

Are There Differences in Arteriovenous Fistulae Created for Hemodialysis between Nephrologists and Vascular Surgeons?

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Significance of the Study

- There is an insufficient number of vascular surgeons and inadequate training for creation of vascular access.
- This requires that an increasing number of nephrologists are involved in forming the vascular access.
- This study shows better results of the nephrologist in terms of better outcomes of arteriovenous fistulas compared to vascular surgeons.
- Thus, there is a need for greater involvement of nephrologists in creating vascular access.

Keywords

Arteriovenous fistulae · Nephrologists · Vascular surgeons · Risk factors

Abstract

Objective: Many studies have reported insufficient support from surgical services, resulting in nephrologists creating arteriovenous fistulas in many centers. The aim of this study was to compare risk factors of arteriovenous fistula dysfunction in patients whose fistulas were created by nephrologists versus vascular surgeons. **Methods:** This was a retrospective, analytical study of interventions by nephrologists and vascular surgeons during a period of 15 years. Out of a total of 1,048 fistulas, 764 (72.9%) were created by nephrologists patients, while vascular surgeons were responsible for 284 (27.1%) fis-

tulae. Laboratory, demographic, and clinical parameters which might affect functioning of these arteriovenous fistulae were analyzed. **Results:** Patients whose arteriovenous fistula was formed by nephrologists differed significantly from those created by vascular surgeons in relation to the preventive character of the arteriovenous fistula ($p = 0.011$), lumen of the vein ($p < 0.001$) and systolic blood pressure ($p = 0.047$). Multivariate logistic regression of arteriovenous fistula dysfunction showed that risk factors were female gender (odds ratio [OR] = 1.56, 95% CI 1.16–2.07), whether the fistulae were created by vascular surgeons or nephrologists (OR = 1.38; 95% CI 1.01–1.89) and the site of the arteriovenous fistula (OR = 0.64; 95% CI 0.48–0.85). **Conclusions:** Arteriovenous fistulae created by vascular surgeons, female gender, and the location are risk factors of dysfunction.

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Introduction

After the introduction of the Cimino-Brescia fistula, in the last few decades, the advent of prosthetic arteriovenous graft and central venous catheters has given physicians the opportunity to choose the most appropriate vascular access for hemodialysis patients. However, the native arteriovenous fistula remains the first choice for vascular access, especially because of the infectious and thrombotic complications more frequently associated with arteriovenous graft and central venous catheters [1, 2].

By 2030, the number of patients with terminal renal failure is expected to increase from 2.6 million to 5.5 million. Financial costs for the care and treatment of patients with terminal renal failure increased to above USD 34 billion in 2011. An arteriovenous fistula is still the best vascular access option that balances medical and economic challenges [3]. Thus, there is general agreement that an arteriovenous fistula is the recommended vascular access for patients with end stage kidney diseases, and all guidelines propose this whenever possible, before initiating dialysis treatment. Vascular access is just one example of the paradox between patient-centered care and population-based quality measures [4].

Creating a permanent vascular access is a significant step in managing the clinical progression of CKDs. It involves early referral to a nephrologist and vascular surgeon to allow sufficient time to plan and create the access and enable it to mature [5]. This should be performed by a vascular surgeon, but the procedure is also carried out by other specialists (urologists, general, and cardiovascular surgeons). Unfortunately, many studies have confirmed insufficient support from surgical services, which is why nephrologists in many centers began to create arteriovenous fistulas themselves [6].

Historically, nephrologists have taken a leading role in the development and application of innovations in terms of vascular access, but, in practice, surgeons and radiologists are doctors who usually perform all the procedures associated with vascular access, and it is assumed that they make the majority of decisions [7]. However, an insufficient number of vascular surgeons and inadequate training for this surgical procedure can lead to “congestion” in the nephrological department. Therefore, an increasing number of nephrologists are involved in forming the vascular access, especially in Central European countries (Italy, Germany, Poland, and Slovenia) [8], as well as in North Macedonia and Serbia. The aim of this study was to determine differ-

ences and risk factors of arteriovenous fistula dysfunction in patients whose fistulas were created by a nephrologist or a vascular surgeon.

