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ORIGINAL ARTICLE
VASCULAR ACCESS

Vascular access as a survival factor for the hemodialysis population: a retrospective study

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ABSTRACT

Background: The creation of vascular access is an essential condition for providing hemodialysis, which remains the only option for most patients suffering from end-stage renal disease. Selection of the type of vascular access affects patients' clinical outcomes, access maintenance frequency, risk of infection and major adverse cardiac events during dialysis. To improve the decision-making process, we performed a retrospective clinical data analysis of dialyzed patients and critically compared the survival rates between two types of vascular access applied during dialysis therapy during a 5 years follow-up period.

Methods: Using nationally representative data from 18 dialysis centers across Slovakia, we explore and compare survival rates of 960 adult patients undergoing hemodialysis using either a central venous catheter (CVC) or an arteriovenous fistula (AVF). Length of dialysis, protein malnutrition and comorbidities were examined as possible covariates that might influence survival rates.

Results: Chances of surviving for a one-year period were higher by 52% in AVF patients compared to CVC patients (HR 1.52; 95% CI 1.27-1.83; $P<0.001$) regardless of age, sex, nutritional status, time spent on dialysis and comorbidities. The presence of cardiac congestion (HR 1.26 [95% CI 1.06-1.50], $P<0.01$) and malnutrition (protein malnutrition: HR 0.98 [95% CI 0.96-1.00], $P<0.05$; lean tissue index: HR 0.79 [95% CI 0.67-0.93], $P<0.01$) decreases chances for survival.

Conclusions: A functional arteriovenous fistula is a significant predictor of survival in the population dependent on hemodialysis, independently of sociodemographic parameters and serious comorbidities. Therefore, if various types of vascular accesses are applicable for the patient, AVF should be prioritized over CVC.

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Key words: Vascular access devices; Renal dialysis; Survival rate.

Out of more than a half-million patients suffering from end-stage renal disease in Europe, 56% are being treated with hemodialysis, 5% are receiving peritoneal dialysis and 39% are living kidney transplants.[1] Based on the 2016 annual statistical report on nephrology care in the Slovak Republic, 4022 patients were treated with maintenance hemodialysis, 471 patients were included on the waiting schedule for transplantation and 115 patients were subjected to renal transplant.[2] Despite the fact that transplantation is the most effective therapy and each year more patients could be provided with this type of therapy (+3% each year), hemodialysis remains the only option for most patients.[1]

Hemodialysis therapy requires vascular access that ideally has both high blood flow in the feeding artery and low downstream resistance.[3] In the initiation of dialysis therapy and creation of vascular access, nephrologists need to carefully consider a multitude of factors, including the patient's clinical condition, demographics, comorbidities, anatomy and personal preferences.[4] There are three main alternatives for vascular access: a native arteriovenous fistula (AVF), a central venous catheter (CVC) and an arteriovenous graft. AVF and CVC are the most frequent types of vascular access used for dialyzed patients.[5] Based on clinical guidelines for hemodialysis therapy, AVF is recommended as the first choice of access for all patients receiving dialysis therapy. AVF is characterized with long functionality and less frequency of complications, revisions and hospital admissions due to infections or malfunction of access. However, AVF is a time-consuming procedure for the patient (requiring a maturation time of up to six weeks), requires operating theatre capacity and is accompanied by the risks of early thrombosis and non-maturation of vascular access after surgery. In contrast, CVC is fully functional for hemodialysis immediately after creation, with the majority of fluoroscopy-guided catheters inserted under local anesthetics in a day-case theatre. However, the creation of the CVC is accompanied by a higher risk of infection and bilateral central venous occlusive disease.[6, 7]

Both types of vascular access have several primary pros and cons, but to get a more objective perspective in their applications, we need to analyze the impact of access type on patient survival rates. Regardless of a patient's age, a comparison of survival rates between AVF and CVC in a cohort of 532 hemodialyzed patients showed that CVC use is associated with higher mortality and morbidity risk ratio than AVF.[8] Another registry-based study confirmed the superior survival conclusion for AVF access compared to CVC access.[9] Among elderly patients, implementation of "fistula first" needs to carefully considered the context of the patient's estimated life expectancy, the existing comorbidities and the likelihood of successful AVF maturation.[10] Analysis of differences in 1-year and 2-year survival among older patients did not confirm the expected differences between vascular access patient groups.[11] The differences in survival rates between access types also disappeared after correction for comorbidity data of patients.[12] Moreover, the overall primarily failure rate of AVF maturation is significantly higher in elderly patients with small vein diameter.[13, 14] Evidence from the literature on the effects of vascular access type on survival rates is inconclusive and requires further studies that include corrections for patients' age, sex, dialysis duration, nutritional data and comorbidities.

