The influence of diabetes mellitus on patency of arteriovenous fistulas for hemodialysis

Influência do diabetes mellitus sobre a perviedade da fístula arteriovenosa para hemodiálise

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Abstract

Background: Failure of arteriovenous fistulas (AVFs) to meet the minimum requirements for hemodialysis (HD) is the greatest cause of morbidity in patients on renal replacement therapy. Identifying risk factors associated with failure of vascular access is crucial to management and success of hemodialysis treatment. **Objective:** To compare mean duration of patency and survival of arteriovenous fistulas created in HD patients with and without diabetes mellitus (DM). **Methods:** This was a retrospective observational study of the medical records for all patients on HD at the Hospital Santa Casa de Misericórdia de Ponta Grossa (Brazil) in February 2014. We analyzed clinical data relating to creation, maintenance and use of AVF for dialysis, comparing mean duration of patency of fistulas currently in use for HD and analyzing survival of previously occluded AVFs. Patient data was allocated to one of two groups for analysis, according to presence or absence of DM. **Results:** Individuals in the DM group had higher mean age (59.97 ± 10.12), shorter time on hemodialysis treatment (25.42 ± 3.21 months), lower mean time before occlusion of arteriovenous fistulas (3.09 ± 11.60 months) and a lower mean rate survival of vascular access to 24 months (50.25%). **Conclusions:** This study concluded that diabetic patients had shorter mean duration of AVF patency and lower rate of access survival to 24 months.

Keywords: renal dialysis; arteriovenous fistula; diabetes mellitus.

Resumo

Contexto: A incapacidade das fístulas arteriovenosas (FAVs) atenderem aos quesitos mínimos para realização da hemodiálise (HD) corresponde a uma das maiores causas de morbidade nos pacientes em terapia renal substitutiva. Identificar os fatores de risco associados com a falência do acesso vascular é fundamental para o manejo e sucesso da terapia hemodialítica. **Objetivo:** Comparar o tempo médio de patência e a sobrevida das fístulas arteriovenosas realizadas nos pacientes portadores de diabetes mellitus com pacientes não portadores de diabetes mellitus (DM) em HD. **Métodos:** Trata-se de um estudo retrospectivo observacional, no qual foram observados os prontuários médicos de todos os pacientes em HD no Hospital Santa Casa de Misericórdia de Ponta Grossa, no período de fevereiro de 2014. Foram analisados dados clínicos referentes à confecção, manutenção e utilização das FAVs como adjuvante na terapia dialítica, comparando o tempo médio de patência das fístulas em uso para HD, bem como a sobrevida das FAVs ocluídas. Os pacientes selecionados foram divididos em dois grupos para comparação, conforme a presença ou ausência de DM. **Resultados:** Os indivíduos do Grupo DM apresentaram maior média de idade (59,97 ± 10,12), menor tempo de acompanhamento no serviço de hemodiálise (25,42 ± 21,03 meses), menor tempo médio até a oclusão da fístula arteriovenosa (9,03 ± 11,60 meses) e menor média de sobrevida dos acessos vasculares em 24 meses (50,25%). **Conclusões:** O estudo concluiu que para os pacientes diabéticos houve um menor tempo médio da patência das FAVs e menor taxa de sobrevida dos acessos em 24 meses.

Palavras-chave: diálise renal; fístula arteriovenosa; diabetes mellitus.

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INTRODUCTION

At the start of the 1960s, Scribner et al.[1] revolutionized nephrology when they developed a Teflon device to create an arteriovenous shunt that could be continuously used for dialysis treatment.[1,2] The Scribner shunt, as it came to be known, caused great interest in the scientific community, which went on to develop other vascular access techniques for chronic hemodialysis (HD) and, as a result, offered better life support for people with chronic end stage kidney disease (ESKD).[3]

The vascular access methods currently available are arteriovenous fistulas (AVFs), which may be autologous or prosthetic, and central venous catheters (CVCs).[4]

According to the 2012 Brazilian Chronic Dialysis Census, it is estimated that more than 95,000 patients are on dialysis treatment in the country, 91.6% of whom are being given HD as standard renal replacement therapy, demonstrating the overwhelming predominance of this modality.[5] Invariably, these patients need vascular access for the dialysis procedure. The ideal vascular access should provide adequate blood flow, allow dialysis sessions lasting many hours, tolerate frequent use, have the capacity to survive for a long period of time and exhibit low rates of complications (thromboses, infections and aneurysms).[3,6]

