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Original Article

Outcomes of Arteriovenous Fistula for Hemodialysis in Pediatric and Adolescent Patients

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Purpose: This retrospective review aimed to report the outcomes of arteriovenous fistula (AVF) and to evaluate the suitability of AVF as a permanent vascular access in pediatric populations.

Materials and Methods: Data were collected for all patients aged 0 to 19 years who underwent AVF creation for hemodialysis between January 2000 and June 2014.

Results: Fifty-two AVFs were created in 47 patients. Mean age was 15.7±3.2 years and mean body weight was 46.7±15.4 kg. Of the 52 AVFs, 43 were radiocephalic AVFs, 7 were brachiocephalic AVFs and 2 were basilic vein transpositions. With a mean follow-up of 49.7±39.2 months, primary patency was 60.5%, 51.4%, and 47.7% at 1, 3, and 5 years, respectively and secondary patency was 82.7%, 79.2% and 79.2% at 1, 3, and 5 years, respectively. Age, body weight, AVF type, the presence of a central venous catheter, use of anticoagulation therapy, and history of vascular access failure were not significantly associated with patency rates. There were 9 cases (17.3%) of primary failure; low body weight was an independent predictor. Excluding cases of primary failure, the mean duration of maturation was 10.0±3.7 weeks. During follow-up, 20 patients (42.6%) underwent kidney transplantation, with a median interval to transplantation of 36 months.

Conclusion: AVF creation in children and adolescents is associated with acceptable long-term durability, primary failure rate and maturation time. Considering the waiting time and limited kidney graft survival, placement of AVFs should be considered primarily even in patients expected to receive transplantation.

Key Words: Arteriovenous fistula, Renal dialysis, Pediatrics

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INTRODUCTION

The number of pediatric patients with end-stage renal disease (ESRD) receiving hemodialysis (HD) has been increasing [1]. Although transplantation is the treatment of choice, other types of renal replacement therapy are required while awaiting a transplant. In pediatric patients, HD is a more commonly used method of renal replacement therapy than peritoneal dialysis [2,3].

The Kidney Disease Outcomes Quality Initiative (K-DOQI) guidelines recommend placement of permanent access in dialysis patients aged 0 to 19 years who weigh >20 kg and are unlikely to receive a transplant within one year [4]. Despite this recommendation, more than 90% of pediatric patients still undergo initiation HD through a central venous catheter (CVC) [5]. The CVC has been widely used as a bridge to transplantation in spite of several disadvantages, including infection and restriction of activity. Technical

difficulties imposed by small vessel diameters and low arterial flow rates are additional reasons for the current low rates of arteriovenous fistula (AVF) creation [6].

Previous studies have focused on the patterns of vascular access for HD to emphasize the need for AVF placement [2,7,8]. There is limited information on the durability and usability of AVFs in patients with ESRD, including those on wait-lists for transplant. The aims of this study were to report the long-term outcomes of AVFs and to evaluate the suitability of AVF as a permanent vascular access in pediatric and adolescent populations.

MATERIALS AND METHODS

A retrospective review of all AVFs created in patients who underwent HD aged 0 to 19 years was performed. Fifty-two AVFs for HD were created in 47 patients between January 2000 and June 2014. Data on patient demographics, etiology of chronic kidney disease, histories of dialysis and transplantation, AVF type, and the results on follow-ups were collected via a retrospective review of medical records. This study was approved by the Institutional Review Board of Seoul National University Hospital (IRB no. H-1507-154-691).

Once the patient and his or her parents chose HD as a renal replacement modality, a vascular surgeon evaluated the patient`s venous and arterial suitability by performing a thorough physical examination. Vein mapping through duplex scan was performed in selected patients after the physical evaluation. The minimum acceptable venous size limit on duplex scan was 2.0 mm.

All AVFs were created according to the standard end-to-side anastomosis method with a continuous running suture. To decrease the extent of dissection and vasospastic response of vessels, flow control was performed with silastic vessel loops instead of vascular clamps. Loupe magnification was used in all cases, and an operating microscope was not used. Preoperative antiplatelet agents and intraoperative heparin were not routinely used. Postoperative management with heparin or antiplatelet agents was performed in selected patients, based on the immediate results of the AVFs: a weak fistula flow after anastomosis and high risk for thrombosis.