Therefore, using nationally representative data from 18 dialysis centers across the Slovak Republic, we explored the 54-months survival of adult patients undergoing hemodialysis using either a CVC or AVF. As the length of dialysis, malnutrition and other comorbidities (*e.g.* cardiac congestion, diabetes nephropathy) might strongly influence the survival, we considered them as well.

Materials and methods

Population

A retrospective cohort study was conducted on a nationally representative sample of adult patients (age ≥18 years), who have received long-term hemodialysis therapy provided by a network of 18 dialysis centers across Slovakia between August 2008 and January 2013 (N.=960). Only patients with the stated type and date of access placement of AVF or CVC and active clinical profile in the database were included in the data collection (N.=960). Patients with missing data were excluded from the data collection (N.=212). The sample of included patients (N.=748) consisted of 406 men (54%) and 342 women (46%). The median age of the sample was 63 years (IQR 54-73).

The study design protocol was reviewed and approved by the Ethics Committee of Fresenius Medical Care Slovakia on 26 October 2012 (Approval number: F/26102012). The methodology of patients' data registration was approved by the ethics committee and the research was conducted according to the principles expressed in the Declaration of Helsinki. In the case of anonymous population-based medical registries, Slovak regulations do not require a participant's written or verbal informed consent. The patients of nephrology clinics were informed about the procedure of registration and anonymization during data collection and recording of medical databases and about the availability and rules of data accessibility. The only exclusion criterion in the study was a patient's disagreement with participation in the study.

Clinical data collection

All adult patients registered in the medical database of the nephrology clinics were screened for the availability of data about vascular access type applied at dialysis initiation, date of access placement and active clinical profile. Demographic data at the time of starting dialysis, etiology of renal disease, initial vascular access type (AVF or CVC), dialysis duration, serum albumin concentration, comorbidities (cardiac congestion, diabetic nephropathy) and cause of death (where appropriate) were extracted and registered from medical databases administered by dialysis center clinicians. Clinical data registered in medical databases did not contain information about the history of changes in vascular access type after the creation of the initial vascular access. Therefore, this information is missing from our database.

Assessment of a patient's body composition and hydration status was done using the Body Composition Monitor (BCM, Fresenius Medical Care, Germany). The BCM is a validated diagnostic tool that uses various objective measurements, such as body plethysmography and dual-energy RTG absorption, for quantification of fluid status (hydration status, total body water)[15] and assessment of body composition (lean tissue index, fat tissue index).[16] BCM monitoring outputs have been validated against standard assessment methods of body fluid status and body composition in hemodialyzed patients.[17-19] Assessments made by BCM were typically done for each patient one time per month, before the start of dialysis, with the patient in a supine position. The assessment procedure was performed and supervised by the trained medical staff of the dialysis center. Patient malnutrition was indicated if the lean tissue index dropped below 10% of the normal value.

Survival data were collected and analyzed among patients at the point of commencing dialysis and death (if occurred) from August 2008 up to January 2013.

Statistical analysis

Patient characteristics were described and statistically compared between the two groups defined by the type of vascular access (AVF patient group *vs.* CVC patient group). Continuous variables are expressed as means, medians, interquartile ranges and standard deviations. Categorical variables are expressed as percentages of the total study population. For comparing the two groups, a Mann–Whitney U-Test for continuous and a χ^2 test for categorical variables were used. Survival rates were analyzed using the Kaplan-Meier method. The independent variables in the stratified Cox regression model were all variables with a level of significance set at P<0.1 in the Mann-Whitney U-Test and the χ^2 test, as appropriate. Cox regression was used to control for age, gender, protein malnutrition, duration of dialysis and selected comorbidities. P values less than 0.05 were accepted as statistically significant. All data analyses were carried out using the statistical software package IBM SPSS 22.0 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.).

