating the ostium and V1 of the vertebral arteries, as well as with pronounced calcinosis and along the course of the vessels, shadowing by bony structures, which can lead to erroneous interpretation and evaluation of the arteries. Similar to CT angiography, magnetic resonance angiography has a high sensitivity that surpasses selective vertebral angiography in terms of intracranial segments. Sensitivity, like CT angiography, decreases when imaging the extracranial segments. Lesions along the course of the extracranial segments are often overestimated. The use of different contrast agents increases the sensitivity of the method, regarding the assessment of high-grade stenosis and ostial lesions. However, selective angiography of the vertebral arteries is the method with the highest sensitivity and accuracy for evaluating extracranial segments.

20% of ischemic strokes in VBS are caused by stenosis of the extra- or intracranial segments of the vertebral arteries. Atherosclerotic plaque is the basis of formation of vascular stenosis. Atherosclerosis is known to be the most common cause of cerebral infarction or TIA in the VBS basin. In addition to hemodynamically significant narrowing of the vascular lumen, the atherosclerotic plaque can also become a site and source of thrombus formation. It is known that dyslipidemia, smoking, hypertension and diabetes are risk factors for the development of atherosclerosis. In the examined 74 patients, the percentage of hypertensives was the highest, namely 97.3%. Patients with dyslipidemia follow - 94.6%, smokers - 56.6%, diabetics - 25.7%. The number of patients with proven stenosis of the vertebral and subclavian arteries, the basis of which is assumed to be atherosclerosis, is 34, or 45.9%, which means that nearly half of the patients studied have prominent atherosclerosis.

AF is also a risk factor that should be addressed. According to statistics, 1/3 of IMIs are caused by embolic complications of AF. In 2-4% of patients, the first clinical manifestation of AF is precisely IMI or TIA. In our patient cohort, 18 or 24.7% had known AF. 4 of them experienced an IMI in the large cerebral hemispheres and 4 in the VBS. Therefore, in 44.4% of patients with AF, a causal relationship between AF and the occurrence of IMI can be assumed, which is slightly more than 10% of the data in the literature.

In all patients in the sample, in addition to angiography of the extracranial segments of the four major arteries supplying blood to the brain: left and right vertebral arteries, left and right common carotid artery, left and right internal carotid artery, truncus brachiocephalicus and both (left and right) subclavian arteries, selective coronary angiography (SCAG) was also performed. The aim of the latter is the contemporary diagnosis and treatment of life-threatening conditions, such as the manifestations of IHD, and also the search for a correlation between the spread of atherosclerosis in two vascular basins - that of the coronary arteries and that of the extracranial segments of the cerebral arteries. 61.6% of the examined had IHD. 45.9% had vertebral or subclavian artery stenosis, which clearly proves that atherosclerosis is a systemic disease that usually involves more than one vascular basin, and the incidence of coronary involvement was 15.7% higher than vertebral artery involvement in patients with risk factors AH, dyslipidemia, diabetes, smoking.

A predilection site for the formation of atherosclerotic plaques in the vertebral arteries is the ostium, which is part of V1. The reason for this is purely anatomical. The right angle of separation of the vertebral arteries from the subclavian arteries, as well as the large difference in diameters between the two vessels create a prerequisite for the formation of ostial stenosis. Affecting any of the remaining segments (V2, V3, V4) by atherosclerotic plaques is associated with some additional factor creating a prerequisite for the formation of stenosis. Such factors are mechanical compression by adjacent bony, muscular or tendon structures, kinking and coiling of the vessel. In the patients examined by us, stenosis of the vertebral arteries was diagnosed in 28 cases. In all of them, atherosclerosis was considered the cause of the stenosis. 16 of these stenosis was determined to be significant. The remaining 12 are hemodynamically insignificant. Significant stenosis is defined as ≥50%, localized along the course of the extracranial segments of the vertebral artery, diagnosed in patients with recurrence of symptoms despite receiving optimal medical therapy (ODT). 15 or 93.8% of significant stenosis are located in V1 ostially. 1 or 6.3% is located in V2. No significant stenosis was found in V3 and

V4. Insignificant stenosis is also most often located ostially - 9 patients or 75%. 2 or 16.7% are stenosis in V2. In one patient (8.3%), two segments of the vertebral artery – V1 and V4 – were affected. The established data confirm the statement that atherosclerosis is the most common cause of the formation of narrowing of the vertebral arteries, and the ostium is the most frequently affected vascular segment.

