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Hemodialysis and peritoneal dialysis access related outcomes in the pediatric and adolescent population☆

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ABSTRACT

Background: There is paucity of comparative data on the objective performance of arteriovenous fistulas (AVF), grafts (AVG), hemodialysis (HD) catheter and peritoneal dialysis (PD) catheter in the pediatric population.
Methods: A retrospective analysis of all patients <21 years in the United States Renal Database System who had an AVF, AVG, HD catheter or PD catheter placed for dialysis access between 1/2007 and 12/2014 was performed. Multivariable cox regression was used to evaluate mortality, patency (primary, primary-assisted and secondary), maturation and catheter survival.
Results: The 11,575 patients studied comprised of 9445 (82%) HD, 1435 (12%) PD, 528 (4.6%) HD to PD and 167 (1.4%) PD to HD patients. The HD subcohort comprised of 1296 (13.7%) AVF initiates, 199 (2.1%) AVG initiates, 1347 (14.3%) AVF converts after initial HD catheter use, 292 (3.1%) AVG converts and 6311 (67%) patients who persistently utilized HD catheters. There was no difference between PD and HD in patients 0–5 (aHR: 1.36; 95% CI: 0.89–2.07; P = 0.15) and 6–12 years (aHR: 1.05; 95% CI: 0.72–1.52; P = 0.8). However, PD was associated with 73% and 76% increase in mortality relative to HD among patients in the 13–17 (aHR: 1.73; 95% CI: 1.35–2.21; P < 0.001) and 18–20 (aHR: 1.76; 95% CI: 1.38–2.24; P < 0.001) age categories. AVG was associated with 78% increase in mortality compared to AVF (aHR: 1.78; 95% CI: 1.41–2.25; P < 0.001). Persistent use of HD catheters was associated with 29% increase in mortality (aHR: 1.29; 95% CI: 1.07–1.57; P = 0.009) compared to initiation and persistent use of AVF. Conversion from HD catheter to AVF was associated with 66% decrease in mortality compared to persistent HD catheter use (aHR: 0.34; 95% CI: 0.28–0.40; P < 0.001). Primary, primary assisted and secondary patency were higher for AVF compared to AVG.
Conclusion: There was no difference in risk adjusted mortality between HD and PD in children less than 13 years. PD is associated with higher mortality compared to HD in adolescents. Initiation of HD with AVF is associated with better patency and patient survival relative to AVG and persistent use of HD catheters in pediatric patients irrespective of transplant potential. Conversion from HD catheter to AVF or AVG in patients who inevitably initiate HD with a catheter is associated with better survival compared to persistent HD catheter use.
Type of study: Retrospective cohort study.
Level of evidence: Level II.

Despite the recent plateau in the prevalence of End Stage Renal Disease (ESRD) in the US pediatric population, overall increase in prevalence was recorded in recent decades: 29.6 per million in 1980 to 86 per million in 2010 [1–3]. Although renal transplantation remains the definitive treatment for ESRD, only 24% of renal transplants are preemptive [4]. Hemodialysis (HD) remains the more prevalent dialysis option for children and adolescents in the US (63%), relative to peritoneal dialysis (PD) [2,5,6]. Few studies have evaluated population based differences in HD versus PD outcomes in pediatric patients.

The mode of HD access is a recognized contributor to survival and adequacy of renal replacement therapy in adults [7–9]. Elucidation of

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factors that impact HD related outcomes in pediatric patients and efforts at improving same, deserve significant attention in view of their longer life expectancy. Unique aspects of the pediatric population including the potential for renal transplantation and preservation of vascular options for future use must be taken into account when planning vascular access for hemodialysis in these patients.

Few studies of relatively small cohorts of less than 200 patients have examined outcomes of arteriovenous fistulas (AVF) and arteriovenous grafts (AVG) in the pediatric population [10–19]. Furthermore, children and young adults are preferential recipients of renal transplants and temporizing with an HD catheter until renal transplantation is common practice in these patients. The complications associated with HD catheter use are known and well documented [20,21]. However, little is known of the impact of prior and persistent HD catheter use on outcomes in the pediatric population. This study is a comprehensive audit of the utilization of HD and PD access, their associated mortality, patency of AVF and AVG, the impact of prior and persistent HD catheters and catheter survival in a population based cohort of children and adolescents.

