Hemodialysis vascular access in children and adolescents: a ten-year retrospective cohort study

Avaliação do acesso vascular para hemodiálise em crianças e adolescentes: um estudo de coorte retrospectivo de 10 anos

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Abstract

Introduction: Vascular access complications have been the major cause of hospitalization among patients with end stage kidney disease (ESKD) on hemodialysis (HD). Despite recommendations to decrease the use of central venous catheters (CVCs), these devices still represent the main access for children and adolescents who start HD. **Objectives and methods:** This was a retrospective cohort study to assess HD vascular access type, complications and causes of failure in children and adolescents aged less than 18 years, who started HD during the 1997-2007 period. **Results:** 251 accesses were studied in 61 patients: 97 arteriovenous fistulas (AVFs) and 154 short-dwelling untunnelled CVCs. 51% of the study patients started HD with a CVC. Patients` mean age at HD start was 12.5 years. The predominant underlying disease was glomerulonephritis (46%). The main cause of CVC removal was infection (35%). Mean untunnelled CVC survival was 40 days. AVF primary failure was detected in 37.8% of the fistulas. The main cause of failure of the functioning AVFs was thrombosis (84%). Infection did not cause any AVF failure. Patients with a CVC had a 34 times higher risk of infection than patients with an AVF. Conclusion: Infection was the major cause of CVC removal, and our results suggest that untunnelled CVCs must be avoided for ESKD children and adolescents on HD, and replaced by AVFs or long-dwelling tunnelled CVCs, whenever feasible. Thrombosis was the main cause of AVF failure, strengthening the

Resumo

Introdução: As intercorrências do acesso vascular têm sido a maior causa de internação entre os pacientes com estágio V da doença renal crônica (DRC) em hemodiálise (HD). Apesar de campanhas para a diminuição do uso de cateter venoso central (CVC) como via de acesso para HD, este ainda representa a principal via de acesso para crianças e adolescentes que iniciam HD. **Objetivos e métodos:** Este estudo tem o objetivo de avaliar, por meio de um coorte retrospectivo, o tipo de acesso vascular inicial, a incidência de complicações dos acessos vasculares e as razões de falência dos acessos em crianças e adolescentes com idade entre 0 e 18 anos que iniciaram HD no período de 1997 a 2007. **Resultados:** Foram estudados 251 acessos em 61 pacientes, sendo 97 fístulas arteriovenosas (FAV) e 154 CVC de curta permanência. Dos pacientes do estudo 51% iniciaram HD pelo CVC. A média de idade dos pacientes no início da HD foi de 12,5 anos. A doença de base predominante foi glomerulopatia (46%). A principal causa de retirada de CVC foi infecção, em 35%. A sobrevida média do CVC foi de 40 dias. A falência primária da FAV foi detectada em 37,8% das FAV confeccionadas. Para as FAV funcionantes, a principal causa de falência foi a trombose (84%). A infecção não foi a causa de nenhuma falência de FAV. Comparando-se os tipos de acesso, constatou-se risco de infecção 34 vezes maior para os pacientes em uso de CVC em relação aos em uso de FAV. **Conclusão:** A infecção foi a maior causa de retirada de CVC temporário. Esse estudo sugere que o CVC temporário deve ser evitado, e, sempre que possível, substituído por FAV ou

need of implementation of a program for early detection of access failure.
Keywords: Renal dialysis. Arteriovenous fistula. Pediatric assistants. Long-dwelling catheters.

CVC de longa permanência. A trombose foi a principal causa de perda da FAV, reforçando a importância de um programa para a detecção precoce da disfunção do acesso.
Palavras-chave: Diálise renal. Fístula arteriovenosa. Assistentes de pediatria. Cateteres de demora.

Introduction

The ideal vascular access, besides providing adequate blood flow, should have satisfactory survival and a low rate of complications.[1] Arteriovenous fistula (AVF) is the type of access that meets these characteristics most closely.