Subjects and Methods

The retrospective, analytical study was conducted at the Center for Nephrology and Dialysis, Urology and Nephrology Clinical Center, Kragujevac, Serbia. It included all surgical interventions carried out for the purpose of creating an arteriovenous fistula for hemodialysis over a period of 15 years. Arteriovenous fistulas were created in the distal and proximal part of the forearm. Among the total number of 1,048 surgical interventions, 671 (64%) were done in men and 377 (36%) in women. For all 764 (72.9%) respondents whose fistula was created by a nephrologist, the operation was performed by the first author. Several vascular surgeons created the fistula in another group of 284 (27.1%) patients.

A minimum criterion for successful use of a fistula for conventional hemodialysis is 2-needle cannulation for 2/3 runs within a month at an average blood flow rate (total blood processed over duration of hemodialysis) of 300 mL/min in a 3.5-h hemodialysis session [9]. If the fistula cannot meet these requirements, it is considered dysfunctional.

From the risk factors for fistula functioning, we evaluated the following parameters: the gender and demography, fistula positioning (fistulas were created in the distal or proximal part of the forearm), time of fistula function, use of central venous catheters for hemodialysis, preoperative ultrasound mapping of blood vessels, preventive formation of a fistula, diameters of arteries and veins used for anastomosis, and values of systolic and diastolic arterial blood pressure. The preferred rule for formation of arteriovenous fistula is to start distally and move proximally in the non-dominant arm, which we adhered to. The technique of surgical creation of an arteriovenous fistula involved end-to-side or end-to-end anastomosis and was a matter of choice. All the risk factors for the functioning of the arteriovenous fistula were estimated in relation to the data about who had created the arteriovenous fistula. As all participants in the study were from 1 dialysis center, they were controlled all the time, from the moment the fistula was created, to its dysfunction.

Blood samples for biochemical tests were obtained in Vacutainer® tubes, in the middle of the week before dialysis. Plasma samples were stored at -20°C. Biochemical analyses were made using the flow cytometric method (Beckman Coulter Inc., Fullerton, CA, USA) or spectrophotometrically on an ILAB-600 instrument (Diamond Diagnostics-333 Fiske Street Holliston, MA, USA) using original reagents. Biochemical parameters represent average values of laboratory tests, in the last year, before fistula dysfunction was noted.

Statistical Analysis

Descriptive statistical methods were used as measures of central tendency, variability, and relative numbers. Statistical hypotheses were tested using the *t*-test, Mann-Whitney test, and χ^2 test. Logistic regression was employed to analyze the relationship between binary outcomes and potential risk factors. *p* values <0.05 were considered significant.

Table 1. Basic demographic, clinical, and biochemical characteristics of the study patients

Variable	Values
Patients, <i>n</i>	1,048
Positioning of arteriovenous fistula, <i>n</i> (%)	
Distal position	455 (43.4)
Proximal position	593 (56.6)
Functioning time of arteriovenous fistula, median (range), months	15.5 (1.0–259.0)
Central venous catheter insertion, yes/no, <i>n</i> (%)	506 (48.4)/540 (51.6)
Preoperative mapping of blood vessels (Doppler), yes/no, <i>n</i> (%)	502 (47.9)/546 (52.1)
Type of fistula in relation to the time of creation, <i>n</i> (%)	382 (36.5)/666 (63.5)
Vein diameter, mean ± SD, mm	2.3±0.4
Artery diameter, mean ± SD, mm	2.3±0.5
Systolic blood pressure, mean ± SD, mm Hg	148.3±25.6
Diastolic blood pressure, mean ± SD, mm Hg	82.6±14.8
Erythrocytes, mean ± SD, ×10 ¹² /L	3.2±0.5
Hemoglobin, mean ± SD, g/L	93.7±14.9
Platelets, mean ± SD, ×10 ⁹	220.6±78.2
Glycemia, mean ± SD, mmol/L	5.8±2.0
Albumin, mean ± SD, g/L	34.6±6.3
Cr, mean ± SD, μmol/L	641.0±236.6
Urea, mean ± SD, mmol/L	25.6±8.6
Cholesterol, mean ± SD, mmol/L	4.5±1.3
Triglycerides, mean ± SD, mmol/L	1.8±0.9
Fibrinogen, mean ± SD, g/L	5.0±1.5

Results

Table 1 shows the average values of biochemical, demographic and clinical parameters in all subjects. The group of subjects, whose arteriovenous fistula was created by the nephrologist differed significantly from the group of patients with arteriovenous fistulae created by vascular surgeons, in relation to the preventive character of the arteriovenous fistula ($p = 0.011$), lumen of the vein ($p < 0.001$), and systolic blood pressure ($p = 0.047$; Table 2).