The frequency distribution of stenosis by gender and age groups is as follows: The only dynamic stenosis was found in a female in the age group 60-69 years. Nine non-significant stenosis located in the V1 segment were distributed in a 2:1 ratio for males, 77.8% in the 60-69 age group and one each (11.1%) in the 70-79 and 80-89 age groups. The two non-significant stenosis located in segment V2 were distributed in a 1:1 ratio between both genders and in age groups 70-79 and 80-89 years. The only non-significant stenosis located simultaneously in two segments was found in a male aged 50-59 years. The 15 significant stenosis located in the V1 segment were distributed in a 4:1 ratio for males, 46.7% in the 60-69 age group, followed by 33.3% in the 70-79 age group, 13.3% in the 50- 59 years and 6.7% - 80-89 years. A significant stenosis located in segment V2 was in a male and in the age group of 70-79 years. Also interesting is the result that all 5 patients with occlusions of the vertebral arteries are male, and 4 of them or 80% are from the age group 60-69 years and only one (20%) - 50-59 years. In conclusion, we can say that the male gender is a risk factor for the formation of stenosis/occlusions of the vertebral arteries. The age group between 60-69 years is most at risk.

Of clinical and diagnostic interest are the dynamic stenosis of the vertebral arteries, causing the syndrome of Bow Hunter. The only method that can accurately make the diagnosis is selective dynamic vertebral angiography. It allows contrast imaging and imaging of the affected artery during rotation of the patient's head. This is one of the advantages of motada over other imaging methods. The disease is rare, with a large number of cases thought to go undiagnosed. Most often, the involvement is in the area of C1-C2, i.e. V3. We diagnosed 1 patient with dynamic stenosis localized precisely in V3. The only treatment method for severe cases with a clinical picture of IMI or TIA is surgery. The clinical presentation of the disease and the angiographic findings are taken into consideration when assessing the need for surgical treatment.

Another pathology of interest is “Steal” syndrome or also called “syndrome of the subclavian thief”. It is caused by high-grade stenosis or complete occlusion of the subclavian artery located in the area between the ostium of the left subclavian artery and the ostium of the left vertebral artery on the left, or in the area between the truncus brachiocephalicus and the ostium of the right vertebral artery on the right. Anatomically, the two vertebral arteries separate precisely from the proximal segments of the left and right subclavian arteries, except for the variations in separation. Depending on the degree of narrowing or obstruction, “Steal” syndrome can be incomplete or complete. We considered it important to image the subclavian arteries in their proximal segments, since the pathology there is directly related to a significant reduction or complete cessation of blood flow to the vertebral arteries. Also, subclavian stenosis can become a source of peripheral embolization in the VBS basin. In these patients, the affected vertebral artery is disconnected from the cerebral blood supply, becoming a collateral connection between the VBS and the subclavian artery. The result is ischemia in the VBS area, due to redirection of blood flow to the affected limb. Selective catheter vertebral angiography allows accurate diagnosis after injection of contrast into the unaffected vertebral artery with subsequent visualization of retrograde blood flow in the affected vertebral artery. In our study we identified 6 patients with subclavian artery stenosis/occlusions. 4 or 66.6% have insignificant stenosis. 1 (16.6%) had complete subclavian artery occlusion and 1 (16.6%) had subtotal occlusion. “Steal” syndrome is visualized in patients with subtotal and total occlusion. After recanalization of the occluded subclavian arteries and stent placement, normal blood flow in the vertebral arteries was restored in both patients. No complications were registered, which proves that interventional treatment in such patients is an accurate and safe diagnostic and therapeutic method.