Although Sheth *et al*.[2] reported that AVF long-term function and survival in children are equivalent to those of adults and to those with long-dwelling tunnelled catheters, AVF construction in children and adolescents is hampered by vessel caliber and shorter length for puncture. In addition, many surgical and nursing teams are not adequately trained to manage these patients.[3] The same holds true for some adolescents, as chronic kidney disease (CKD) frequently leads to stunting and low weight.

Vascular access complications account for the high morbidity related to hemodialysis (HD), being the main reason for hospitalization of patients on this treatment, thus increasing costs.[4]

In spite of the Kidney Disease Outcomes Quality Initiative (K/DOQI) recommendation to prioritize AVF as initial vascular access, and the evidence pointing to increased morbidity and mortality of adult patients with central venous catheters (CVCs),[5] studies have shown that most pediatric patients still begin HD with a CVC, instead of an AVF or prosthetic graft.[6,7]

Infection and thrombosis are the most frequent catheter-related complications.[8] Besides being serious events, these complications further impair the patient`s clinical picture and jeopardize future accesses. Furthermore, each access has its own length of patency, and each patient has a limited number of sites for AVF construction, with no further available site after years on HD being a common finding. Zaritsky[9] compared the complication rates of different access types and concluded that CVC was strongly associated with infections and higher morbidity rates, compared with AVF. The rate of complications, chiefly infections, may be reduced when an aseptic technique is used for catheter manipulation.[10]

The aim of this study was to assess the complication rates of and reasons for access failure in a group of children and adolescents on HD in the city of Belo Horizonte (MG), Brazil.

Methods

We undertook a retrospective cohort study to assess the HD vascular access of 61 CKD patients. All patients starting HD under the age of 18 years, registered with the HD centers of Belo Horizonte (MG), Brazil, during the period from January 1997 through December 2007, and who remained on HD for 6 months or more, were included. The data were collected until December 2008. The number of patients and each patient`s registration center were provided by the municipal nephrology commission. Patients who did not sign their informed consent, who had no recording of their physical examination, and who had started HD due to chronification of acute kidney failure were excluded. The exclusions aimed to avoid misinterpretation of the causes of access complications, once these patients are exposed to other variables which interfere with their clinical evolution.

The number of patients provided by the municipal nephrology commission was 90. Of this total, 18 died before the beginning of the study (5 because of vascular access failure), and 9 were transferred to dialysis centers elsewhere. Two additional patients were excluded because their medical records were incomplete.

The study was approved by the institutional ethics committees of the Federal University of Minas Gerais and Belo Horizonte Health Authority. The patients or their carers signed their informed consent. The medical records were surveyed for information concerning the vascular accesses, from the beginning of HD to December 2008 or treatment interruption, either because of kidney transplantation or change to another treatment modality.

Besides anthropometric data (sex, age, underlying disease, date of HD start and patient`s origin) we collected all data concerning the existing accesses. As for AVFs, we investigated: the number of previous failed access construction attempts; the number of previous patent AVFs and their length of use; failure cause; type (native or prosthetic) and the time elapsing from construction to first puncture. As for CVCs, we investigated: insertion site; number of catheters inserted; indwelling time and; reason for removal. All CVC-related or AVF-related infectious events were registered.

After analysis of the medical records, the patients were examined with the aim of collecting information that was not present in the records, chiefly regarding previously failed AVF construction attempts. This information was not available from the records when the attempts were made prior to the patient`s registration with the dialysis center.

Data categorization was based on the following definitions:

Infection – Because of the impossibility to identify the infection-confirming results of the blood cultures in the records, a CVC infection was considered to exist when CVC removal was due to fever, without any other infectious source, and/or when antibiotics were started.

Thrombosis – Thrombosis was considered to have been the outcome of AVFs and CVCs when no blood flow was achieved, in spite of attempts to relieve obstruction.