One major cause of dialysis–related morbidity is vascular access that fails to meet the minimum conditions for successful treatment.[6,7] This is clearly demonstrated by the observation that vascular access complications are the most prevalent of the major causes of hospital admission.[8] These complications (such as thrombosis and infection) may occur early on, before the access has been used for hemodialysis (primary failure or early occlusion), or later, when they occur after a certain period of successful use of the AVF.[9]

There are several factors associated with AVF failures: the type of material used to construct the vascular access (autologous or prosthetic), whether the location is distal (radiocephalic) or proximal (brachiocephalic and brachiobasilic), the age of the patient, history of smoking, use of a central venous catheter during construction of the AVF, and presence of comorbidities such as metabolic syndrome and diabetes mellitus (DM).[10-12]

Globally, DM is the most prevalent chronic disease among patients with ESKD, with systemic arterial hypertension (SAH) in second place.[13] In Brazil, these figures are reversed, and 35.1% of patients with ESKD have SAH, while 28.5% have DM.[5] However, it should be acknowledged that DM associated with ESKD has been becoming increasingly predominant within the Brazilian epidemiological profile and if the trend continues it will reach worldwide prevalence rates in the next few years.[14,15]

Considering the increasing role of diabetes mellitus as a cause of ESKD in our country, and the challenges involved in constructing AVFs in certain groups of patients, the primary objective of this study was to compare the mean duration of patency of occluded AVFs before this event, and the survival rates of arteriovenous fistulas constructed in patients with diabetes mellitus, with the same outcomes in patients who do not have diabetes mellitus, in patients given hemodialysis treatment at the Hospital Santa Casa de Misericórdia de Ponta Grossa (Parana, Brazil).

MATERIALS AND METHODS

Data were collected from the medical records of all patients on hemodialysis at the Hospital Santa Casa de Misericórdia de Ponta Grossa in February 2014. Patients with the following characteristics were included: (1) diagnosed with end stage kidney disease; (2) using hemodialysis as renal replacement therapy method; (3) current or prior use of an AVF as vascular access for dialysis treatment.

Patients were divided into two groups, depending on presence or absence of diabetes mellitus. Patients were assigned to the DM Group if they were on treatment with insulin or oral hypoglycemics or if they had a prior diagnosis of DM on their patient medical record. Patients were assigned to the NDM Group if they were on dialysis treatment but did not have DM as a comorbidity.

Sociocultural data were collected using an epidemiological questionnaire covering the following information: age, sex, ethnicity, educational level, place of residence and smoking habits.

Clinical data were collected using a structured research protocol covering the following information that was harvested from medical records: (1) time on dialysis treatment; (2) number of AVFs created since starting treatment; (3) mean duration of patency of previous AVFs, defined as cumulative or secondary patency (time elapsed from the date of creation to the date access was abandoned);[9] (4) mean duration of patency of AVFs currently in use up to the study cutoff; (5) time taken for AVF to mature (from creation until first puncture for HD); (6) anatomic site of AVF creation; (7) presence of infectious processes involving AVF since starting treatment; (8) prior use of a central venous catheter (CVC) for dialysis (9) use of CVC as access for initial dialysis treatment; and

(10) presence of systemic arterial hypertension as an associated comorbidity.

The term premature occlusion was used to describe fistulas that occluded before 30 days, without attaining the necessary maturity for HD use. Results are first given for patent fistulas that were still in use for HD up to the study cutoff, and then the results for fistulas that had already occluded by that point are listed.

This study was analyzed and approved by the Research Ethics Committee at the Hospital Santa Casa de Misericórdia de Ponta Grossa under number 561.520/2014 (COEP). Patients were given free and informed consent forms, which they read and then signed to indicate their agreement to study participation.

The single-tailed Student's *t* test was used to detect statistical differences between means for groups and Fisher's test was used for dichotomous statistical differences. Results are expressed as mean ± standard deviation (SD). The Kaplan-Meier test was used to analyze AVF survival and the log-rank test was used to compare rates. Differences for which $p < 0.05$ were considered significant. Results were analyzed using MedCalc 13 (Belgium).

RESULTS

A total of 160 patients were recruited, 49 of them were allocated to the DM Group and 99 patients were allocated to the NDM Group, while 12 patients did not meet the inclusion criteria, making a total sample of 148 patients. Mean age differed between the two groups, at 59.97 years (± 10.12) for the diabetic patients and 52.54 years (± 14.83) for non-diabetic patients ($p = 0.0010$). There were no significant differences in educational level or smoking habits. Both groups exhibited a predominance of males, accounting for 69.39% in the DM Group and 51.52% in the NDM Group ($p = 0.0510$) (Table 1).