Multivariate logistics analysis, with a dysfunctional arteriovenous fistula as the dependent variable, included those risk factors of arteriovenous fistula dysfunction that were statistically significant in the univariate logistic regression models at the probability level of 0.05, and which, based on previous research, are considered to be important for arteriovenous fistula dysfunction. The model contained the 6 risk factors listed in Table 3; all risk factors were statistically significant ($\chi^2 = 23.660$; $DF = 5$; $p = 0.001$). There was no significant multicollinearity between the risk factors. Statistically significant risk factors of arteriovenous fistula dysfunction, in the multivariate logistic regression model, were female gender ($B = 0.439$; $p = 0.003$), with an odds ratio (OR) of 1.56, arteriovenous fistula creation by vascular surgeon or ne-

phrologist ($B = 0.325$; $p = 0.041$; $OR = 1.38$), and location of the arteriovenous fistula ($B = -0.454$; $p = 0.002$; $OR = 0.64$) (Table 3).

Discussion

After the introduction of the Cimino-Brescia fistula, in the last few decades, the advent of prosthetic arteriovenous graft and central venous catheters has given physicians the opportunity to choose the most appropriate vascular access for hemodialysis patients. However, the native arteriovenous fistula remains the first choice for vascular access, especially because of the infectious and thrombotic complications more frequently associated with arteriovenous graft and central venous catheters [1, 2].

Central venous catheters are most commonly used for incident hemodialysis patients. But, catheters are associated with the greatest risk of adverse events, which include infection, catheter dysfunction from thrombosis, occlusion of a central vein, and inadequate blood flow leading to poor dialysis adequacy [10]. Almost 57% of our patients had a central venous catheter implanted during their treatment.

Table 2. Correlation of laboratory, demographic, and clinical characteristics of patients with an arteriovenous fistula, created by a nephrologist or vascular surgeon

Variable	Groups of respondents		p value
	arteriovenous fistula created by a nephrologist (n = 764/72.9%)	arteriovenous fistula created by a vascular surgeon (n = 284/27.1%)	
Age, mean ± SD, years	61.8±11.8	61.1±11.3	0.793
Gender, n/%			
Male	484/63.4	187/65.8	0.455
Female	280/36.6	97/34.2	
Position of arteriovenous fistula, n/%			
Distal position	323/42.3	132/46.5	0.223
Proximal position	441/57.7	152/53.5	
Functioning time of arteriovenous fistula, median (range), months	18.0 (1.0–252.0)	12.0 (1.0–259.0)	0.206
Central venous catheter insertion, n (%)	359 (47.1)	147 (51.9)	0.160
Preoperative mapping of blood vessels (Doppler), n (%)	362 (47.4)	140 (49.3)	0.582
Preventative creation of AVF, yes/no, n (%)	296 (38.7)/468 (61.3)	86 (30.3)/198 (69.7)	0.011*
Vein diameter, mean ± SD, mm	2.3±0.4	2.0±0.3	<0.001*
Artery diameter, mean ± SD, mm	2.3±0.5	2.2±0.4	0.189
Systolic blood pressure, mean ± SD, mm Hg	148.8±25.6	141.9±23.8	0.047*
Diastolic blood pressure, mean ± SD, mm Hg	82.6±14.8	82.0±14.5	0.776
Erythrocytes, mean±SD, ×10 ¹² /L	3.1±0.5	3.1±0.5	0.583
Hemoglobin, mean±SD, g/L	93.6±15.3	94.00±13.7	0.691
Platelets, mean±SD, ×10 ⁹	219.4±75.0	223.8±86.0	0.484
Glycemia, mmol/L, mean ± SD	5.8±1.9	5.8±2.0	0.690
Albumin, mean ± SD, g/L	34.7±6.2	34.0±6.6	0.118
Cr, mean ± SD, μmol/L	646.1±239.3	626.2±228.4	0.248
Urea, mean ± SD, mmol/L	25.7±8.8	25.4±8.1	0.614
Cholesterol, mean ± SD, mmol/L	4.5±1.3	4.6±1.4	0.142
Triglycerides, mean ± SD, mmol/L	1.8±0.9	1.9±0.9	0.295
Fibrinogen, mean ± SD, g/L	5.0±1.5	5.1±1.4	0.569