Primary failure – Primary failure was considered to have occurred when the AVF did not provide adequate flow since its construction, or when flow was interrupted, in a previously unused AVF, within the first four weeks after its construction.

The collected data were processed and analyzed with the Excel (2000) and SPSS (11.5 for Windows) programs. The patients were divided in groups according to the type of vascular access used in their first HD session: AVF or CVC. We described the data with frequency tables, medians and means. Categorical data were shown in proportions and expressed as percentages. The chi-squared test, with Yates correction, was used for proportion comparison.

Results

251 HD vascular accesses were investigated in 61 patients. 97 were permanent accesses (94 AVFs and 3 prostheses) and 154 were short-dwelling CVCs. Of these 61 patients, 31 (51%) had a CVC and 30 (49%) had an AVF as the initial access. Mean age at HD start was 12.5 years (range: 2.9 - 17.8) for those starting with a CVC, and 13.1 years (range: 7.7 - 17.0) for those starting with an AVF. The most frequent underlying disease was glomerulopathy (28 patients, 46%), followed by uropathy (21 patients, 34%). The demographic data are presented in Table 1.

Mean weight at HD start was 32 kg (range: 15 - 58) and 34 kg (range: 8 - 59) for AVF and CVC patients, respectively. As for patients weighing 15 Kg or less, 3 started HD with a CVC and 1 with an AVF. The mean indwelling time of the 154 CVCs was 41 days (range: 0 - 207).

For the 31 CVC patients, mean time between HD start and AVF use (first puncture) was 105 days (range: 16 - 447). During this period, these 31 patients used a mean of 4 CVCs/patient.

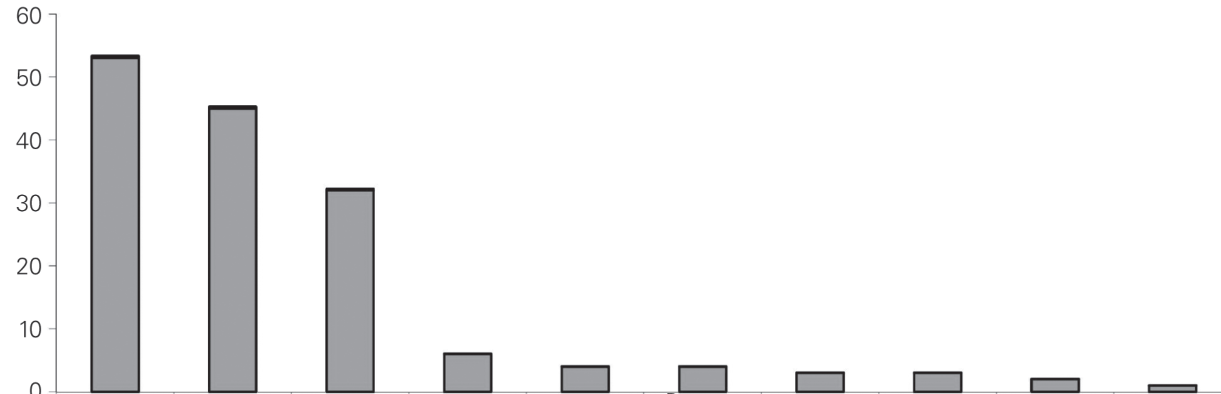
Infection was the most frequent complication in CVC patients, being responsible for 53 (35%) of CVC removals, of the 154 studied (Figure 1).