The clinical picture of patients with hemodynamic disorders of the vertebral arteries is characterized by numerous symptoms and syndromes. The clinical diversity is due to the complex anatomy of the vertebral arteries, consisting of extra- and intracranial segments, giving off numerous lateral branches that are involved in the blood supply of vital brain structures. The cerebellum, stem, inner ear, labyrinth, vermis, occipital, mediobasal surface of the temporal lobe, mesencephalon, diencephalon, choroid plexus, parts of lateral ventricle and third ventricle, part of thalamus and corpus callosum are a large part of the areas receiving blood from vertebral arteries and their branches. Participation in the circle of Willis, by means of the left and right posterior cerebral arteries, is key to adequate cerebral blood supply, and its symmetrical structure is responsible for the correct distribution of blood flow and its collateral compensation in case of blockage of one of the cerebral arteries.

The pathology of the vertebral arteries proceeds clinically with characteristic symptoms and trunk syndromes. In extracranial stenosis or occlusions of one of the vertebral arteries, clinical symptoms may not occur if the blood supply from the contralateral vertebral artery is adequate. In order for a clinical picture to develop as a result of a hemodynamic disturbance along the course of one artery, a second factor preventing normal blood flow in the other artery is also necessary. Such factors may be plaques, stenosis, hypoplasia, aplasia, poorly functioning circle of Willis, vascular spasm. The most characteristic symptoms of patients with VBVI are: dizziness, nausea, hemianopsia, cortical blindness, diplopia, impaired facial sensation, vertigo, dysphagia, dysarthria, hemiplegia, hemianesthesia, coordination disorders, alternating syndromes of the medulla oblongata and pons, myoclonus of the eyes muscles, tongue, soft palate, larynx and diaphragm, drop attacks, episodes of amnesia and confusion. The listed symptoms are combined into trunk syndromes - alternating and non-alternating. The syndromes of a.vertebralis - for the most part, namely in about 70% of heart attacks, are preceded by a transient ischemic attack (TIA) and are embolic. The above-described symptoms and syndrome are revealed when taking a neurological status, supported by instrumental studies such as Doppler sonography, CT, MRI, transcatheter angiography. All 74 patients in our study had a neurological status taken, and anamnestic and accompanying medical record data suggestive of VBVI were used. We have described the most characteristic and most common symptoms of vertebral artery pathology, as they are vertigo, weakness, dizziness, unsteady gait, ataxia, headache, blurred vision, vomiting, nausea, and diplopia. According to the literature, dizziness and dyscoordination disorders such as unsteady gait and ataxia are the most common symptoms. According to the results we obtained, patients with vertigo had the largest relative share (28.8%), followed by those with weakness and dizziness with 6.8% each. Three of the studied symptoms - unstable gait, ataxia, headache - were represented by 3 cases each or 4.1%.

Single cases of impaired vision, vomiting and nausea (1.4%) were also found, and patients with diplopia were not diagnosed. For the only symptom with statistical representation, the largest number of cases (9 or 42.9%) were from the 60-69 age group, followed by 70-79 years with 8 or 38.1%, and in the 40-49 age group there are no patients.

From the obtained distribution (number/%) according to the type of cerebrovascular accidents experienced (cerebral stroke in the large hemispheres; cerebral stroke in VBS; TIA) - in general for the group and by gender and age groups, it is clear that from the considered indicators with the most a large relative share (40.5%) is IMI large hemispheres, followed by IMI VBS with 24.3%. The least (only one or 1.4%) were patients with TIA. Of the patients who survived IMI in the large hemispheres, males predominated - 56.7%, compared to 43.3% for females. Patients with an experienced IMI in VBS are predominately for females - 55.6% and 44.4% for males. The only TIA was in a male patient. IMIs in large hemispheres have representatives in all age groups, but they are the most (40%) in the group 60-69 years, followed by 70-79 with 33.3%. The youngest age group 40-49 has one patient. Patients with IMI in VBS are most in the 70-79 age group, followed by those in the 60-69 and 80-89 age groups, and are completely absent in the youngest age groups. The TIA patient is from the age group of 60-69 years. We can conclude that the riskiest age group for IMI in the large hemispheres is 60-69, and for IMI in VBS 70-79 years. We established the presence of a statistically reliable relationship between IMI in the VBS and age, expressed in a significantly greater mean age in patients with IMI in the VBS compared to those with IMI in the large hemispheres. 94.6% of our patients have dyslipidemia. As mentioned above, atherosclerosis is a major risk factor for IMI, but statistically, IMI in large hemispheres is caused by atherosclerosis in 25% of cases, and IMI in VBS in 20%. We hypothesize an earlier atherosclerotic involvement of the carotids than the vertebral arteries, but this will be the subject of further studies. The male gender again prevails in terms of IMI in the large hemispheres with 13.4%.

