The Predictive Significance of Doppler Parameters on the Arteriovenous Fistula Maturation for Hemodialysis—A Single Center Experience

Abstract

Background: Doppler ultrasound examination of blood vessels has a significant role in planning and identifying parameters that affect the functioning and maturation of arteriovenous fistula (AVF). Our goal was to determine the predictive parameters of Doppler ultrasound, measured at different time distances, which affect the maturation of AVF for hemodialysis. **Materials and Methods:** The research was a retrospective cohort study. The criteria for selecting patients in our study was the existence of information on ultrasound examinations of the lumen of blood vessels before the creation of AVF, as well as lumens of fistula conduits and blood flow measurements, at time intervals of 6–8 weeks and 2–4 months, after the creation of AVF, which we recorded in 105 patients. The respondents were divided into two groups: a group of patients with immature, and mature fistulas. Basic demographic data, clinical characteristics of the responders and laboratory parameters were analyzed. **Results:** By comparing clinical and laboratory parameters between the group of subjects with and without AVF maturation, a statistically significant difference was determined between the lumen of the proximal radial vein ($p = 0.008$) and the lumen of the distal radial vein ($p = 0.001$). The diameter of the fistulous veins ($p = 0.037$), and the blood flow through the AVF 6–8 weeks ($p = 0.001$) and 2–4 months ($p = 0.001$) after its creation were statistically significantly higher in subjects with mature fistulas. By univariate regression analysis, brachial vein ($p = 0.04$), proximal ($p = 0.011$) and distal radial artery ($p = 0.001$), fistula vein, after 6–8 weeks ($p = 0.002$), blood flow through AVF 6–8 weeks ($p = 0.001$) and 2–4 months ($p = 0.001$) after AVF creation, are statistically significant parameters. Predictive parameters of AVF maturation are AVF blood flow after 6–8 weeks ($p = 0.010$) and AVF blood flow after 2–4 months ($p = 0.001$). **Conclusion:** Our research confirmed that greater the blood flow through AVF, at time intervals of 6–8 weeks and 2–4 months after creation, the better the maturation.

Keywords: *Hemodialysis, Arteriovenous fistula, Functionality, Ultrasound examination, Doppler parameters*

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Introduction

The global incidence of chronic kidney disease is increasing, with an estimated prevalence rate of 8%–16%. About 1.5 million patients with end-stage renal disease worldwide use hemodialysis as a kidney replacement therapy. The National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI) suggests the use of arteriovenous fistula (AVF) wherever possible because of its cost-effectiveness and practicality, lower complication rate, long-term durability, and high patency rate, which improve patient's quality of life and survival rates.[1]

In case of AVF, the most recent studies have shown one- and two-year patency rates of 60% and 51%.[2] Data from the dialysis outcomes and practice patterns study (DOPPS) show that the patency of AVF is relatively high in Europe (83%), while in the United Kingdom, it is only 68%.[3] Age, hemoglobin, hematocrit, and calcium–phosphorus products were shown to be independent factors associated with late AVF failure in hemodialysis patients.[4] There is a growing problem with the outcome of AVF for hemodialysis, in elderly hemodialysis patients.[5] In such a trend, Doppler ultrasound examination of blood vessels used to create AVF, plays

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a significant role, providing useful information in the the identification of parameters of dysfunction and maturation of AVF.[6]

The 2019 updated NKF KDOQI guidelines recommend selective preoperative ultrasound, only in patients at high risk of failure. On the other hand, the 2017 Spanish access guidelines recommend routine preoperative ultrasound mapping of blood vessels in all patients.[7-9]

Our research aimed to indicate our experiences regarding the determination of predictive parameters of Doppler ultrasound, measured at different time intervals, on the outcome of AVF for hemodialysis.

Materials and Methods

The research was organized at the Nephrology and Dialysis Clinic of the University Clinical Center Kragujevac, Serbia, as a retrospective cohort study that included data collection to identify predictive Doppler parameters of AVF functioning and maturation. In 15 years, AVF was performed in our clinic on 1202 patients. The largest number of AVFs in our study was created by the first author (nephrologist), who has decades of experience in creating AVFs.