Table 1 Patients` clinical features in relation to the initial vascular access

	Start with CVC	Start with AVF	TOTAL
N	31 (51%)	30 (49%)	61
Sex			
F	15 (48%)	13 (43%)	28 (46%)
M	16 (52%)	17 (57%)	33 (54%)
Age			
< 10	10 (32%)	4 (13%)	14 (23%)
> 10	21 (68%)	26 (57%)	47 (77%)
Weight			
≤ 20 kg	7 (23%)	7 (23%)	14 (23%)
> 20 kg	24 (77%)	23 (77%)	47 (77%)
Procedence			
OUT/CAPD/TX	14 (45%)	30 (100%)	44 (72%)
ER	17 (55%)	–	17 (28%)
Underlying disease			
Uropatia	8 (26%)	13 (43%)	21 (34%)
Glomerulopathy	16 (52%)	12 (40%)	28 (46%)
Tubulopathy	4 (13%)	2 (7%)	6 (10%)
Systemic disease	2 (6%)	1 (3%)	3 (5%)
Miscelaneous	–	1 (3%)	1 (2%)
Indeterminate	1 (3%)	1 (3%)	2 (3%)

CVC: Central venous catheter; AVF: Arteriovenous fistula; N: number; F: female; M: male; OUT: Outpatient; CAPD: Continuous Ambulatory Peritoneal Dialysis; TX: transplantation; ER: Emergency room.

Figure 1. Reasons for CVC removal.



	Infection	AVF	Thrombosis	Exteriorization	Kinking	Puncture failure	Bleeding	No flow	Malposition	Transplantation
%	35%	29%	21%	4%	3%	3%	2%	2%	1%	1%
number	53	45	32	6	4	4	3	3	2	1

AVF: arteriovenous fistula; CVC: central venous catheter

The predominant site for catheter insertion was the internal jugular vein (88 cases), followed by the subclavian vein (38 cases) and femoral vein (26 cases).

151 AVFs were constructed in 61 patients; 57 AVFs suffered primary failure (37.8%) and were not counted in the other steps of the study. The remaining 94 AVFs had their features analyzed. 21 of the 30 patients starting HD with an AVF had this access as the sole one. 2 patients developed venous hypertension which required AVF closure, with the construction of another AVF in the contralateral limb. These two hypertensive fistulas were only closed when the new AVF became usable, after observation of the maturation time, no catheter being necessary.

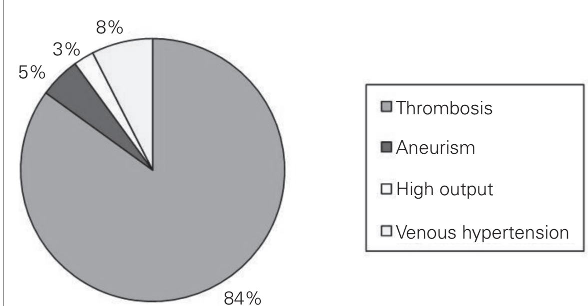
Of the 94 AVFs studied, 55 remained patent until the end of data collection. The causes of failure of 39 AVFs are described in Figure 2. Thrombosis was the most frequent cause of AVF failure, occurring in 84% (33 AVFs). 9 patients lost more than 1 AVF.

Although thrombosis led to access failure in 33 AVFs (84%), thrombectomy was performed in only 6 fístulas (all successfully), a short-dwelling CVC being necessary in 4 patients.

Two fistulas (5%) with aneurysm formation and one high-output fistula (3%), although functioning, were closed due to the risk of rupture.

No AVF was lost due to infection (Figure 2). CVC entailed a 34 times greater risk of infection, compared with AVF.

Figure 2. Causes of AVF loss.



AVF: Arteriovenous fistula

Discussion

The number of patients reaching CKD stage 5, with the consequent need of renal replacement therapy, has increased each year.[11] This high and growing rate of CKD stage 5 patients among the adult and pediatric populations has been considered a CKD epidemic, and has demanded a significant share of the resources allocated to health care. The rate of CKD stage 5 patients among the pediatric population has remained fairly constant, being approximately 14/million population below 19 years of age/year.[12] Considering that the pediatric population corresponds to 40% of the 4 million people inhabiting the Belo Horizonte metropolitan area, 224 people under the age of 19 years should be expected to reach CKD stage 5 each year. Yet, this has not been observed, even considering that many children start dialysis through the peritoneal route. The centers caring for CKD children in the metropolitan area of Belo Horizonte, and chiefly those offering dialysis, do not receive 224 CKD stage 5 children and adolescents each year. This strengthens the supposition that most of these patients do not have access to primary care centers which could screen for CKD and refer to specialized care for adequate diagnosis, prevention and treatment. It must be highlighted that many CKD stage 5 adult patients had disease onset during childhood. Pediatricians and pediatric nephrologists should therefore liaise with one another, aiming the early diagnosis, prevention and optimal management of CKD starting during childhood.[12,13]