The number of patients with an experienced IMI in VBS is 18. In four of them, significant stenosis of the extracranial segments of the vertebral arteries were diagnosed. These are patients with stenosis ≥50%, in whom we assume a causal relationship between the angiographically established stenosis and the clinical diagnosis of IMI. The percentage of these cases is 22%, which is consistent with the 20% reported in the literature for IMI in VBS caused by vertebral artery stenosis.

Selective transcatheter vertebral angiography is an invasive study that is the “gold standard” for the diagnosis of hemodynamic disorders affecting the extracranial segments of the vertebral arteries. Vertebral angiography depicts with high resolution the causes of hemodynamic changes, such as: anomalies, stenosis, occlusions, dynamic stenosis, dissections, aneurysms, kinking, “steal” syndrome, collaterals. An advantage of the method over other imaging methods is the possibility and accuracy in evaluating the ostium of the vertebral arteries, which is the place most often affected by atherosclerosis. The angiograph is the only method that allows performing dynamic angiography, which proves the dynamic stenosis along the course of the extracranial segments of the vertebral arteries.

According to the recommendations of the American Heart Association and the American Stroke Association, patients indicated for selective vertebral angiography are those who have clinical signs of cerebellar ischemia or ischemia in the posterior cerebral circulation, and at the same time are considered suitable for interventional treatment. These are patients in whom non-invasive methods (MRI, CT, Doppler) did not provide sufficiently clear and accurate data on the pathology present and are referred for digital subtraction angiography. Recommendations are class 2a, level of evidence C. In our study, the indications for selective vertebral angiography are expanded, as we consider the method to be readily available and safe, even though it is invasive. These are patients with anamnestic, clinical and instrumental data suspicious for ischemia in the VBS area. It concerns patients who report having experienced a cerebrovascular accident in the past, have medical documentation proving a cerebrovascular event (IMI or TIA), show deviations in the neurological status and are suspected of ischemia in VBS, have an imaging study (MRI, CT, Doppler), which proves pathology in the VBS basin. Accepting these broad indications, we try to prove our thesis that selective catheter angiography of the vertebral arteries is an accurate and safe method of diagnosis in these patients, prevailing over other imaging methods, thanks to the high resolution, the possibility of different projections of the target segment and the ability to perform dynamic angiography.

All patient angiograms are performed in an angiography room equipped with an angiograph. Vascular access is through the right radial artery or the right femoral artery. 22.9% were angiographies performed through the right femoral artery. In 5% of patients, the examination was performed through the left radial artery, due to the impossibility of performing it from the right side. Right radial access was used in 72% of cases. It is preferred because it is gentler and safer for the patient. Data are on the entire sample of diagnoses plus interventions. In cases of severe, insurmountable vascular spasm, marked tortuosity, highly curved artery, presence of accessory radial artery, “high” separation of radial and ulnar arteries from the brachial artery, left radial or transfemoral access is undertaken. Femoral access is preferred for interventional treatment of the vertebral arteries following diagnosis. In this way, the obstacles described above are avoided and a better stability and support of the system, necessary for carrying out an intervention, is provided. According to data from the European Society of Vascular Surgery in 2023, 93% of transcatheter interventions of the vertebral arteries were performed through femoral access. Radial access was used in 5% and brachial in 3%. In 90.9% of cases with intervention of the vertebral arteries, we used transfemoral access from the right common femoral artery. In the remaining 9.1%, the access is radial through the right radial artery. Brachial vascular access was not used because of the high risk of vascular complications. In conclusion, we can say that there are no established recommendations in the literature for vascular access when performing diagnostic selective transcatheter vertebral angiography. In the interventions of the vertebral arteries, the preferred and recommended approach is the transfemoral one. In our study, the preferred access for diagnostic examination was the radial. If it is impossible to perform the examination transradially, an alternative transfemoral access is used. A large percentage of the interventions (90.9%) were performed through the generally accepted transfemoral access. An alternative method, with favourable anatomy, is the transradial method.