There was a significant difference between the groups in terms of time on hemodialysis treatment. The group of non-diabetic patients had a mean duration of 63.09 (± 53.19) months of treatment, which was considerably longer than the diabetic patients, who had mean hemodialysis duration of 25.42 (± 21.03) months ($p = 0.0001$). Although systemic arterial hypertension is an important risk factor associated with chronic kidney disease (CKD), its prevalence was similar between the groups at 87.86% of the DM Group patients and 88.89% of the patients in the NDM Group. There were no significant differences between the groups in terms of prior use of CVCs or the number of patients who started dialysis treatment via this type of access (Table 1).

For analysis of patent AVFs, 137 individuals had a fistula for HD access and in 11 patients a CVC was used as access route. The mean duration of patency for AVFs currently in use was 18.96 (± 13.40) months in the DM Group (n = 46) and 44.29 (± 43.77) months in

Table 1. Sociocultural and clinical patient data.

Variable	DM Group	NDM Group	
N	49	99	
Mean age (SD)	59.97 (10.12)	52.54 (14.83)	0.0010
Males (%)	34 (69.39%)	51 (51.52%)	0.0517
Skin color			
White	45 (91.84%)	85 (85.86%)	0.4267
Black	4 (8.16%)	14 (14.14%)	0.4267
Educational level			
Illiterate	04 (8.16%)	3 (3.03%)	0.2202
Primary school incomplete	09 (18.37%)	14 (14.14)	0.6302
Primary school graduated	22 (44.90%)	54 (54.54%)	0.2977
Secondary school incomplete	01 (2.04%)	4 (4.04%)	1.0000
Secondary school graduated	13 (26.53%)	23 (23.23)	0.6870
Higher education incomplete	01 (2.04%)	1 (1.01%)	1.0000
Higher education graduated	0 (0%)	0 (0%)	1.0000
Smokers	6 (12.24%)	21 (21.21%)	0.2583
Mean time on HD (months)	25.42 (± 21.03)	63.09 (± 53.19)	0.0001
SAH	46 (87.86%)	88 (88.89%)	0.3886
Prior use of CVC	37 (75.51%)	78 (78.79%)	0.6781
Treatment started via CVC	32 (71.11%)	69 (69.70%)	0.7078

HD - hemodialysis; SAH - systemic arterial hypertension; CVC - central venous catheter.

the NDM Group (n = 91) (p = 0.0002). When fistulas were categorized by duration of patency into 1, 12 and 24-month groups, there was no significant difference between DM and NDM groups in terms of the prevalence of AVFs with less than 12 months' patency (32.61% in the DM Group vs. 22.08% in the NDM Group; p = 0.3040). Analysis of AVFs that remained patent for 12 and 24 months revealed greater prevalence in the DM Group (39.13%) (p = 0.0268). However, analysis of the rate of AVFs that remained patent for more than 24 months revealed that the proportion in the DM Group (28.26%) was significantly lower than the proportion in the NDM Group (56.04%) (p = 0.0020). Another notable difference between the groups was related to the time taken for AVFs to mature, since 25 (54.35%) of the 49 patients in the DM Group had a vascular access puncture performed before the full 30 days' maturation period had elapsed, compared to just 31 (34.07%) of the 99 patients in the NDM Group (p = 0.0277). The remaining analyses of data on patent AVFs did not detect significant difference between the groups, in terms of current use of CVC, prosthetic grafts, autologous AVF or anatomic site of vascular access (Table 2).

The data on AVFs occluded prior to the study cutoff showed that there was no significant difference in the prevalence of patients who had had occluded fistulas (p = 0.1493), since 26 (53.06%) patients in the DM Group, and 66 (66.67%) patients in the NDM Group had had occlusions previously, including premature and late AVF losses (Table 3). There were a total of 49 occluded AVFs in the DM Group, 29 (59.18%) of which were late occlusions and 20 (40.82%) of which were premature occlusions. There were 121 occluded AVFs in the NDM Group, 71 (58.68%) late occlusions and 50 (41.32%) premature occlusions. Analysis of the time elapsed until AVF occlusion revealed that the mean time was 9.03 (± 11.60) months in the DM

Table 2. Characteristics of patent arteriovenous fistulas currently in use for HD.