We reviewed Doppler ultrasound data, preoperative, then 6–8 weeks and 2–4 months after the creation of AVF. Out of the total number of 1202 patients in whom AVF was created, 664 (55%) subjects did not have data on a Doppler ultrasound examination, while 538 (45%) subjects had at least one Doppler ultrasound examination (preoperatively or in the first 6–8 weeks or 2–4 months, after the creation of AVF). Of the 538 patients who had at least one Doppler ultrasound examination of blood vessels, 235 (43.7%) had only preoperative Doppler of blood vessels, 198 (36.8%) patients had a preoperative Doppler as well as after 6–8 weeks AVF creation, while 105 patients had done all three ultrasound examinations (preoperative, 6–8 weeks and 2–4 months after AVF creation).

The criterion for selecting patients in our study is the existence of data on three ultrasound examinations (preoperative measurement of the lumen of blood vessels, measurement of the lumen of the vein fistula and blood flow, in time intervals of 6–8 weeks and 2–4 months, after creation of AVF).

An ultrasound examination was performed on a Shimadzu SDU-2200, Tokyo, Japan, using Doppler B mode ultrasonography and a 7.5 MHz resolution probe. Our target group was patients who had all three planned Doppler findings.

A trained nephrologist from our center performed all Doppler ultrasound examinations.

The pre-operative protocol of ultrasound examination of blood vessels for the creation of AVF for hemodialysis is representative of the routine work-up at the study institution. According to the clinical guidelines, an arterial and venous measurement location was selected in both the forearm and upper arm. The protocol consisted of complete scanning of the veins (cephalic in the forearm and upper arm, median cubital, basilic in the upper arm, and subclavian) for continuity, and diameters measured. After that, the arteries (subclavian, brachial, radial, and ulnar) were assessed for any stenoses, including diameter and flow measurements, halfway between the radial styloid process and elbow crease or upper arm.[10] Unfortunately, we have no data regarding the use of surgical and endovascular interventions to promote and maintain AVF patency.

We analyzed the demographic and gender characteristics of the patients, etiological cause of renal failure, fistula location (radiocephalic, radiobasilic, or brachiocephalic), type of AVFs concerning the time of creation (before or after starting hemodialysis treatment), type of anastomosis (end-to-side or end-to-end), information about site catheter insertion for hemodialysis, systolic and diastolic components of blood pressure, mean arterial blood pressure and data on the fistula functioning (maturation). In all respondents, the lumen of the artery and vein was measured intraoperatively for the creation of AVF. Doppler ultrasound measured, in addition, the diameter of arteries and their access veins and of blood flow through the AVF.

Of the laboratory variables, we analyzed the parameters that are routinely controlled in our institution for hospitalized patients and which, according to our experience, could affect AVF maturation. Laboratory variables represent the mean values of total biochemical parameters that were recorded in time frames defined by the criteria of this study.

The study was approved by the ethics committee of the Clinical Center Kragujevac, by the Helsinki Declaration for Medical Research. Institutional Review Board approval was obtained, and the study was given authorization to waive the consent of the patients, given its retrospective nature.

Statistical methods

The data were analyzed using SPSS for Windows, version 19. Measures of central tendency and variability, as well as relative numbers were used to describe the variables. Differences in the investigated parameters were assessed using the Chi-square test and t-test. To examine associations between independent variables of interest and AVF maturation, we performed a logistic regression analysis of factors associated with AVF maturation.

To avoid the risk of over-adjustments,to find spuriously low correlations, and maintain adequate power, we tended to follow the one-in-ten statistical rule that explains how many predictors per participant number can be estimated from the data when doing regression analysis and therefore we created models in which we included parameters that are similar in terms of the characteristics they describe in the studied population ("Clinical and laboratory characteristics of patients", "Doppler before placement of AVF", "Doppler 6-8 weeks after AVF placement" and "Doppler 2–4 months after AVF placement"), and only if they showed a significant association in the univariate regression analysis with the outcome variable.