Selective transcatheter vertebral angiography and subclavian artery angiography is performed using well-known and widely used guides and catheters in the field of invasive diagnostics. A 0.035" J-guide, a hydrophilic 0.035" or 0.020" J-guide, or a coronary 0.014" guide are among the most commonly used. Preferred diagnostic catheters for examination of the cerebral and subclavian arteries are: 5Fr JR Catheter, JL, Vertebral Catheter, Multipurpose Catheter, Simmons Catheter. Each artery is imaged in at least two different projections. Special attention is paid to the ostiums of the vertebral arteries, since they are the most frequently affected segments along the course of the arteries. In the case of diagnosed lesions, additional projections are made, which allow a complete diagnostic specification of the affected segment with an assessment of subsequent behaviour and treatment. Dynamic stenosis along the course of the vertebral arteries are captured in four projections, one of which is dynamic angiography during rotation of the patient's head. To avoid bony structures that often impede accurate visualization of the vertebral arteries, digital subtraction angiography is used.

The biggest advantage of transcatheter selective vertebral angiography over other methods (MRI, CT, Doppler) is that the method is not only diagnostic but also therapeutic. This enables the patient to receive immediate interventional treatment if deemed suitable. According to the recommendations in the literature reference, patients with stenosis ≥50% and ≤99%, localized along the course of the extracranial segments of the vertebral artery and clinically manifest recurrent neurological symptoms, despite taking optimal drug therapy, are indicated for interventional treatment. The recommendations are class 2b, level of evidence B. The cases we accepted as suitable for interventional treatment were discussed by a medical team consisting of a clinical cardiologist, a clinical neurologist and an invasive cardiologist. To perform the procedure, 6Fr guiding catheters or desile catheters are used, which are threaded over an exchangeable 0.035" J-guide or a hydrophilic one. The ostium of the vessel is cannulated in cases where ostial stenosis is not registered. In case of ostial involvement of the artery, the guiding catheter is positioned as close as possible to the ostium with the tip directed towards the vascular lumen. An embolic protective device is not routinely used during the procedure because of the high risk of dissection or vascular spasm complicating and making the intervention difficult. The latter are due to the characteristics of vertebral arteries such as the small caliber of the vessel compared to that of the carotid arteries, the tortuous in most cases first segment, the angle of separation of the artery relative to the subclavian artery and the tendency to spasm. There are already studies on the benefits and risks of the use of a vascular protective device in intervention of the extracranial segments of the vertebral arteries, which recommend their use in vertebral arteries with a large caliber >3.5 mm and a favorable separation angle. In other cases, their use carries the risk of vascular complications. Our interventions were carried out without the use of protection and no embolic incidents were recorded.

A coronary 0.014" guidewire is selectively placed in the vertebral artery, the tip of which is positioned distally intracranially. The degree of stenosis is determined by the distal size of the artery. The target stenosis for stenting are, as mentioned above, between 50-99%. High-grade >70% and critical >95% stenosis, as well as subtotal occlusions, are predilated with a small balloon, providing easy and trouble-free access of the stent to the target lesion. Predilation is performed with a simple 'semicompliant' balloon. A 'Non-compliant' balloon is used in marked calcinosis, usually affecting the ostium of the vessel. Balloon predilatation is also performed when direct stent passage through the stenosis is not feasible. The usual diameter of balloons used for predilation is 2.0-2.5mm, expanded to 8-14atm. In 7 or 63.6% of the vertebral arteries intervened by us, balloon predilatation was used. It is important to note that 10 of the 11 vertebral artery stentings were in V1, and only 1 in V2.

At this stage, no specific vertebral stents exist. Self-expanding stents are rarely used. They have a larger diameter in the folded state, which makes it difficult to pass through the stenosis, especially through the ostial ones, which, as it turned out, are the most common. The use of "monorail" or "over the wire" stent systems for vertebral stenosis is extremely rare and is determined by the experience of the operator.