According to the North American Pediatric Renal Transplantation Cooperative Study (NAPRTCS),[6] 77.7% of the children in the USA start HD with a CVC, against 12.3% with an AVF and 7.3% with a prosthesis. In our study, 31 patients (51%) started HD with a CVC (Table 1). Of these, 17 were initially assessed at an emergency facility, suggesting that their CKD had not been previously diagnosed.

There are few studies assessing the complications and survival of temporary catheters. Short-dwelling and long-dwelling catheters are removed for a number of reasons. Although thrombotic occlusion with flow disruption is more common than infection, CVC-related infection is the main barrier to the use of long-dwelling catheters, being the main reason for catheter removal and the main cause of morbidity and mortality among dialysis patients.[14] Data from the United States Renal Data System (USRDS) indicate that the rate of sepsis remains on the increase among dialysis patients, with the rate of hospital admissions for treatment of vascular access infection having doubled in the last decade.[15] CVC patients have admission rates that are 20 times higher than those with AVF as their HD vascular access.[9] Dialysis programs should monitor the vascular access, chiefly catheter-related infections and their features: incidence, bacteriological profile and evolution. Biofilm formation on the CVC internal and external surfaces is considered an important factor for the colonization process. Biofilm, which is produced by a combination of host-derived factors (fibrinogen, fibrin, fibronectin and extracellular polysaccharides) and microbial products (glycocalix), plays a pivotal role in bacterial resistance.[15]

Goldstein *et al.*[16] evaluated 23 patients using 78 CVCs (56 short-dwelling and 22 long-dwelling), during a 5-year period. The catheters were mostly (39%) electively removed in their study, when an AVF became the vascular access or when the patient underwent kidney transplantation. Those authors reported a short-dwelling CVC removal rate due to infection of 7%, with a mean catheter survival of 31 days, whereas for long-dwelling catheters, infection-related removal rate was 36%, but with a mean catheter survival of 123 days. Mean time till infection was 11 days (range: 7 - 157) for short-dwelling catheters and 211 days (range: 129 - 971) for long-dwelling ones, a finding that strengthens the superiority of long-dwelling CVCs for vascular access in children who need HD for more than 10 days, and who do not have a permanent vascular access. In our study, 35% of the short-dwelling catheters were removed because of infection. (Figure 2), exposing the patients to higher morbidity and mortality. Literature reports[16,17] indicate that short-dwelling catheters should be used for a short period of time, preferably less than one month. This hampers comparison with our study, in which a large number of patients (36%) had the loss of their CVC as reason for the insertion of another CVC, indicating that, in these cases, the CVC was not being used with the perspective of a change to a permanent access.

Successive CVC changes could have been minimized with a wider use of long-dwelling CVCs, something that did not commonly occur in the dialysis centers we studied, as these devices are difficult to obtain, need to be imported, are costly and are not reimbursed by the Brazilian Unified Health System (*Sistema Único de Saúde* – SUS). Since 2009, long-dwelling catheters have been used at the dialysis unit of the UFMG Hospital das Clínicas, in children and adults without a permanent access, and who need chronic dialysis.

