

# Ultrasound Diagnostics of Hemodynamic Changes in Arteriovenous Fistula for Hemodialysis: Review

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**Abstract** — The socio-economic significance of chronic kidney disease in the terminal stage is due to the fact that expensive methods of treatment are required, the number of patients on hemodialysis increases annually and most of them are of working age. The most preferred vascular access for hemodialysis treatment is an arteriovenous fistula, yet its dysfunction occurs in more than 30% of patients. Adequate long-term functioning of the fistula depends on its successful maturation, timely diagnosis and elimination of possible complications of permanent vascular access. The main method for diagnosing dysfunction of an arteriovenous fistula is duplex ultrasound, which allows determining the diameters, the state of the walls and blood vessels lumen, the access flow, identifying such complications as stenosis of inflow artery, anastomotic zone and outflow vein, fistula thrombosis, hand ischemia. Ultrasound diagnosis of vascular access complications allows for their timely correction, which increases the duration of fistula adequate functioning.

**Keywords** — arteriovenous fistula, hemodialysis, duplex ultrasound, stenosis, thrombosis, hand ischemia.

## I. INTRODUCTION

Chronic kidney disease occupies a special place among chronic non-communicable diseases since in the terminal stage it leads to a sharp decrease in the patients' quality of life and requires expensive treatment methods [6]. The share of hemodialysis among other methods of renal replacement therapy is up to 95 %. In the world, more than 2 million patients with terminal renal disease are on hemodialysis [5], and the dialysis population is increasing every year. The socio-economic significance of the disease is determined by the fact that the majority of patients are of working age – the average age in different countries varies from 49 to 65 years [3].

The most preferred vascular access for hemodialysis is the arteriovenous fistula since it is associated with a lower risk of infectious complications and lower mortality compared with the arteriovenous graft and a permanent tunneled catheter. However, arteriovenous fistula dysfunction occurs in more than 30 % of patients, and the maximum duration of its functioning rarely exceeds 4 years. At the same time, the patient's stay on hemodialysis therapy can reach 20 years or more [2, 4, 6, 15, 22, 26, 27, 32]. Effective long-term treatment depends largely on the successful maturation and functioning of permanent vascular access. Given the limited vascular resource in patients, one should strive to maximize the duration of an already formed arteriovenous fistula functioning by timely diagnosis and correction of its

complications. The main method for diagnosing vascular access dysfunction is duplex ultrasound [1, 7, 21, 25, 31].

## II. CHANGES IN HEMODYNAMIC PARAMETERS IN ARTERIOVENOUS FISTULA DURING ITS MATURATION

Much attention is paid in the literature to changing of the hemodynamic parameters in the maturing arteriovenous fistula. Immediately after the formation of a fistula, due to a significant pressure gradient between the inflow artery and the outflow vein, there is a sharp increase in blood flow to the artery. Despite the fact that intraoperative measurement of access flow does not reflect real data due to vascular spasm and it is believed that the data may be underestimated, most arteriovenous fistulas immediately after the fistula formation show a 5–10 fold increase in access flow. For example, during the radiocephalic fistula formation, blood flow in the radial artery may increase from 20 to 200 ml/min immediately after surgery. The range of access flow values can vary greatly between different patients and is on average 50–500 ml/min. In the proximal (shoulder) arteriovenous fistula the blood flow, measured intraoperatively immediately after fistula formation, averages 700–1000 ml/min and increases by 50–100 % with an increase in the vessel diameter [2, 3, 5]. The inflow artery lengthens and expands over time to ensure adequate blood flow. An increase in the diameter and length of the artery is accompanied by its aneurysmal degeneration in the late stages due to atrophy of the smooth muscle cells of the media [2].

The size of the superimposed anastomosis plays an important role in the fistula maturation and the increase in access flow. Studies have shown that when the fistula diameter is about 20 % of the inflow artery diameter, there is no significant change in blood flow and ripening of the fistula. During the anastomosis formation with a size of about 75 % of the artery diameter, the blood flow in the arteriovenous fistula increases significantly, and with a subsequent increase in the size of the anastomosis, a further, but moderate increase in the blood flow is observed in the outflow vein [2]. Other authors believe that when the anastomosis diameter is 1.5 times the inflow artery diameter, the blood flow increases 5.6 times, and if the diameter exceeds 3 times, the access flow increases 8 times. In this case, remodeling occurs in the anastomosis itself, which increases in size, which leads to an additional increase in the arteriovenous fistula blood flow [3].