Variable	DM GROUP (n = 49)	NDM GROUP (n = 99)	P
Mean duration of patency	18.96 (± 13.40)	44.29 (± 43.77)	0.0002
Type of vascular access:			
FAVs	46 (93.88%)	91 (91.91%)	1.0000
Radiocephalic	28 (57.14%)	49 (49.49%)	0.3894
Brachiocephalic	10 (20.40%)	26 (26.26%)	0.5425
Brachiobasilic	6 (12.24%)	16 (16.16%)	0.6283
Femoro-femoral	1 (2.04%)	0	0.3311
Prosthetic	1 (2.04%)	0	0.3311
CVC	3 (6.12%)	8 (8.08%)	1.0000
AVFs patent at:			
< 12 months	15 (32.61%)	21 (23.08%)	0.3040
12-24 months	18 (39.13%)	19 (20.88%)	0.0268
>24 months	13 (28.26%)	51 (56.04%)	0.0022
Maturation time < 30 days	25 (54.35%)	31 (34.07%)	0.0277

AVF - arteriovenous fistula; HD - hemodialysis; CVC - central venous catheter.

Table 3. Analysis of arteriovenous fistulas occluded prior to study cutoff.

Variable	DM Group (n = 26)	NDM Group (n = 66)	p
Number of occlusions	49	121	
Premature occlusion*	20 (40.82%)	50 (41.82)	1.0000
Late occlusion†	29 (59.18%)	71 (58.68%)	1.0000
Mean time to occlusion (months)	9.03 (± 11.60)	15.97 (± 27.92)	0.0952
Mean time to occlusion (months) for late-occluded accesses	14.62 (± 12.39)	26.15 (± 32.58)	0.0338
Survival of late-occluded AVFs	n = 29	n = 71	
Patent at 12 months	15 (51.72%)	38 (53.52%)	1.0000
Patent at 24 months	5 (17.24%)	28 (39.44%)	0.0300

AVF - arteriovenous fistulas. *Occlusion of access before it was used for hemodialysis (primary failure). †Occlusion of access that had successfully been used for hemodialysis.

Group and 15.97 (± 27.92) months in the NDM Group and the difference between them was not significant (p = 0.0952). However, excluding the premature occlusions from the analysis revealed that AVFs that underwent late occlusion exhibited significant difference between groups in terms of mean time before occlusion, which was 14.62 (± 12.39) months in the DM Group and 26.15 (± 32.58) months in the NDM Group (p = 0.0338) (Table 3).

When late-occluded AVFs were further broken down by patency at 12 and 24 months, it was found that the 12-month patency rate was 51.72% among diabetic patients and 53.52% for non-diabetic patients (p = 1), but that 24-month patency was significantly different between the groups, since 39.44% of the late-occluded AVFs in the NDM Group were still patent after 2 years, whereas in the DM Group just 17.24% survived to 24 months (p = 0.0368) (Table 3).

Analysis of the results of the Kaplan-Meier survival test showed that in the DM Group the AVFs exhibited 78.95% likelihood of patency after 1 month. In the NDM Group this probability was 76.42%. Extending the analysis to 12 months revealed that the DM Group AVFs exhibited a 64.21% likelihood of patency, compared with 60.85% of the AVFs in the NDM Group. Notwithstanding, the 24-month patency rates showed that AVFs in DM Group patients were less likely to be patent, with 50.25% patency, compared to 55.21% for the NDM Group (p = 0.3800) (Figure 1).

DISCUSSION

With regard to the prevalence of DM among ESKD patients, the national scenario was illustrated by the 2012 Brazilian Chronic Dialysis Census,[5] revealing that 28.5% of patients on dialysis treatment also have diabetes as an associated comorbidity, which is a slightly lower figure than was found in the present study (33.10%). A study conducted in 2009 in the South of Brazil by Burmeister et al.[15] reported that 37.9% of the hemodialysis patients studied also had DM. These epidemiological data suggest that there are significant regional differences in DM rates among hemodialysis patients.

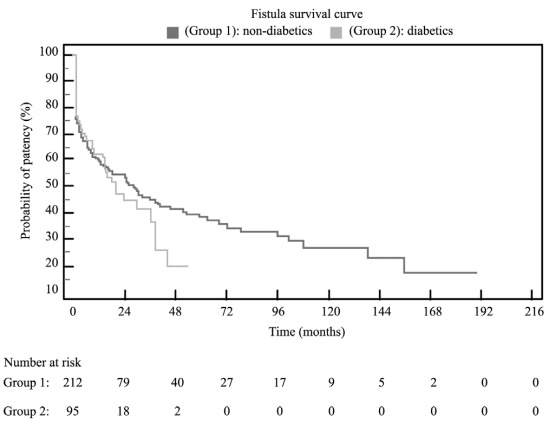

Figure 1. Survival curve for arteriovenous fistulas, in months.