Coronary stents are used that have good radial strength, a fine profile, minimal shortening upon expansion, and good patency through tortuous vessels. There are two types of coronary stents – bare metal stents (BMS) and drug eluting stents (DES). Bare metal stents (BMS) were used in 4 of our patients. 7 patients were stented with drug-eluting stents (DES). Sizes are from 2.0-4.0mm for BMS and from 3.5-4.0mm for DES. The lengths are selected to completely cover the stenosis, with the proximal and distal ends of the stent covering 2-3 mm of healthy vessel area. Expansion is at 8-16 atm. Stents, which are placed ostially, prolapse 1-2 mm into the lumen of the subclavian artery, after which balloon postdilatation is mandatory, i.e. called "flair" targeting proximal stent optimization. In case of poor expansion of the stent in the area of the stenosis, balloon postdilatation is performed. These cases in our study are 7. Post-dilatation is performed with "non-compliant" balloons, which allow a high-pressure impact on the stenosis. The diameter of the balloons matches the diameter of the stent and the length is a few millimetres shorter or equivalent to the stent. In case of an unsatisfactory result of the expansion, a balloon with a diameter of 0.25-0.5 mm larger than that of the used stent is taken.

An important condition is that the balloon does not go beyond the borders of the stent to avoid vascular complications such as dissection. Balloon postdilations are necessary in severe high-grade stenosis with pronounced calcinosis, usually located in the ostium of the artery.

Still, endovascular treatment of extracranial vertebral artery stenosis remains a major challenge with insufficient long-term results due to the lack of sufficient randomized clinical trials. In summary, the two types of stents showed no significant difference in terms of technical success and procedural complications. Patients stented with BMS reported more often the occurrence of cerebral symptoms – 11.3%, compared to 2.8% of patients with DES. Also, BMS had a higher reintervention rate of 19.2% versus 4.8% for DES. This is explained by the lower rate of restenosis in DES patients, which is due to the drug effect and suppression of endothelial proliferation and inflammation. Drug-eluting stents also show an advantage in patients with diabetes. The percentage of significant in-stent restenoses, meaning stenosis >50%, varies widely, regardless of the type of stent used – BMS or DES. Data from follow-up studies regarding restenosis in patients with BMS ranged from 0-48% per cent restenosis. In patients with DES, the percentage is from 0-63%. Variations in the percentage, as well as the higher number in DES compared to BMS, can be explained by the different length of the follow-up period in the individual studies, the type and duration of drug therapy after stenting performed, the diameter of the stent used. The high frequency of restenosis is generally associated with the pronounced tortuosity of the extracranial segments of the vertebral arteries. Data in the literature review regarding periprocedural complications also vary.

Table 3

Review of the long term results of previous studies on endovascular stent treatment of extracranial vertebral artery stenosis

Studies	Stent type	Number of patients	Number of treated stenosis	Complication rate (%)		Follow-up	
				Technical	Clinical	Period (mo)	Rate of significant restenosis[2] (%)
Lin et al[74]	Bare stent	58	67	0	7	11	25
Albuquerque et al[11]	Bare stent	33	33	3	0	16	43
Chastain et al[12]	Bare stent	50	55	2	0	6	10
Weber et al[75]	Bare stent	38	38	2	1	11	38
Cloud et al[76]	Bare stent	14	14	0	0	20	9
SYLVIA[1]study[77]	Bare stent	18	18	-	-	6	43
Akins et al[78]	Bare stent	7	7	0	0	36	43
Taylor et al[79]	Bare stent	44	48	0	0	7	48
Hatano et al[80]	Bare stent	117	117	0	0	6	10
Lin et al[81]	Bare stent	80	90	0	0	12	28
Jenkins et al[16]	Bare stent	32	38	0	0	10	3
Karamehev et al[82]	Bare stent, DES	10	12	0	0	34	10
Lin et al[27]	DES	11	11	0	0	8	0
Zhou et al[30]	DES	86	92	0	0	12	17
Gupta et al[83]	DES	27	27	0	2	6	7
Akins et al[78]	DES	5	5	0	0	17	0
Edgell et al[84]	DES	5	5	0	0	15	0
Vajda et al[85]	DES	48	52	0	0	7	12
Lugmayr et al[86]	DES	7	8	0	0	6	63

Open in a separate window

[1]Stenting of symptomatic atherosclerotic lesions in the vertebral or intracranial arteries; [2]significant restenosis indicates that it is equal or higher than 50% stenosis. DES: Drug-eluting stents.

Table 3: Summary of clinical trial results for interventional treatment of vertebral arteries in extracranial segments.