Results

A total of 960 patients were screened for inclusive and exclusive criteria, from which 748 (response rate 77.9%) were included in the data extraction and statistical analysis. The median time of observation was 17 months (IQR 10-33 months) and the longest period of observation was 54 months. The patients' gender, age and clinical characteristics are summarized in Table I. During 54-months follow-up, 107 patients died (Figure 1). We found a higher application of AVF among the patients followed in our study (AVF=478, 63.9% *vs.* CVC=270, 36.1%). More frequent use of AVF was a result of an effective following of guidelines and recommendations for vascular access management in clinical care by nephrology clinics in the Slovak Republic.

For the assessment of differences in survival rates and death occurrence among patients, we constructed a Kaplan-Meier mortality curve for both types of vascular access (Figure 2). Kaplan-Meier plots showed higher mortality during the first 5 years on hemodialysis in patients with CVC compared to patients with AVF vascular access.

In the fully adjusted Cox proportional hazard analyses (Table II) we found an increased chance for survival in patients receiving hemodialysis by use of AVF (HR 1.52 [95% CI 1.27-1.83], P<0.001). Because diabetic and cardiac comorbidities strongly affect patient survival rates, we realized proportional hazard models for both parameters. We observed an increased chance of survival for patients who do not suffer with cardiac congestion (HR 1.26 [95% CI 1.06-1.50], P<0.01) or malnutrition (protein malnutrition: HR 0.98 [95% CI 0.96-1.00], P<0.05; lean tissue index: HR 0.79 [95% CI 0.67-0.93], P<0.01). However, there was no significant difference in the chance of survival by age, gender, duration of dialysis and the presence

TABLE I.—*Gender, age and clinical characteristics of the AVF and CVC patient groups.*

Parameters	AVF	CVC	AVF *vs.* CVC
Gender N.(%)			
Male	278 (57.1)	128 (49.0)	
Female	209 (42.9)	133 (51.0)	P<0.05
Age (years)			
Mean (SD)	60.8 (14.4)	63.5 (13.8)	
Median (IQR)	61.0 (53.0-72.0)	65.0 (55.0-73.5)	ns
Serum albumin (g/L)			
Mean (SD)	39.00 (3.97)	35.89 (5.23)	
Median (IQR)	39.40 (36.90-41.30)	36.90 (33.30-39.05)	P<0.001
Duration of dialysis (years)			
Mean (SD)	1226.57 (1683.17)	699.82 (1541.61)	
Median (IQR)	576.00 (58.00-1687.00)	55.00 (20-671.00)	P<0.001
Lean tissue index (n(%))			
Low (≤10%)	202 (41.5)	116 (44.4)	
Optimal (>10%)	285 (58.5)	145 (55.6)	ns
Diabetic nephropathy (N.[%])			
Yes	126 (25.9)	82 (31.4)	
No	361 (74.1)	179 (68.6)	ns
Cardiac congestion (N.[%])			
Yes	271 (56.8)	171 (66.3)	
No	206 (43.2)	87 (33.7)	P<0.05
Mortality (N.[%])			
Dead	56 (11.5)	51 (19.5)	
Alive	431 (88.5)	210 (80.5)	P<0.01

AVF: AVF group characteristics; CVC: CVC group characteristics; AVF *vs.* CVC: level of statistical significance of the differences between AVF and CVC characteristics indicated by statistical comparison (χ^2 and Mann-Whitney Test).