Increased access flow in the fistula affects the blood flow in the artery below the anastomosis. With a small fistula

diameter, the blood flow direction in the distal part of the radial artery does not change. As the anastomosis size increases, the blood flow becomes bidirectional: anterograde to systole, retrograde to diastole. With a large amount of fistula blood flow completely changes the direction to retrograde. Significant dilation of the artery distal portion does not occur due to small access flow [2, 3, 5]. In the case of retrograde blood flow in the distal portion of the radial artery, blood flows through the ulnar artery through the arterial palmar arch into the fistula vein. The volume of blood entering the arteriovenous fistula from the distal part of the radial artery can reach 20–30 %. When this occurs, an increase in the blood flow in the ulnar, anterior interosseous arteries and collateral branches on the forearm to compensate for the lack of blood supply to the hand [2].

The concept of "fistula maturation" also includes an increase in the vein diameter and the thickening of its wall (the process of the vein arterialization) [5]. A sharp increase in the fistula access flow leads to an increase in shear stress in the outflow vein. Thus, the magnitude of the shear stress ranges from  $-12 \text{ dyn/cm}^2$  in the direct portion of the fistula vein to  $+112 \text{ dyn cm}^2$  in the bending zones and closer to the anastomosis, which causes activation of the release of NO, prostacyclin and EDHF, increasing the concentration of cGMP in the vascular wall, which in turn, leads to relaxation of smooth muscles and the vein dilatation. At the same time, cytoskeleton reconstruction and hyperplasia of neointima and media occur, leading to a relative decrease in the diameter of the vein. NO and prostacyclin limit the hypertrophy of the vascular wall, but its thickness should be sufficient for the timely closure of the defect from the dialysis needle after puncture and prevent the hematomas development. The ratio of these mechanisms has a significant impact on the arteriovenous fistula maturation [2, 5, 32, 33]. Vein's large branches within 10 cm from the anastomosis, which take away a large amount of blood can prevent its maturation. Therefore, special attention should be paid to the vein branches detection during the pre-operative assessment of the vascular topography with a view to their timely ligation [9]. It has been established that the minimum diameter of the outflow vein, suitable for punctures and adequate hemodialysis, is 4–6 mm with a depth of no more than 5–6 mm [9, 10, 26, 27, 32, 33].

### III. THE OPTIMAL VALUES OF ACCESS FLOW IN THE ARTERIOVENOUS FISTULA

Among the authors, there is no consensus on the target value of the blood flow parameter in the fistula. It is believed that the minimum access flow capable of providing adequate blood flow through the dialyzer is 350–400 ml/min, and the higher the speed, the greater the likelihood of long-term successful functioning of the arteriovenous fistula and the lower the risk of fistula thrombosis [2, 32]. H. Huijbregts et al. determined that with the fall of access flow for every 100 ml/min, the likelihood of complications increases by 10–15 % depending on the level of arteriovenous fistula formation [19]. However, with an increase in blood flow in the fistula, the load on the right heart chambers increases and the risk of developing chronic heart failure increases. It has been proven that access flow in a fistula should not exceed 30 % of the cardiac output, averaging no

more than 1500–2000 ml/min [1, 32, 34]. There is also evidence of the effect of high blood flow in the arteriovenous fistula on the development of complications such as hand ischemia and the outflow vein stenosis. Access flow values in the fistula that are recommended in the literature range significantly in different authors: from 350 to 2000 ml/min [1–3, 10, 13, 18, 27, 30, 32, 33]. According to the American and European clinical recommendations, the optimal blood flow rate is not less than 600 ml/min [32, 33].

The literature provides data on other parameters that are able to predict the maturation effectiveness and the duration of the arteriovenous fistula functioning. So, fistulas, superimposed on the radial artery with the blood flow of more than 20 ml/min, in the future often function more adequately. Arteriovenous fistulas with an intraoperative blood flow of about 230 ml/min have a greater likelihood of maturation as compared with fistulas with a small intraoperative access flow (average 98 ml/min) [5, 23]. Most often, the blood flow values in the fistula and the size of the outflow vein a month after the formation of the fistula are used as predictors of effective arteriovenous fistula maturation. With a vein diameter of more than 4 mm and the access flow of 500 ml/min and higher, the fistula adequately functions in 95 % of cases, with 1 criterion in 74–76 % and only 33 % of cases if none of the criteria exists. It has been proven that veins with a diameter of less than 2.5 mm prior to fistula overlay have poor maturation ability as well as arteries with a diameter of less than 2 mm, so some authors do not recommend the formation of a fistula between vessels of this size [6, 9, 10, 26, 27].