Results

Table 1 shows the correlation of sociodemographic, clinical and laboratory characteristics of the subjects, which represent the aggregate mean values of the biochemical

Table 1: Respondents' characteristics, comparison of the investigated demographic, clinical and laboratory parameters of the group of patients with and without maturation AVF

Variables		Maturation AVF	Immature AVF	p-value
		Mean ± SD	Mean ± SD	
Age		58.78 ± 9.38	57.09 ± 11.91	0.59
Gender N (%)	Male	39 (70.9)	28 (56)	0.11
	Female	16 (29.1)	22 (44)	
Etiology of end-stage kidney disease N (%)	Diabetes mellitus	7 (12.7)	10 (20)	0.33
	Hypertensive nephropathy	19 (34.5)	13 (26)	
	Polycystic kidneys	10 (18.2)	6 (12)	
	Tubulointerstitial disease	3 (5.5)	6 (12)	
	Glomerular disease	0 (0.0)	2 (4)	
	Others	16 (29.1)	13 (26)	
RBC		3.19 ± 0.47	3.46 ± 1.82	0.91
WBC		7.48 ± 1.92	7.94 ± 2.59	0.60
HGB		97.11 ± 15.83	94.95 ± 15.13	0.60
PLT		231.54 ± 92.18	241.53 ± 96.7	0.43
Protein electrophoresis		66.79 ± 10.16	64.49 ± 8.57	0.39
Albumin (g/L)		36.30 ± 5.92	34.49 ± 6.2	0.26
Glucose (mmol/L)		5.90 ± 1.80	5.80 ± 1.7	0.69
Urea (mmol/L)		26.91 ± 9.67	25.26 ± 10.48	0.24
Creatinine (mmol/L)		665.67 ± 252.62	631.81 ± 342.9	0.18
Uric acid		448.21 ± 165.26	427.68 ± 143.4	0.43
ALP		88.47 ± 38.22	94.06 ± 42.4	0.91
K		4.90 ± 0.84	4.95 ± 0.83	0.69
Ca		2.11 ± 0.27	2.16 ± 0.19	0.89
Systolic blood pressure (mmHg)		152.47 ± 19.56	150.97 ± 26.65	0.74
Diastolic blood pressure (mmHg)		86.70 ± 13.71	85.72 ± 14.73	0.93
Mean blood pressure (mmHg)		112.47 ± 18.91	110.89 ± 22.83	0.72
Cholesterol		5.04 ± 1.67	4.87 ± 1.59	0.77
Triglyceride (mmol/L)		2.15 ± 1.43	1.94 ± 1.01	0.96
HDL (mmol/L)		1.10 ± 0.28	1.07 ± 0.43	0.24
LDL (mmol/L)		3.67 ± 1.69	2.78 ± 1.61	0.15
Location of AVF N (%)	Distal	24 (43.6)	20 (40)	0.76
	Proximal	31 (56.4)	30 (60)	
Type of anastomosis N (%)	T-L	43 (78.2)	42 (84)	0.45
	T-T	12 (21.8)	8 (16)	
Catheter insertion site N (%)	Jugular vein	19 (34.5)	22 (44)	0.32
	Femoral vein	36 (65.5)	28 (56)	
Type of AVF N (%)	Before starting HD	20 (36.4)	20 (40)	0.70
	After starting HD	35 (63.6)	30 (60)	

AVF: Arteriovenous fistula; ESR: Erythrocyte; RBC: Red blood cell; WBC: White blood cell; HGB: Hemoglobin; PLT: Platelet count; Alb: Albumin; Glu: Glucose; Cr: Creatinine; ALP:Alkaline phosphatase; K: Potassium; Ca: Calcium; Trig: Triglycerides; HDL: High density lipoprotein; LDL: Low density lipoprotein; AVF: Arteriovenous fistula; T-L: Termino-lateral; T-T: Termino-terminal; HD: Hemodialysis.

parameters recorded during the time frames of this study. Our results did not establish statistically significant differences, concerning the examined variables.

The cephalic vein, in the group of patients with functional fistulas, had a statistically significant larger lumen (2.74 ± 0.56 mm), compared to the group of patients with immature fistulas (2.30 ± 0.37 mm); (p = 0.008). The distal radial artery had a statistically significant (p = 0.001) higher mean value (2.12 ± 0.2 mm) in the group of patients who had maturation fistulas compared to the group of patients with maturation fistulas (1.93 ± 0.29 mm) [Table 2].

Patients with maturation AVF, 6–8 weeks after its creation, had a statistically significant larger fistula vein lumen, compared to the group of respondents, who did not have maturation fistulas (6.03 ± 1.82 vs. 5.24 ± 1.88 mm; p = 0.037). Higher blood flow through the AVF was registered in the group of patients with a functional AVF in both controlled time intervals, 6–8 weeks (684.4 ± 354.6 vs. 355.1 ± 269.6 mL/min; p = 0.001) and 2–4 months (834.91 ± 271.6 vs. 302.9 ± 158.5 mL/min; p = 0.001) after AVF creation [Table 3].