Patients were evaluated through physical examinations on the first postoperative day and at 2 and 6 weeks after AVF creation. The decision of whether AVF may be used for HD was made at 6 to 8 weeks after AVF creation with duplex ultrasonography. Further follow-up with duplex ultrasonography was performed when delayed maturation or surgical complications were detected. If the AVF had not matured successfully 8 to 10 weeks after the initial operation, intervention for correctable causes was undertaken.

Primary patency (i.e., intervention-free access survival) was defined as the interval from AVF creation until any intervention designed to maintain or re-establish patency; simply, it is the time interval of patency. Primary-assisted patency (i.e., thrombosis-free access survival) was defined as the interval from AVF creation until access thrombosis, or the time interval of patency, including intervening manipulations designed to maintain the functionality of a patent AVF. Secondary patency was defined as the time interval from AVF creation until access failure or thrombosis, or the time interval of patency including intervening manipulations designed to re-establish the functionality in a thrombosed AVF [9]. Primary failure is defined as the inability to use the AVF even once.

Continuous data were summarized as median with ranges, and categorical data were summarized as proportions and percentages. Logistic regression analysis was used to determine predictors of primary failure. The Kaplan-Meier method was used to calculate graft and patient survival rates. Cox proportional hazards multivariate regression models were used to estimate the relative risks for access failure. A P-value of <0.05 was considered statistically significant. All statistical analyses were performed with PASW Statistics ver. 18.0 software (IBM Co., Armonk, NY, USA).

RESULTS

1) Patient characteristics

Median age was 17 (range, 8-19) years: 0-9 (n=3), 10-14 (n=12), 15-19 (n=32). Median body weight was 45 (range, 22-98) kg. Thirty-two male and 15 female patients were included in this study. The etiologies of chronic kidney disease were glomerulonephritis in 20 patients (42.6%), urologic causes in 8 (17.0%), hypo-dysplasia in 4 (8.5%), Alport syndrome in 4 (8.5%), nephrectomy due to malignant disease in 1 (2.1%), polycystic kidney disease in 1 (2.1%), others, including renal coloboma syndrome, neurofibromatosis, Henoch–Schönlein purpura, myelomeningocele, amyloidosis, in 5 (10.6%), and unknown cause in 4 (8.5%). At the time of AVF creation, 21 patients (44.7%) were undergoing HD through a CVC, 17 patients (36.2%) had not undergone renal replacement therapy, and 9 patients (19.1%) decided to convert from peritoneal dialysis to HD due to complications or insufficient dialysis. Fifteen patients (31.9%) had a previous history of transplant (Table 1).

Table 1. Patient demographics (n=47)

Characteristic	Value
Age (y)	17 (8-19)
Body weight (kg)	45 (22-98)
Female	15 (31.9)
The etiology of chronic kidney disease	
Glomerulonephritis	20 (42.6)
Urologic causes	8 (17.0)
Hypo-dysplasia	4 (8.5)
Alport syndrome	4 (8.5)
Nephrectomy due to malignant disease	1 (2.1)
Polycystic kidney disease	1 (2.1)
Others	5 (10.6)
Unknown	4 (8.5)
Renal replacement therapy	
Hemodialysis through central venous catheter	21 (44.7)
Peritoneal dialysis	17 (36.2)
No dialysis yet	9 (19.1)
Previous history of a kidney transplant	
None	32 (68.1)
Once	13 (27.7)
Twice	2 (4.3)

Values are presented as median (range) or number (%).

2) Perioperative evaluation and management

Of the 52 AVFs, 43 cases were radiocephalic AVFs, 7 cases were brachiocephalic AVFs and 2 cases were forearm basilic vein transpositions. Arteriovenous grafts with prosthetic material were not performed in any of the patients. Preoperative vein mapping was performed in 12 cases and all of them were performed after January 2012 according to the revised center protocol for vascular access creation, which favored routine duplex mapping. The median diameter of the vein and artery were 27 (range, 21-47) mm and 20 (range, 14-31) mm, respectively. Ten patients were treated postoperatively with low molecular weight heparin (LMWH) and 7 of them had taken aspirin based on the immediate results of the AVFs (Table 2).