Children are more exposed to catheter infection than adults, once placement is generally performed under sedation, in the hospital environment, thus increasing exposure to hospital-acquired pathogens. Studies have pointed to *Staphylococcus* as the main cause of CVC infection, followed by Gram-negative bacteria, such as *E.coli*, *Enterobacter* and *Xanthomonas*.[16] We could not detect the causative agent in our study, because in most cases the bacteriological results had not been entered in the medical records. Weijmer *et al.*[18] reported a long-dwelling CVC infection rate of 2.9/1,000 catheters/day, significantly lower than the short-dwelling CVC infection rate (12.8/1,000 catheters/day;

$p < 0.001$). Other studies[19-22] have also reported a higher infection rate for short-dwelling catheters (3.8 to 6.6 episodes/1,000 days) than for long-dwelling ones (1.6 to 5.5 episodes/1,000 days). CVC-related bacteremia was diagnosed in 81% of children aged 13.9 ± 4.6 years, on long-dwelling CVC chronic HD. The isolates consisted of Gram-positive bacteria in 67%, Gram-negative bacteria in 14% and multiple agents in 19%. Systemic antibiotic therapy cured bacteremia in 34%; in 23%, cure included the use of an antibiotic-sealed catheter. CVC change occurred in 43% of the catheters, strengthening the evidence that catheter-related bacteremia remains the main responsible for catheter failure.[23]

We found that 21% of the CVCs were lost because of thrombosis (Figure 1), with no statistically significant correlation between the insertion site and infection and/or thrombosis.

For some children, CVC is the only access option. The preferred site for CVC insertion should be the right internal jugular vein, followed by the right external jugular vein, left internal and external jugular veins, and right and left femoral veins, the subclavian vein being best avoided due to the risk of stenosis.[14] CVC insertion in the right internal jugular vein affords straighter access to the right atrium, compared to the left vessels, and also carries a lower risk of infection, compared with the other sites. CVC insertion in the left jugular vein not only jeopardizes the success of a future permanent access in the left upper limb, but is also associated with poorer blood flow and higher rates of stenosis and thrombosis. Implantation in the femoral and translombar veins is associated with higher infection rates. In addition to infection, thrombosis is frequent with insertions in the femoral vein, such occurrence having the potential to preclude future transplantations. CVC-induced central vein stenosis is related to the insertion site, number of catheters used, CVC indwelling time and the occurrence of infection. 25% of the CVCs in our study were inserted in the right or left subclavian vein. Other studies have reported even higher rates of subclavian use, reaching 82% of the insertions,[7,24] thus increasing the risk of thrombosis and making it more difficult to later construct an AVF in the ipsilateral upper limb. Yet, according to the NAPRTCS registry,[6] CVC use remains frequent and unabated, most CVCs being inserted in the subclavian vein (54.6%), followed by the jugular (40.1%) and femoral (4.4%) veins. In our study, the subclavian vein was the preferred CVC insertion site until the last decade. As the untoward effects of such use were published, vascular surgeons started changing to the jugular and femoral veins. In spite of reduced use of the subclavian vein, however, central vein stenosis remains very common.[25] In our study, 21% of the CVCs were lost due to thrombosis (Figure 1).

While some authors state that the construction of an AVF using the same techniques employed in adults is feasible even in lower weight children,[26] this does not reflect real practice. Most studies of vascular access in low-weight children[24,27,28] have reported a higher rate of CVC use than of AVF use, mainly due to surgical difficulties. This is especially relevant because of the correlation between CVC use and mortality.[28,29] We detected a 3:1 CVC/AVF ratio in patients weighing less than 15 kg. Most patients aged 10 years or less started treatment with a CVC (10 patients with mean weight = 18.6 ± 6.9 kg), in comparison with those who started with an AVF (4 patients with mean weight = 22.0 ± 6.3 kg). AVF patency success is directly related to the patient`s clinical status, age, weight, sex and primary disease, and also to the surgical technique employed and the experience of the multiprofessional team. Setting a permanent vascular access in the pediatric population is technically more challenging. Although microsurgery can improve the technical results,[30-32] the surgeon`s experience seems to be the most significant factor for success of the procedure.[33]