* Statistically significant.

Table 3. Multivariate logistic regression with dysfunctional arteriovenous fistula as the dependent variable

	B	p value	OR	95% CI	
				lower	upper
Gender	0.439	0.003*	1.56	1.16	2.07
Age	-0.003	0.666	0.99	0.98	1.01
Who created the arteriovenous fistula	0.325	0.041*	1.38	1.01	1.89
Arteriovenous fistula location	-0.454	0.002*	0.64	0.48	0.85
Preventative creation of AVF	-0.288	0.172	0.75	0.50	1.13
Central venous catheter	0.376	0.065	1.46	0.98	2.17

OR, odds ratio; B, regression coefficient; CI, confidence interval. * Statistically significant.

The normal hemostatic reaction is initiated by damage to the blood vessel wall and the exposure of sub-endothelial structures to blood flow, resulting in the formation of a thrombus [11]. Fibrinogen and other adhesive proteins bind causing platelets to aggregate. High levels of plasma fibrinogen may trigger thrombus formation in arteriovenous fistula [12]. Fibrinogen values in our study did not show a statistically significant value.

The risks incurred by “early” and “late” placement of fistula are not equal. Delaying placement of a fistula incurs the risk of starting hemodialysis with a catheter and all its substantial complications and costs, while early fistula placement incurs a rather modest increase in cumulative access procedures. The major health imperative in this population is trying to increase fistula use and reduce the number of catheters needed at dialysis initiation. Waiting for the optimal time for fistula placement incurs the risk of increasing the number of patients who start hemodialysis with a catheter [13]. All these parameters should be taken into account, if nephrologists agree to deal with the creation of vascular access, which indicates great caution on this job.

Arteriovenous fistulae are recommended by many national clinical guidelines for vascular access, but there is concern about whether these general guidelines also apply to the female population [14, 15]. Vernaglione et al. [16] found that arteriovenous fistulae may function poorly in women, with a failure rate of 50%. Inequality of gender distribution in published studies limits assessment of the possible influence of gender on the functioning of the arteriovenous fistula, which is why any correlation between gender and vascular access function remains controversial [17]. The proportion of women in our study groups was similar (Table 2). However, in the multivariate logistic regression model, statistically significant risk factors of dysfunction of the arteriovenous fistula included female gender, and we found that women have a 50% greater chance of arteriovenous fistula dysfunction.

It is important to evaluate whether nephrologists ought to be authorized to create arteriovenous fistulas for their patients. Experience shows that this should be considered favorably. García-Trío et al. [18] found no difference in the rate of functioning of the arteriovenous fistula, whether created by vascular surgeons or by nephrologists [17]. Therefore, nephrologists in many dialysis centers in Europe have begun to conduct this procedure [19]. It is currently believed that countries where nephrologists have a significant role in professional coordination, including involvement in the organization

of treatment, are achieving better results [7]. Yet, due to the lack of specific information in the literature that indicates the primary specificity of physicians creating vascular access, it is difficult to evaluate the experience of nephrologists, in relation to that of surgeons [20]. The inability for a nephrologist to make a timely decision on an adequate vascular access is often a cause for disappointments among medical professionals engaged in the treatment of patients with end stage kidney diseases. This is the reason why training nephrologists to create vascular access is being pursued in many nephrology centers. Data on the comparison of the efficacy of functional vascular access creation between nephrologists and vascular surgeons is almost nonexistent in the available literature.