Comparison of epidemiological data between groups with and without DM revealed that the mean of age of the DM patients was higher, which has also been observed in other studies in the literature,[12,14] which have identified DM as the most prevalent comorbidity among older patients using AVFs for hemodialysis.[16] However, the duration of hemodialysis treatment was significantly shorter in the DM Group, which might be explained by the higher mortality rate among diabetic patients on HD.[17,18] On the other hand, the longer duration of treatment in the NDM Group may have its causes in the earlier onset of ESKD cases that are related to causes of CKD other than diabetes[7] (Table 1).

According to the recommendations in the National Kidney Foundation – Kidney Disease Outcomes Quality Initiative (NKF – KDOQI) guidelines,[6] an autologous arteriovenous fistula is the approach that comes closest to an ideal access for dialysis treatment, since it is associated with lower rates of complications, lower costs and greater durability. In this study we observed greater than 90% utilization of autologous AVFs as access in both groups, with no distinction between them, showing that DM did not prove to be a limiting factor to choosing "fistula first", as the literature recommends.[19,20] Notwithstanding, it was also observed that more than 50% of the DM patients had their AVFs punctured for use before 30 days had elapsed since creation (p = 0.0277), which is the minimum period recommended by the NKF-KDOQI to allow an autologous AVF to mature, since premature puncture of the access can result in increased incidence of infiltration and compression of the anastomoses, causing permanent loss of the AVF.[6] The morbidity and mortality linked with employing a CVC for dialysis access figures among the principal motives related to premature puncture of AVFs, whether because of the risk of developing complications, such as infection of the catheter, or because of the increased discomfort attributed to employing this method.[21,22] As an alternative, it is recommended that patients with CKD should be referred to a specialist as early as possible to discuss methods for renal replacement therapy,[23] particularly individuals who have chronic comorbidities, since they invariably exhibit greater chances of progression to ESKD. When the treatment

chosen is HD, an AVF should be created when the patient reaches stage 4 CKD (glomerular filtration rate <30mL/min/1.73m^2), thereby providing sufficient time for the access to mature, so that it is available when dialysis treatment is started.[6]

International studies have demonstrated that DM is an important risk factor for premature occlusion of vascular accesses before they are ready for puncture.[24-26] However, the data collected in this study did not reveal differences between the rates of premature occlusion in accesses created in diabetic and non-diabetic patients (Figure 1), since accesses attained maturity in more than 70% of cases in both groups, confirming data published elsewhere in the Brazilian literature.[10] The restricted number of premature occlusions of vascular accesses among the diabetic patients may be the result of good management of DM treatment.[25]

Although they had been on treatment for shorter periods, patients in the DM Group exhibited similar prevalence rates of later occlusions (Table 3) when compared with non-diabetic patients, showing that the occurrence of occlusion of accesses is more frequent among the diabetic patients, allowing for the length of time on dialysis treatment.[22]

The data on survival rates of accesses, illustrated by the Kaplan-Meier curve (Figure 1), demonstrate that at 12 months the AVFs in the diabetic patients in this study did not have lower patency rates, in contrast with what was reported in a meta-analysis published in 2014 by Al-Jaishi et al.[27] This can be explained by the fact that the mean time elapsed before late occlusion of AVFs in the DM Group (which was approximately 14 months) was beyond the 12-month analysis cutoff.

However, the univariate analysis of cumulative patency at 24 months shows that there was a significant reduction in patency among the patients in the DM Group, following the pattern that is generally described in the literature.[27] This result is related to the greater number of vascular access occlusions observed from 12 to 24 months after creation of the AVFs in this group.

This study suffers from certain limitations, including the small number of patients, which did not provide significant results for AVF survival according to the Kaplan-Meier test, although it did show that accesses in the DM Group had lower survival rates at 24 months and this might have been significant with a larger sample size. Another probable limiting factor is the lack of standardization of institution of surgical treatment to create the AVFs, which is the result of the fact that these procedures were conducted by different teams of professionals over the years.

In terms of conclusions, it was observed that in the sample studied diabetic patients had lower duration of use, lower patency of AVFs that later occluded and also lower rates of access survival at 24 months, when compared with non-diabetic patients.

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