### IV. STENOTIC LESIONS OF BLOOD VESSELS THAT FORM THE ARTERIOVENOUS FISTULA

Fistulas with hemodynamic parameters that have not reached target values cannot be used for effective hemodialysis. With the help of duplex ultrasound, it is possible to identify the arteriovenous fistula complications, which prevent its successful maturation [15, 27, 31]. One of the most frequent complications of vascular access is stenosis. Atherosclerotic changes and diabetes mellitus can be causes of inflow artery stenosis. Outflow vein stenosis is associated with high access flow, multiple punctures in the local zone, turbulent blood flow and vibration, which permanently injure the vein wall [3, 6, 10, 16]. Histological studies demonstrate the accumulation of myofibroblasts, fibroblasts, and fibrocytes in the subendothelial intimal layer, which is an indication of increased metabolic activity of cells, which develops as a result of the above damaging factors [3, 10, 28]. The stenotic area can be detected in duplex ultrasound in the B-mode as a section for reducing the vessel lumen by at least 50 % [27]. However, taking into account the possible unevenness of the outflow vein diameter during long-term functioning of the fistula, its tortuosity with the formation of acute angles, as well as to assess the hemodynamic significance of stenosis, other criteria should be used. The indicators of blood flow in the place of the alleged stenosis and 2 cm below are determined, the ratio of the peak systolic velocity in the place of stenosis and in the proximal area is calculated. If this ratio exceeds 2:1, then stenosis of more than 50 % of the inflow artery or the draining vein is diagnosed. For stenosis of the

anastomotic zone, this indicator is 3:1 or more, and an increase in the peak systolic velocity in the anastomotic zone of more than 400–500 cm/s is also taken into account [9, 27, 29]. Some authors recommend comparing the blood flow rate in the stenotic zone and in the distal section, while they believe that with more than 50 % stenosis, the ratio is more than 2 for stenosis of an artery and vein, 3 or more for anastomotic stenosis at a peak systolic velocity of more than 400 cm/sec in the stenotic area for all localizations [8].

Hemodynamically significant stenoses lead to a decrease in access flow in the distal zones. It has been established that the presence of stenosis of more than 50 % is indicated by a decrease in blood flow of less than 500 ml/min, as well as a decrease in access flow by 25 % compared with the data from the previous study [8, 11, 12, 24, 27, 29, 32]. As an auxiliary criterion for significant stenosis of the outflow vein F. Fahrtaş and co-authors propose the diameter of the vein free lumen in the stenosis area of less than 2.7 mm with a sensitivity of 90 % and specificity of 80 % [17].

In the absence of inflow artery stenosis or the fistula vein at low blood flow in the arteriovenous fistula, the search should be continued in order to identify the subclavian and internal jugular vein stenosis [27, 33]. According to the literature, the frequency of central stenosis is from 5 to 20 %. Their most frequent cause is previous vein catheterization [4, 33]. Timely diagnosis of ipsilateral stenosis of the subclavian and internal jugular veins, as well as the distal portions of the cephalica or basilica veins during the preoperative stage, is of particular importance to reduce the risk of vascular access dysfunction [4].

#### V. ARTERIOVENOUS FISTULA THROMBOSIS

A decrease in the fistula access flow as a result of stenosis leads to the blood clots formation [6, 11, 12, 32]. According to different authors, arteriovenous fistula thrombosis occurs in 70–95 % of cases, and fistula stenosis is found in 85 % of thrombosed accesses. Other causes of thrombosis are a violation of the rheological properties of blood associated with an increase in uremic toxins in patients with chronic kidney disease, as well as low systemic blood pressure and permanent vessel injury due to repeated punctures in the local area [2, 29]. It has been established that to reduce blood clots formation, a fistula with an outflow vein length sufficient for punctures – at least 30–35 cm is required [7]. Studies have shown that the risk of thrombosis is significantly reduced with minimum access flow in the fistula of about 580 ml/min [20]. In addition to visualizing thrombotic masses in the vessel lumen, ultrasound criteria for arteriovenous fistula thrombosis include the absence of vein compressibility and impaired blood flow phasicity during breathing [8].