3) Patency

The mean follow-up duration for all AVFs was 49.7±39.2 months. At 1, 3 and 5 years, the primary patency rates for all AVFs, including cases of primary failure, were 60.5%, 51.4%, and 47.7%, respectively; primary assisted patency rates were 78.8%, 75.6%, and 72.1%, respectively; and secondary patency rates were 82.7%, 79.2% and 79.2%, respectively (Fig. 1).

Table 2. Baseline characteristics of vascular access (n=52)

Characteristic	AVFs
Type of AVF	
Radio-cephalic	43 (82.7)
Brachio-cephalic	7 (13.5)
Basilic vein transposition	2 (3.8)
Preoperative evaluation	
Duplex scan	12 (23.1)
Physical examination only	40 (76.9)
Measured vessel (mm)	
Artery	27 (21-47)
Vein	20 (14-31)
Perioperative anti-thrombotics	
None	42 (80.8)
LMWH	3 (5.8)
LMWH followed by aspirin	7 (13.5)

Values are presented as number (%) or median (range).
AVF, arteriovenous fistula; LMWH, low molecular weight heparin.

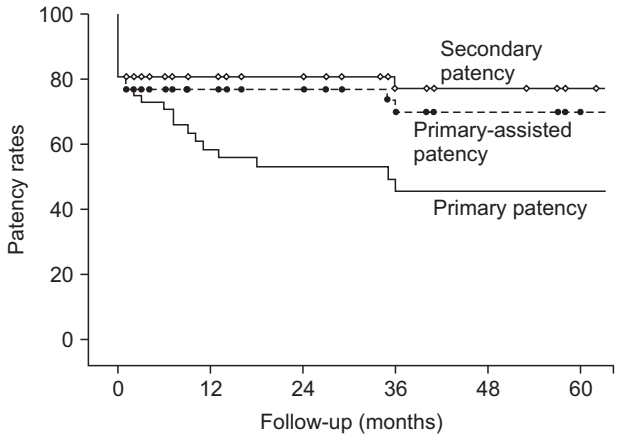

Fig. 1. Kaplan–Meier curves show, primary-assisted, and secondary patency rates of 52 arteriovenous fistulas in 47 patients.

When age was evaluated as a continuous variable, there was a tendency toward improved primary patency with increasing age; however the tendency was not statistically significant (hazard ratio, 0.832; 95% confidence interval [CI], 0.678-1.020; P=0.077) (Table 3). Results of Cox regression analysis indicated that no other factor, including sex, body weight, AVF type, the presence of a CVC, previous history of vascular access failure, and use of anticoagulation therapy was significantly associated with primary patency.

When the patients were grouped as <13 or >13 years old (the fourth quartile of age), there was a tendency for increased primary (39.2% vs. 65.3% at 1-year, P=0.05) and

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Table 3. Cox proportional hazard regression multivariate analysis for predictors of poor primary patency

Parameter	HR (95% CI)	P-value
Age (y)	0.832 (0.678-1.020)	0.077
Body weight	0.976 (0.933-1.020)	0.284
Female	1.047 (0.342-3.201)	0.936
Type of vascular access (R-C AVF)	1.216 (0.141-10.483)	0.858
Presence of a CVC	1.720 (0.761-3.884)	0.192
History of vascular access failure	2.713 (0.539-13.652)	0.226
Anticoagulation therapy	0.339 (0.077-1.505)	0.155

HR, hazard ratio; CI, confidence interval; R-C AVF, radio-cephalic arteriovenous fistula; CVC, central venous catheter.

primary-assisted patency (57.1% vs. 84.2% at 1-year, P=0.05) in older patients. There was no significant difference in secondary patency (71.4% vs. 84.2% at 1-year, P=0.12).