In our study over a 15-year period, 72.9% of all arteriovenous fistulas were created by a nephrologist. The results showed that those created by vascular surgeons had a 38% greater chance of failure. The better results of the nephrologist in terms of fistula functionality in relation to vascular surgeons can be interpreted not only by insufficient motivation of vascular surgeons but also by more detailed preoperative examination of the blood vessels used to create the anastomosis. One can assume that most nephrologists perform a thorough clinical examination and radiological diagnosis to help identify the optimal location and quality of blood vessels for a successful anastomosis. The possible reasons behind the increased risk of fistula dysfunction among vascular surgeons may be attributable to surgeons being overloaded within their own surgical program, as well as insufficient training. Also, the possible reasons behind the increased risk of fistula dysfunction among vascular surgeons may be the lower number of procedures conducted by vascular surgeons compared to nephrologists.

However, the skill and experience of the surgeon is an important parameter that influences the success of the intervention. The risk of primary thrombosis of the arteriovenous fistula was 34% lower if it had been created by surgeons who had already created at least 25 fistulas previously [6]. The DOPPS study confirmed that in Australia, New Zealand, Germany, and Japan, 50–72% of patients with end-stage kidney diseases initiated hemodialysis with an arteriovenous fistula compared with 16% in the USA [5, 21–24]. The skill and experience of the nephrologist who created all the fistulas in our study are based on 30 years of experience with over 3,000 operative interventions in creating arteriovenous fistulae and resolving their complications. The vascular surgeons involved in the creation of fistulas in

this study also had many years of experience, with several dozen fistulas done individually. This speaks in favor of the cumulative experience of the operators who created fistulas for our patients. In our study, the overall rate of patients, who started hemodialysis with vascular access, was 36.4%. The rate of preventive fistulas created by the nephrologist was 38.7% and that for vascular surgeons was 30.2%, the difference between the groups being statistically significant. However, in the multivariate logistic regression model, the predictive significance of a preventive arteriovenous fistula was not confirmed.

The risk of thrombosis of the primary fistula is much greater for a fistula on the forearm than on the upper arm (20%). Upper arm fistulas have a greater chance of maturation, compared to a forearm fistula [4]. In Pescara (Italy), in 98% of cases, the vascular access was placed and examined by a nephrologist in an outpatient setting, among which 80.2% were distal and 10.6% proximal arteriovenous fistulae [20]. In our study, there were 42.3% distal and 57.7% proximal fistulae in the group of subjects operated on by the nephrologist. There were 46.5% distal and 53.5% proximal fistulas among the patients whose fistula was created by a vascular surgeon. The difference between the groups is not statistically significant, but in the multivariate logistic regression model, statistically significant risk factors of dysfunction of the arteriovenous fistula included the location of the arteriovenous fistula. Namely, proximal localization of the fistula had a 36% greater chance of dysfunction. Although certain dialysis regimens or hemodynamic parameters used during dialysis might influence fistula dysfunction, we did not consider these parameters; this could be a limiting data for our investigation.

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Conclusions

Arteriovenous fistulas, in our study, created by vascular surgeons are more likely to be dysfunctional than fistulas created by a nephrologist. The women in our study were more likely to have a dysfunctional fistula. Likewise, fistulas that are created in the proximal region of the forearm were less likely to function. The main result of our study indicates the need for greater involvement of nephrologists in creating vascular access, given the better outcomes of arteriovenous fistulas compared to vascular surgeons.

Statement of Ethics

All the enrolled patients provided written informed consent, and the study protocol was approved by the institutional review board. All study procedures were conducted according to the Declaration of Helsinki.

Conflict of Interest Statement

The authors declare that there are no conflicts of interest.

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Author Contributions

Radojica Stolic designed the protocol, reviewed the literature, analyzed the data, and critically reviewed and wrote the manuscript. Zoran Bukumiric analyzed the data and performed a statistical analysis of the data. Vekoslav Mitrovic, Maja Sipic, Biljana Krdzic, Goran Relic, Gordana Nikolic, Sasa Sovtic, and Naja Suljkovic participated in study design, read, and approved the final manuscript.

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