Another risk factor for arteriovenous fistula thrombosis is the aneurysmal dilation of the fistula vein. Its formation is facilitated by numerous punctures, localization in the area of fusion with the inflow veins, in the valve apparatus area, as well as in the rigid zones formed as a result of previous surgical interventions or catheterizations [4, 10, 14]. The turbulent nature of the blood flow in the aneurysm leads to the settling of platelets on the endothelium in places with low

blood flow rates with subsequent agglutination and activation of the fibrin coagulation process [10].

#### VI. HAND ISCHEMIA

Another complication of the arteriovenous fistula functioning is hand ischemia. The frequency of the complication is from 5 to 20 %, and the incidence of hand ischemia without obvious clinical manifestations is from 67 to 95 % [2, 5, 8]. The question of what factors lead to its development is controversial. Among the most frequently indicated reasons for the hand ischemia formation are: high access flow in the fistula (more than 750–1900 ml/min), retrograde blood flow in the distal part of the inflow artery, stenotic lesion of the inflow vessel, and peripheral artery disease [2, 4–8, 27]. However, studies have shown that not all patients with large volumetric discharges by fistula or inflow artery stenosis have hand ischemia. The isolated presence of retrograde blood flow in the artery distal to the fistula, which occurs in 80–90 % of patients, does not lead to the hand ischemia [2, 4–6]. The discharge of blood from the artery directly into the vein, bypassing the microvasculature of the hand, high blood flow in the fistula, the narrowing of the inflow artery normally leads to an increase in heart rate, cardiac output, access flow in the ulnar artery and to the development of collateral branches in the forearm to compensate for blood flow deficit in hand [6]. It has been proven that patients suffering from diabetes are more likely to develop hand ischemia as a result of disruption of the blood flow autoregulation mechanisms against the background of microangiopathy [5–7, 18, 33]. Thus, the hand ischemia is a multifactorial pathology, the forearm arteries condition that are not involved in the arteriovenous fistula formation, the hand microvasculature and the violation of the compensatory mechanisms of blood flow regulation play a decisive role in its development [3, 8].

#### VII. CONCLUSION

The topicality of the problem of hemodialysis replacement therapy is stipulated both with the increase in the number of patients on hemodialysis and the high incidence of vascular access complications. The duration and quality of life of patients depend on many factors, the most important of which is the efficiency of arteriovenous fistula functioning for hemodialysis. Various approaches to ultrasound assessment of its maturation, normal functioning and diagnosis of complications have been given. It has been established that during the formation of an anastomosis with a size of about 75 % of the artery diameter, the blood flow in the arteriovenous fistula increases and conditions for its normal maturation are created, and when the anastomosis diameter is about 20 % of the inflow artery diameter, fistula does not mature. It is believed that the minimum outflow vein diameter, suitable for puncture and adequate hemodialysis, is 4–6 mm with a depth of no more than 5–6 mm. In the literature, there is no consensus about the optimal value of the access flow in the arteriovenous fistula, and the figures vary significantly among different authors (from 350 to 2000 ml/min). The criteria for significant stenosis of vessels forming arteriovenous fistula are: the diameter of the vein free lumen in the stenotic zone less than 2.7 mm, the decrease of access flow distal to the

stenosis to less than 500 ml/min, the ratio of the maximum linear velocity in the place of stenosis and in the proximal part more than 2:1 (for stenosis of the anastomotic zone 3:1 and more). The main factors for the occurrence of arteriovenous fistula thrombosis are considered to be a disorder of the rheological properties of blood, a decrease in systemic arterial pressure, a permanent trauma of the vessel due to repeated punctures in the local area, dilation of the outflow vein and a decrease in access flow. The frequency of hand ischemia is from 5 to 20 %. Among the reasons for the formation of hand ischemia, high blood flow in the fistula, stenosis of the inflow artery, damage to the forearm arteries not involved in the formation of arteriovenous fistula, and the hand microvasculature, as well as disorder of the compensatory mechanisms of blood flow autoregulation are of major importance. Thus, regular duplex ultrasound performing allows detecting the arteriovenous fistula complications and makes it possible to carry out their timely correction.

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