In univariate analysis, smaller volumes of brachial vein (p = 0.040), larger volumes of the proximal radial vein (p = 0.011) and distal radial artery (p = 0.001), before the fistula creation, a larger vein fistula (p = 0.002) and higher flow through the AVF (p = 0.001) at 6–8 weeks, as well as higher flow through the AVF 2–4 months (p = 0.001) after its creation are predictive parameters of AVF maturation. The data representing the univariate analysis of the investigated variables are shown in Supplementary Table 1.

Multivariable statistical analysis showed that greater volume of the proximal radial vein (p = 0.050), and blood flow through the AVF at 6–8 weeks (p = 0.001) and 2–4 months (p = 0.001) after the creation of the anastomosis, were predictive parameters of AVF maturation. Data having statistically significant values by univariate analysis were analyzed by multivariate analysis and the results are presented in Supplementary Table 2.

Discussion

The use of Doppler ultrasound by physicians performing vascular access surgery has increased the number of cases in which AVF can be created with native vessels.[11,12] According to the recently published Guidelines of the European Association for Vascular Surgery on Vascular Access, preoperative Doppler ultrasound mapping is recommended for all patients planning AVF based on the results of randomized controlled trials and meta-analyses that give Doppler ultrasound strength of recommendation class I and the highest level of evidence — A.[13-15] Unfortunately, many hemodialysis centers are neither equipped nor trained for this procedure. In 15 years, 1202 AVFs were performed in the Hemodialysis Center,

Table 2: Doppler characteristics of blood vessels before placement of AVF

Variables	Maturation AVF	Immature AVF	p value
	Mean ± SD	Mean ± SD	
Intraoperative vein diameter (mm)	2.37 ± 0.53	2.50 ± 0.52	0.35
Intraoperative artery diameter (mm)	2.58 ± 0.69	2.52 ± 0.48	0.81
Brachial artery (mm)	4.26 ± 0.41	4.29 ± 0.88	0.92
Brachial vein (mm)	3.73 ± 0.54	3.28 ± 0.64	0.07
Proximal radial artery (mm)	3.35 ± 0.59	2.98 ± 0.64	0.10
Proximal radial vein (mm)	2.74 ± 0.56	2.30 ± 0.37	0.008*
Peak systolic velocity cm/s	50.38 ± 21.15	53.64 ± 25.25	0.95
The middle third of the radial artery (mm)	2.34 ± 0.32	2.21 ± 0.31	0.21
The middle third of the saphenous vein (mm)	2.10 ± 0.33	1.89 ± 0.20	0.062
Distal radial artery (mm)	2.12 ± 0.20	1.93 ± 0.29	0.001*
Distal saphenous vein (mm)	2.02 ± 0.33	1.70 ± 0.48	0.10

AVF: Arteriovenous fistula; *statistically significant value.

Table 3: Doppler characteristics versus time-distance after AVF placement

Variables	Maturation AVF	Immature AVF	p value
	Mean ± SD	Mean ± SD	
Fistula vein (mm) after 6-8 weeks	6.03 ± 1.82	5.24 ± 1.88	0.037*
Lumen of the accessory branch of the fistula vein (mm) after 6-8 weeks	5.50 ± 2.06	4.41 ± 1.05	0.134
Flow (ml) after 6-8 weeks	684.44 ± 354.62	355.10 ± 269.64	0.001*
Flow (ml) after 2-4 months	834.91 ± 271.60	302.95 ± 158.52	0.001*

AVF: Arteriovenous fistula; *statistically significant value.

Nephrology Clinic and University Clinical Center Kragujevac. Of these, 538 (45%) patients underwent at least one ultrasound examination of blood vessels to create AVF.

The one-year patency level and maturation of radiocephalic AVF are similar for men and women, while the ratio of the relationship between AVF success rate and age is unclear and no definitive conclusions can be drawn.[13] The results of our study did not establish that gender and age are significantly related to AVF maturation. The median age of our respondents is 58 years, slightly younger than usually reported in other studies, and therefore difficult to compare with other studies.