Although permanent vascular access has afforded good results in children weighing less than 10-15 kg, AVF maturation may require 4-6 months, making it difficult to schedule the construction of a timely permanent access in young children who, frequently, reach the dialysis center at an advanced stage of their kidney disease, thus precluding the previous setting of a permanent access.[34-36]

Primary AVF failure is described in the literature and found at varied rates, both in adults and children. This rate has ranged from 10%, reported by Sanabia *et al*. in Spain, in 1993,[35] with microsurgical techniques for AVF construction, to 33%, reported by Sheth *et al*., in the USA, in 2002.[2] The latter figure is closer to our observation of 37.8% primary AVF failures. Literature results suggest that primary failure correlates more with the surgeon`s expertise, surgical technique and vessel integrity than with vein caliber or patient`s size or age.[2] In order to minimize the technical problems which jeopardize the success of vascular accesses, especially AVF and prostheses, some dialysis centers included in our study have more recently hired experienced vascular surgeons to construct the accesses. Prischl *et al.*[37] have shown that the surgeon`s experience was the main determinant of AVF patency. This has also been our observation: better AVF patency is reached when experienced surgeons are responsible for the construction.

Thrombosis is one of the main causes of AVF failure.[26,33] Approximately 80% of thrombotic events are related to venous stasis produced by stenotic lesions.[38] Excessive vessel compression after needle withdrawal, to avoid bleeding, and intradialytic and post-dialytic hypotensive episodes, which are frequent in children, are also important causes of thrombosis.[39] Although not computed in this study, our long experience in HD pediatric units has shown that hypotension is frequent during HD sessions, chiefly with inadequate ultrafiltration calculation or removal of too much water too fast. 84% of the AVF failures we observed were due to thrombosis (Figure 2). Studies have shown reduced AVF failure after implementation of access surveillance measures, with early stenosis detection through physical examination and radiological investigation.[40] We reported a 100% success rate of the attempts to recover the thrombosed access, although this practice was used in a small percentage of thrombosed AVFs.

AVF failure due to thrombosis occurred in two of the three children weighing less than 15 kg, with survival times of 129 and 214 days. Prior to the start of the study, four children weighing less than 15 kg died due to thrombosis-related AVF failure, after failure of their peritoneal dialysis. Multiple temporary catheters had to be inserted in different sites, leading to stenosis of central vessels, which precluded the use of any type of vascular access, including prostheses, and even renal transplantation. This dramatic situation is a reflex of many factors: the long period the children remain on HD, the impossibility of performing peritoneal dialysis because of repeat peritonitis, an inadequate choice of the dialysis modality,[41] the incapacity of the family to face the treatment challenges, and the delay to receive a kidney graft.

Besides the limitations which are inherent to a retrospective study, such as memory gaps and missing data, the poor quality of some medical records was a limitation we had to overcome. Seeking data quality improvement, we investigated the nursing records and the surgical catheter insertion log book, thus solving doubts concerning dates and incorrect or missing data in the medical records.

The small number of vascular surgeons trained to construct an AVF in children and low-weight adolescents must be highlighted. Pediatric dialysis centers should have a professional trained in microsurgery of small caliber vessels. Furthermore, the renal transplantation policy should be stimulated, prioritizing children as recipients and reducing the period on dialysis.

Conclusions:

Our results confirm literature data pointing to short-dwelling CVC infection as the main cause of access failure. These findings strengthen the need to construct a permanent access, such as an AVF, whose infection rate was 0%, as early as possible. If a catheter is necessary for patients on chronic HD, we recommend the use of long-dwelling CVC, as this practice will allow longer indwelling times with lower infection rates. If the insertion of a short-dwelling CVC is inevitable, this should remain in use the shortest time possible, replacement with a long-dwelling catheter being made whenever prolonged treatment is foreseen.

Thrombosis was the main cause of AVF failure, strengthening the need to implement a program for early detection of access dysfunction. Such program will allow the early diagnosis of stenoses, avoiding the development of thrombosis and increasing access survival.

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