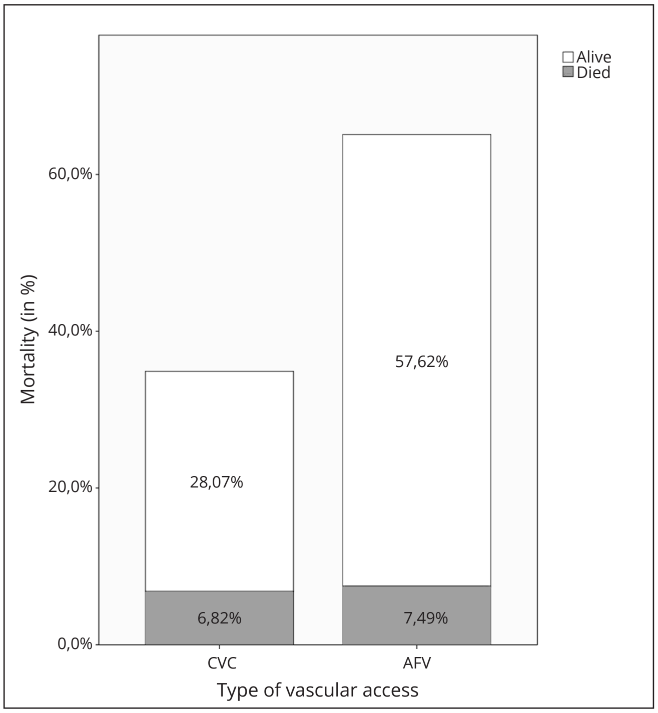

Figure 1.—Differences in survival and death of patients by type of vascular access.

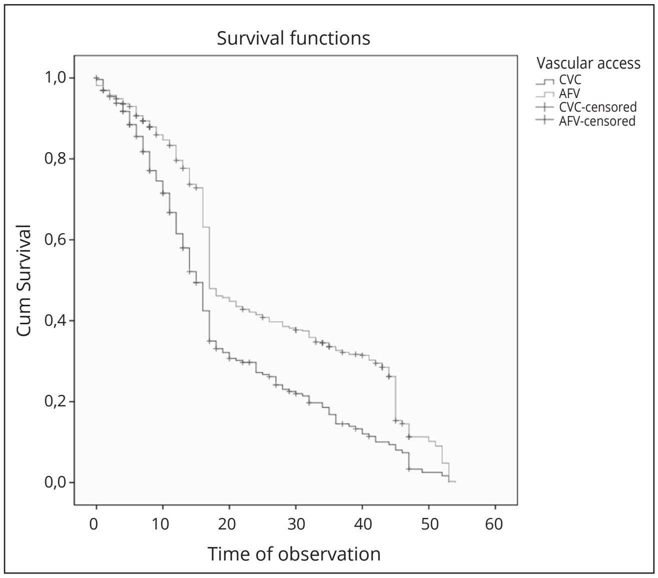

Figure 2.—Differences in survival/mortality between AVF and CVC over 5 years.

of diabetic nephropathy. Chances of surviving were higher by 52% in patients receiving hemodialysis by use of AVF in comparison to those receiving it by use of CVC.

Table II.—*Cox's regression model for age, gender, protein malnutrition, total days spent on dialysis, lean tissue index, the presence of diabetic nephropathy and cardiac congestion and type of vascular access.*

χ^2=59.64	HR	95% Confidence Interval		Significance
		Down	Up	
Age	0.99	0.99	1.00	ns
Gender: female *vs.* male	1.02	0.87	1.21	ns
Protein malnutrition	0.98	0.96	1.00	P<0.05
Duration of dialysis	1.00	1.00	1.00	ns
Lean tissue index: optimal *vs.* low	0.79	0.67	0.93	P<0.01
Diabetic nephropathy: no *vs.* yes	0.90	0.75	1.08	ns
Cardiac congestion: no *vs.* yes	1.26	1.06	1.50	P<0.01
Vascular access: AVF *vs.* CVC	1.52	1.27	1.83	P<0.001

Because the decision about the type of vascular access during initiation of dialysis is definitive for a patient's further clinical prognosis, we made a comparison of survival risks between the groups of AVF and CVC vascular access carriers. Overall, the results presented above show that patients with AVF achieved a higher survival rate than those with CVC. It is not surprising that lower survival rates were confirmed for patients diagnosed with cardiac congestion and malnutrition. These two health conditions related to poor prognosis and higher hospitalization frequencies among hemodialyzed patients.

Discussion

Vascular access for hemodialyzed patients plays a significant role in determining their further life on dialysis. In this study, we assessed survival rates among adult patients undergoing hemodialysis and compared the differences in rates between patients using either a CVC or AVF in the initiation of dialysis. For consideration of other factors that might affect the survival rate, we conducted a separate risks analysis for dialysis duration, the presence of protein malnutrition and two selected comorbidities.