4) Primary failure

There were 9 cases (17.3%) of primary failure. These failures occurred in 8 patients with a 17-year-old male patient experiencing two primary failures. The cases of primary failure included 6 radiocephalic AVFs, 2 brachiocephalic AVFs and 1 basilic vein transposition. The median age of the patients was 16 (range, 7-19) years and the median body weight was 32 (range, 22-62) kg. Three of these patients underwent vein mapping and the diameters of veins were 22, 27, and 36 mm, respectively and the diameters of arteries were 14, 17, and 19 mm, respectively. Four of them were subjected to anticoagulation therapy due to weak fistula flow after anastomosis or high risk for thrombosis. Primary failure occurred more frequently in patients with small body weight, when body weight was evaluated as a continuous variable (odds ratio, 0.907; 95% CI, 0.842-0.977; P=0.010).

Among the patients with primary failure, a 7-year-old boy who was treated with LMWH showed a coagulation abnormality and developed a hematoma, which was believed to be the cause for the AVF thrombosis. A 12-year-old boy kept his arm flexed for several hours and was found to have a thrombosed brachiocephalic AVF 9 days after the initial surgery. The parents no longer consented to revision of the AVF due to fear of re-thrombosis; they opted for peritoneal dialysis.

5) Maturation and complications

Excluding the cases of primary failure, the mean duration of maturation was 10.0±3.7 weeks. During the study period, 36 interventions were performed in 15 AVFs. Twelve of 36 procedures were performed during the first year after AVF creation. The mean number of interventions per AVF, including both endovascular therapy and surgery, was 0.84±1.88, which amounted to 0.20 interventions per 12 access-months. The most common procedure was balloon angioplasty for stenosis (n=23). The locations of the stenosis were juxta-anastomosis (n=13), outflow vein (n=4), multiple stenosis in outflow veins (n=5), and artery (n=1). No patient showed stenosis in the anastomosis or central veins. Others included interposition graft for stenosis (n=1), proximalization of arterial inflow (n=3), branch ligation for delayed maturation (n=2), thrombectomy (n=3), and excision of aneurysm (n=3).

6) Long-term outcomes of patients

During the study period, 20 patients (42.6%) underwent kidney transplantation and 4 of them returned to HD due to graft failure. The median duration between the AVF creation and kidney transplantation was 36 (range, 3-87) months. Among the rest of the patients, 19 patients (40.4%) continued HD, 2 patients (4.3%) converted to peritoneal dialysis and 6 patients (12.8%) were transferred to another center and were lost to follow-up.

Among the 8 patients with primary failure, 1 patient converted to peritoneal dialysis and 7 patients continued HD: 5 with a newly created functional AVF and 2 with CVC. During follow-up, 4 of them underwent kidney transplantation at 71, 64, 18, and 5 months after AVF creation.

DISCUSSION

The feasibility of AVF creation in pediatric populations has been established and recommendations have also been documented [4]. The primary patency rates in pediatric populations at 6 months to 2 years have been reported to be as approximately 50%-65%, which is similar to the results in adults [6,10-12]. A few recent studies are available showing the excellent outcomes in children [13]. Wartman et al. [14] evaluated the outcomes of 101 AVFs and demonstrated primary and secondary patency rates at 2 years as 83% and 92%, respectively.

Although these documented outcomes are acceptable, some have considered the incidence of primary failure to be sufficiently high to be a barrier for AVF placement in children and adolescents [1]. The longer maturation time in children than that in adults and the technical difficulties imposed by small diameters of the vessels are other reasons for a reluctance to create AVFs in children [11].

Based on such factors, CVCs have remained as the most commonly used access in children on chronic HD [1]. As is

well known, CVC-related infections are very common and are the leading cause of morbidity and mortality in children receiving HD therapy [3]. With the success of Fistula First Breakthrough Initiative, the prevalence of native AVF was on the rise and the general perception with regard to AVFs had changed [14]. However, an AVF rate increase has not been observed in the pediatric and adolescent populations. Almost 60% of children still use a CVC for long-term dialysis and 89% of children start HD via a CVC in the United States [15,16].