The percentage of deaths occurring as a complication of the intervention was between 0 and 3.2%. The percentage (3.2%) is the same for cerebrovascular accidents, such as IMI in VBS or TIA. During long-term follow-up for an average period of 4.7 years, no strokes were registered in VBS in both groups of patients – stented with BMS and DES. In the patients we intervened with, a minor complication was registered in 1 patient, expressed in a post-procedural headache, which was controlled with the administration of an analgesic. Serious side effects such as death and cerebrovascular accident (IMI, TIA) were not recorded. From the performed diagnostic angiograms, no complications were reported either.

Interventional treatment of the subclavian artery was performed in two patients. One has registered total occlusion of the left subclavian artery and "steal" syndrome on the affected side. The other with significant 70% ostial stenosis and delayed blood flow in the vertebral artery. Both interventions were performed through a right femoral access. 6Fr guiding catheters type JR 3.5 positioned in the subclavian artery were used. The target lesion was traversed in both cases with a coronary 0.014" guidewire, which was placed distally in a segment of the brachial artery. In both cases, balloon predilatation was performed with 4.0 and 5.0 mm balloons. BMS placed on a dilatation balloon were used for stenting. The size of the stents is 7.0/18mm and 7.0/60mm, expanded to 8atm. Balloon postdilatation was performed in both patients. A very good angiographic result was achieved with restoration of blood flow in the subclavian arteries, leading to elimination of the "steal" syndrome in one patient and normalization of blood flow in the vertebral artery in the other. Periprocedural complications were not recorded.

Extremely important for maintaining the good results of the interventional treatment of the vertebral and subclavian arteries is the long-term implementation of ODT.

The latter includes antithrombotic therapy, lipid-lowering therapy and therapy to control other risk factors such as AH and DM.

Specific recommendations regarding the type and duration of antithrombotic therapy in patients with stented vertebral arteries are still lacking. At this stage, the behaviour of these patients is similar to carotid artery stenting. The patient receives dual antiplatelet therapy including Aspirin and Clopidogrel in loading doses on the day of stenting, which are 325 mg for Aspirin and 300 mg for Clopidogrel, after which they switch to maintenance doses - 75-325 mg for Aspirin and 75 mg for Clopidogrel. The duration of combined therapy is minimum 4 weeks, after which the patient can remain permanently on monotherapy with Clopidogrel 75 mg daily. The same recommendations apply to subclavian artery interventions.

Lipid-lowering therapy is with statins, with or without the addition of Ezetimibe until a target LDL level of <1.8mmol/L is reached.

Surgical treatment of vertebral artery stenosis includes endarterectomy and reconstruction. Treatment options for ostial lesions are: transposition to the ipsilateral common carotid artery; vertebral artery reimplantation; venous bypass from the subclavian artery; endarterectomy with access through the subclavian artery. Endarterectomy of ostial and proximal stenosis of the extracranial segments of the vertebral arteries has been performed through a supraclavicular incision and access since the 1960s, and the success rate of the method varies. Difficult access to the ostiums makes the procedure technically very difficult to perform. For this reason, some surgeons resort to a clavicle osteotomy to provide better access. Complications of these interventions are frequent and include lymphocele, fistulas, paralysis of the vocal cords, pneumothorax. Therefore, endovascular treatment is preferred over endarterectomy.

Reconstruction of the proximal segments manifests itself in transposition of the vertebral artery to the common or internal carotid artery, and less often to the subclavian artery or thyrocervical truncus. Transposition is often combined with endarterectomy. Results of studies of proximal segment reconstruction have shown a relatively low incidence of major complications such as stroke with subsequent fatal outcome as a result of the intervention, namely less than 2%. At

10-year follow-up, however, this rate dramatically increased to 92%. Complications of stroke and death in distal extracranial segment reconstruction were 6% for early and 80% for late at 5-year follow-up.

Other complications of the reconstruction are Horner's syndrome (10%), thrombosis (11%), less often paralysis of the vocal cords, damage to the phrenic nerve.

Surgical treatment of extracranial vertebral artery stenosis can be an alternative to endovascular treatment in centres with extensive experience and a team of experienced surgeons. In centres that do not have experience with this type of intervention, surgical treatment is completely replaced by interventional treatment.