Autogenous AVF maturation was defined as access use for effective dialysis using 2 needles for 75% or more of the dialysis sessions over 4 weeks.[16] If they did not meet this criterion, they were considered non-mature. The start of hemodialysis on time, through mature and functional vascular access, results in a successful outcome in treating patients with chronic kidney disease.[17] However, a randomized controlled trial of early versus late initiation of dialysis showed no difference in survival or clinical outcomes between early (GFR $>$ 10 mL/min at 1.73 m^2) and late initiation of hemodialysis (GFR $<$ 10 mL/min at 1.73 m^2).[11,18] Slightly more than half of our respondents (52.4%) had a fistula created before hemodialysis, which is not by the recommendations and findings that have been stated. We suspect that, partly due to the late referral of the patient to a nephrologist, or due to retrospective data collection, some data were lost or not adequately displayed in the patient's medical records.

Maturation begins with the formation of the anastomosis. It is followed by vascular remodeling that includes an increase in diameter and arterial and venous blood flow, allowing repeated venipuncture and a sufficient flow rate for adequate hemodialysis.[19] All vascular modifications occur rapidly within four weeks after AVF creation and then slow down over the next two months. This indicated that testing for AVF maturity could begin at least four weeks after its creation.[20,21] To provide the flow of 350–500 mL/min required for dialysis, the blood flow in the fistula should be at least 250–350 mL greater than the dialysis flow to prevent recirculation. Thus, the minimum flow rate of the autologous fistula is 500 mL/min to prevent the collapse of the cannulation segment during dialysis. Most fistulas that function well have a flow rate in the range of 800–1500 mL/min.[13] Recorded blood flow through AVFs in our study, both after 6–8 weeks (684 mL/min) and after 2–4 months (834.9 mL/min), had statistically significant higher values, in patients with functional fistulas. Likewise, the statistical model of multiple regression determined that the blood flow through the AVF is a significant predictive factor of the functionality of the fistula, regardless of the time distance when it was verified, which shows the importance of this Doppler parameter for the function and maturation of the AVF.

The detailed and precise preoperative and postoperative vascular Doppler ultrasound evaluation contributes to a better understanding of the parameters for increased functional maturation rate.[22] In fact, postoperative Doppler ultrasound evaluation may become the critical strategy for maintaining and improving the functional maturation rate of AVF.[23] Our results [Supplementary Tables 1 and 2] are similar to the previous study.[22,23] They showed that apart from the venous diameter, blood flow through the AVF, 6–8 weeks and 2–4 months after the creation of AVF, also influenced the functional maturation rate of AVF.

The lumen of the artery and vein is another nonmodifiable parameter influencing AVF maturation. There are different perspectives on the correlation between arterial lumen and AVF functionality. Therefore, indicating an ideal threshold for the diameter of the radial artery is inappropriate: the likelihood of AVF patency and survival increases with the diameter of the artery used to create the fistula.[11,24] Our results showed that the lumen of the radial artery was significantly larger in patients with functional AVFs. However, the multivariate logistic analysis did not confirm the predictive significance of the arterial lumen for the maturation of the AVF, regardless of the time interval of the ultrasound examination.

Maturation AVF requires sufficient enlargement of the fistula vein lumen, which is thought to be induced by the increased blood flow acutely by 5–10 times due to directly shunting arterial blood to the vein and accompanying hemodynamic parameters.[25] The diameter of the fistula vein can also increase rapidly 4–8 weeks after fistula creation. There is a high degree of correlation between AVF flow velocity and venous diameter, indicating that flow is the primary determinant of final venous diameter,[11,26-28] but, there is still no scientifically documented data on the minimum diameter of veins,[29] which would indicate a successful AVF maturation. The results of our study determined a statistically significantly larger lumen of the vein, which was used for anastomosis in patients who had maturation fistulas, compared to the group of respondents who had immature fistulas. However, the multiple regression statistical model did not confirm the predictive significance of the lumen of the vein for the maturation of the AVF.

As limiting factors in our research, we can mention the retrospective methodology of the study, which may introduce inherent weaknesses in its design, due to the possibility of confounding and bias. Likewise, we presented our own experiences, which are based on the practical work of one center, so perhaps, the results of our research cannot be generalized to other centers.

The results of our research confirmed the predictive significance of blood flow through the AVF at time intervals of 6–8 weeks and 2–4 months after creation, that is, greater the blood flow, the better is the maturation of AVF.

Conflicts of interest

There are no conflicts of interest.

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