Our data suggest that AVF is a superior type of vascular access from the perspective of patients' all-cause mortality. Patients dialyzed through AVF had a 52% higher chance of survival compared to patients with CVC regardless of age, sex, nutritional status, time spent on dialysis and also the presence of diabetes mellitus and cardiac weakness. Several other studies reported similar differences in outcomes of survival rates and all-cause mortality risks among dialyzed patients. Werner-Gibbings *et al.*[20] performed a 12-months follow-up of dialyzed patients and found 82% survival in AVF patients, while survival in CVC patients was only around 45%. The difference between AVF and CVC patient carriers on survival rates reported in that study is slightly lower than the survival difference observed in our study. This could be caused by the age-specific selection of patients. In our study, we analyzed adult dialyzed patients, while the above-mentioned study included only patients over 80 years old. A multivariate analysis reported by Ozeki *et al.*[21] revealed that CVC vascular access was associated with a higher risk of mortality in comparison to AVF (AVF, HR 1.60; CVC HR, 2.26). This difference in mortality rates between groups is in line with our observations. The higher mortality risk for CVC was also confirmed by the study published by Soleymanian *et al.*[8] In the unadjusted and full adjustment Cox models, where AVF patients were set as a reference, the HR of death for patients with CVC was, respectively, 2.17 (95% CI: 1.51-3.11) and 1.58 (95% CI: 1.01-2.51). Regardless of the existence of evidence denying the survival rate differences between AVF and CVC,[8, 12, 13, 22] we are strongly convinced that application of AVF brings important clinical and prognostics advantages for further patient life on dialysis. Improvements in endovascular treatment achieved in recent years[23] have strengthened the position of AVF as the choice of a long-term vascular approach in the dialyzed population, with the potential to maintain an appropriate quality of life[24] and lower morbidity and the frequency of cardiovascular and diabetic comorbidities among dialyzed patients.[25, 26] Another strong argument for AVF application is a cost-effectiveness analysis of access-related procedures and complications. Based on an analysis published by Al-Balas *et al.*,[7] the application of CVC at the initiation of dialysis is connected with much higher costs for maintenance procedures and hospitalizations than other vascular access options (Supplementary Digital Material 1: Supplementary Table I). These facts were reflected and documented in vascular access trends in nephrology surgery[27] and were also reviewed in the development of guidelines for clinical nephrologists.[25, 28]

Interestingly, we did not find a significant difference between vascular access groups in the presence of diabetic nephropathy. A slightly higher proportion of patients with diabetic nephropathy in the CVC group is likely explained by knowledge of the higher frequency of complications and failure during maturation of AVF among these patients (Supplementary Digital Material 2: Supplementary Table II). In addition, AVF not only increases the chance of survival but also reduces the risk of systemic infections that are incomparably higher in CVC.[4, 8, 9, 28, 29] This is, of course, linked to both direct and indirect healthcare costs.[7, 8, 11]

Strengths and limitations of the study

The main strength of this study is the follow-up for 5 years, which enabled us to explore vascular access and other factors, including major comorbidities such as malnutrition, cardiac congestion and diabetes mellitus, as predictors of mortality in dialysis patients. Moreover, all consecutive patients originated from 18 dialysis centers over Slovakia.

In this retrospective study, we included only data which were registered into medical databases during the observation period. Thus, we were unable to compare the mortality prediction using the Charlson Comorbidity Index (CCI) separately due to missing data on participants who died. Another limitation may be the lack of certain additional information based on the changing of vascular access types during this period. These factors may play an important role in mortality risk on the dialyzed population. Therefore, these data should be considered in future research. Another limitation that should be considered is the period of primary data acquisition, which was taken from databases reporting entry between the 2008 and 2013.

Conclusions

Functional arteriovenous fistula is a significant predictor survival in the dialyzed population, independently of sociodemographic parameters and serious comorbidities. Patients on dialysis with arteriovenous couplings have almost a 52% higher chance of survival than respondents with the central venous catheter for a year after inclusion in regular dialysis treatment.

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