7. CONCLUSIONS

- 39.1% of patients with Dg: circulatory failure in VBS have angiographic changes of the vertebral arteries.
- 82.7% of angiographic changes are located in the ostial segments of the vert. Art. A. Lower % are in V2 (10.3%) and V3 (3.2%).
- The most common risk factor for angiographic changes of extracranial segments of vertebral arteries is dyslipidemia.
- 61.6% of patients with Dg circulatory failure in VBS have coronary artery disease.
- Selective catheter angiography of the vertebral arteries is an accurate and safe method for Dg in these patients.
- Interventional treatment in them is a safe and effective method for restoring normal circulation in VBS.

8. CONTRIBUTIONS

- For the first time in Bulgaria, a prospective study of the vertebral arteries in patients with diagnosed insufficiency of the blood supply in VBS was performed with the help of selective catheter angiography.
- By means of selective catheter angiography of the vertebral arteries, the frequency, localization and characteristics of the stenosis of the vertebral arteries were clarified.
- An attempt was made to clarify the role of risk factors in patients diagnosed with "Vertebrobasilar vascular insufficiency".
- Catheter interventions of significant stenosis of the vertebral arteries were performed, according to accepted recommendations in international guidelines.

9. PUBLICATIONS AND PARTICIPATION IN SCIENTIFIC FORUMS RELATED TO THE DISSERTATION

9.1 Publications

1. N. Ivanov, Anatomy, dysontogenesis, pathophysiology and pathogenesis of vertebrobasilar artery diseases, Interventional Cardiology Forum, 2022, Issue 2: 5-11, DOI: 10.3897/icf.2.e80540
2. N. Ivanov, Clinical case of a patient with Bow Hunter's Syndrome, Interventional Cardiology Forum, 2022, issue 2: 48-51, DOI: 10.3897/icf.2.e94644
3. N. Ivanov, Clinical picture of patients with vertebrobasilar vascular insufficiency, Interventional Cardiology Forum, 2023, issue 3: 30-38, DOI: 10.3897/icf.3.e113300

4. N. Ivanov, Catheter angiography and interventional treatment of patients with a possible violation of blood supply in the vertebrobasilar system - own experience, Forum for interventional cardiology, - 2023, issue 3: 49-60, DOI: 10.3897/icf.3.e115581
5. Pl. Gatsov, N. Ivanov, H. Kamakh, Occluded left subclavian artery without development of the „subclavian thief“ syndrome, BULGARIAN CARDIOLOGY, 2018, issue 4, 45-48, ISSN 1310-7488
6. Nikolai Ivanov, Plamen Gatzov, Indications and technical implementation of vertebral artery catheter angiography, Journal of Biomedical & Clinical Research (JBCR), 2019, volume 12, 32, ISSN 1313-6917.
7. Plamen Gatzov, Nikolai Ivanov, Indications and technical implementation of vertebral arteries catheter interventions, Journal of Biomedical & Clinical Research (JBCR), 2019, volume 12, 36, ISSN 1313-6917.

9.2 Reports at scientific forums

1. N. Ivanov, Clinical case of a patient with "Bow Hunter's syndrome", VIII BULGARIAN COURSE on CORONARY PHYSIOLOGY and PHYSIOLOGY OF NON-CORONARY VESSELS, 21-22.11.2020, Holiday Inn hotel, Sofia
2. Pl. Gatsov, N. Ivanov, Case of simultaneous recanalization of left subclavian and left vertebral arteries, XVII National Congress of Cardiology, 29.09.-02.10.2022, c.c. Albena
3. N. Ivanov, CLINICAL CASE – DYNAMIC STENOSIS OF LICA, X Jubilee Bulgarian course on coronary physiology and physiology of non-coronary vessels, 24-26.06.2022, Imperial hotel, Plovdiv
4. N. Ivanov, Pl. Gatzov, Indications and technical implementation of vertebral artery catheter angiography, Jubilee scientific conference "45 years Medical University – Pleven", 31.10-02.11.2019, Pleven

5. Pl. Gatzov, N. Ivanov, Indications and technical implementation of vertebral arteries catheter interventions - Jubilee scientific conference “45 years of Medical University – Pleven”, 31.10-02.11.2019, Pleven