This study showed an acceptable incidence of primary failure. By undertaking careful preoperative evaluation and providing postoperative care, the risk of primary failure can be lowered. A small body weight was a significant factor influencing primary failure; therefore, proper vein selection is required especially in small children. The patency rates achieved in this study were comparable to those in adult patients [17]. Thus, placement of AVFs in children and adolescents should be actively considered when a permanent vascular access for long-term HD is required.

Excluding cases of primary failure, 15 of 43 AVFs (34.9%) required later interventions. This was not a small proportion. However more than one-third of them were performed in the first year after AVF creation and the incidence of interventions decreased by about half in the second year. Even though endovascular or surgical treatment was required to achieve maturation and early patency, mid- and long-term patency were maintained without the need for frequent interventions. During the first year after AVF creation, active surveillance and timely intervention are important to achieve a favorable outcome.

One reason suggested for the high prevalence of CVC use in pediatric patients is that many patients expect to receive a kidney transplant within a short period. In this study, 20 of 47 patients (42.6%) underwent kidney transplantation, yet the waiting time for a kidney transplant was not short. The median waiting time was 36 months and the longest interval was 81 months. According to the annual reports of the United States Renal Data System, 60% of pediatric HD patients would not receive a transplant within the first year of HD initiation [14]. The reported waiting time for a kidney transplant in patients aged 6-10 and 11-18 years were 507 and 1,396 days, respectively, in Korea [18]. The actual waiting time for a transplant was longer than expected; thus, the rationale for using a CVC is invalid. AVF creation should be considered primarily even in patients with plans for transplantation if a living donor is not available.

In addition, many pediatric patients might live longer than the graft survival and must return to HD. Therefore, a strategy for development of a long-term plan for vascular access is necessary to avoid CVC use and central vein stenosis. In addition, 13 of the 47 patients experienced peritoneal dialysis-associated complications or peritoneal dialysis catheter insertion failure. In this group of patients, long-term maintenance of HD is essential and AVF creation is required to avoid the use of CVCs.

Weak arterial inflow and small vein diameter are inevitable in children. Several methods, such as the use of microsurgical techniques, have been attempted to overcome these difficulties and increase patency in small children. Bagolan et al. [10] reported that adoption of microsurgical techniques significantly lowered the primary failure rate. Even though we achieved comparable results to that study without using a microscope, we think microsurgical techniques are worth adopting in some subgroups of patients, such as those with low body weight [1,10,19,20].

Antiplatelet medications and cessation of anti-hypertensive medications were other methods recommended [16]. However, there are few evidences supporting the routine use of antithrombotic therapy. Preoperative duplex is one of the preferred methods to improve AVF maturation rates and highly recommended these days. It may improve outcomes of AVF, although not mandatory [21]. This study included patients who underwent AVF creation before preoperative vein mapping was typically performed, and only some had data on duplex scan. Further study with duplex results is needed to prove the importance of preoperative vein mapping in pediatric patients.

Many patients with failed AVFs were non-compliant to instructions and precautions due to age or mental retardation accompanying the original disease. During the early postoperative period, especially in a pediatric population, close supervision is required so as to not compress the AVF site by bending the arm for a long time. To achieve successful postoperative care and patient education levels, a multidisciplinary team that includes vascular surgeons, nephrologists, and HD nurses is important [1,15].

This study had several limitations. First, it involved a small number of patients, which limited the power of the statistical analyses, and the study`s retrospective nature imparted inherent biases. Second, only a small proportion of patients were aged less than 10 years and further study with a greater proportion of young children is required to show any unique or specific results of AVFs in young pediatric populations.

CONCLUSION

In conclusion, creation of AVF for HD in children and adolescents is feasible and shows acceptable long-term durability. The incidence of primary failure and the dura-

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tion required for maturation were comparable to those reported in contemporary studies of adult populations. Considering the long duration on a waiting list and limited graft survival of a transplanted kidney, placement of AVF for maintenance HD should be considered primarily even in patients expecting kidney transplantation.

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