1. Methods

1.1. Study cohort

A retrospective analysis of patients <21 years who underwent placement of an AVF, AVG, HD catheter or PD catheter between January 1, 2007 and December 31, 2014 in the United States Renal Database System (USRDS) was performed. The USRDS is a prospective database of all ESRD patients receiving renal replacement therapy in the United States. This database is maintained by integrating patient specific data from the Center for Medicare and Medicaid service (CMS), Center for Disease Control, United Network for Organ Sharing (UNOS) and ESRD networks. Annual reports published since 1988 include patient demographics, hospitalizations and procedures, and mortality and cost, among other parameters [22]. The age cutoff of 21 years was used in accordance with the definition by the American Academy of Pediatrics [23]; and results were further stratified into patients 0–5 years, 6–12 years, 13–17 years and 18–20 years to evaluate sub group differences. This study was approved by the Johns Hopkins Institutional Review Board and the need for individual patient consent was waived. Data on patients' initial HD access type, demographic and medical characteristics were collected from CMS Form 2728, “End Stage Renal Disease Medical Evidence Report”. Follow-up data were obtained from the USRDS-Medicare linked institutional claims database thus assumed to be complete. Treatment groups and interventions were identified using current procedure terminology codes: arteriovenous fistula: 36818, 36819, 36820, 36821, 36825; arteriovenous graft: 36830; HD catheter placement: 36557, 36558; HD catheter removal: 36581, 36589; PD catheter placement: 49324, 49418, 49421; PD catheter removal: 49422; PD catheter revision: 49325; angioplasty: 35475, 35476, 75962, 75978; stenting: 37205, 75960; thrombectomy/thrombolysis: 36831, 36833, 36870; AVF/AVG revision: 36832, 36833.

1.2. Study outcomes

The primary outcomes of this study were mortality, AVF and AVG maturation, patency (primary, primary assisted and secondary), and catheter survival. Patient mortality data were collected from CMS form 2746, “ESRD Death Notification Form”. AVF and AVG patency was defined in accordance with Society for Vascular Surgery standards [24]. Primary patency was the interval from AV access creation to the first intervention performed to maintain or reestablish patency or access thrombosis. Primary assisted patency was the interval from AV access placement to the first intervention to relieve thrombosis. Secondary patency was interval from AV access creation to thrombosis/abandonment and subsequent replacement with a new HD catheter, AVF or AVG. AV access maturartion was the interval from placement to use. HD and PD catheter survival was the interval between placement and removal.

1.3. Statistical methods

Descriptive analyses of the study groups were performed using chi-square, Student t-tests and analysis of variance as appropriate. Kaplan–Meier, log rank tests, univariable and multivariable Cox regression analyses were employed to evaluate the outcomes adjusting for baseline characteristics; and inferences were made from the risk adjusted analyses. The variables included in the multivariable regression were: age, gender, race, diabetes, hypertension, functional dependence/immobility, cancer, subsequent renal transplantation. Patients who imitated HD via catheter and later had AVF or AVG placed but did not achieve HD catheter free dialysis (HD-CFD) were considered to have failed to mature the AVF or AVG. Failure was deemed to have occurred on the date a subsequent access (AVF, AVG) was placed or by the time the patient was expected to achieve HD-CFD and continued to be dialyzed through HD catheter, whichever comes first. Probability scores were computed based on the probability of attaining HD-CFD per patient characteristics. The probability scores were generated using regression models that predict attainment of CFD based on patient characteristics in the cohort of patients who did and did not achieve CFD. The expected time to HD-CFD for each patient was calculated as the median time to HD-CFD for patients within the same centile of propensity scores. Eligible patients were censored on the date of death, kidney transplant or at the end of the study. Relative mortality for patients who converted from HD catheter to permanent HD access was computed adjusting for patient characteristics, duration of prior HD catheter exposure, etiology of ESRD and receipt of renal transplant. Statistical models were built based on predictive variables from univariate analyses, prior literature, guidance of likelihood ratio tests and Akaike's information indices with a goal to achieve model parsimony. All analyses were performed using Stata 14.1 statistical software (StataCorp, College Station, Texas), and statistical significance was accepted at $P < .05$.

2. Results

2.1. Patient distribution and access utilization

There were 11,575 patients studied. Of these, 9445 (82%) received renal replacement therapy via HD, 1435 (12%) via PD, 528 (4.6%) commenced with HD but converted to PD during the study period while 167 (1.4%) commenced with PD and later converted to HD. The mode of initial vascular access in the 9445 patients who utilized HD all through the study period was HD catheter in 7950 (84%) patients, AVF in 1296 (14%) patients and AVG in 199 (2%) patients (Fig. 1). During the study period, 1347 (17%) patients who initiated HD via catheter converted to AVF, while 292 (4%) converted to AVG, leaving 6311 (79%) patients who persistently dialyzed via HD catheter during the study period. The patient characteristics are listed in Tables 1–3. Median follow up was 25.6 (range: 10.2–52.2) months for HD patients, 33.1 (range: 12.0–62.5) months for PD patients, 24.4 (range: 10.2–44.0) months for patients who converted from HD to PD and 35.7 (range: 19.2–60.7) months for patients who converted from HD to PD.

2.2. Access related patient mortality

Kaplan Meier estimates of patient survival comparing patients who received HD vs. PD all through the study period were 95 vs 93% at 1 year, 83 vs 75% at 5 years and 79 vs 66% at 7 years ($p < 0.001$) (Fig. 2, Table 4). The risk adjusted analyses showed 53% increase in mortality for PD-only patients (aHR: 1.53; 95% CI: 1.32–1.77; $P < 0.001$); and 30% increase in mortality for those who converted from HD to PD (aHR: 1.30; 95% CI: 1.01–1.68; $P = 0.039$) compared to patients who remained on HD through the study period. There was no significant difference in

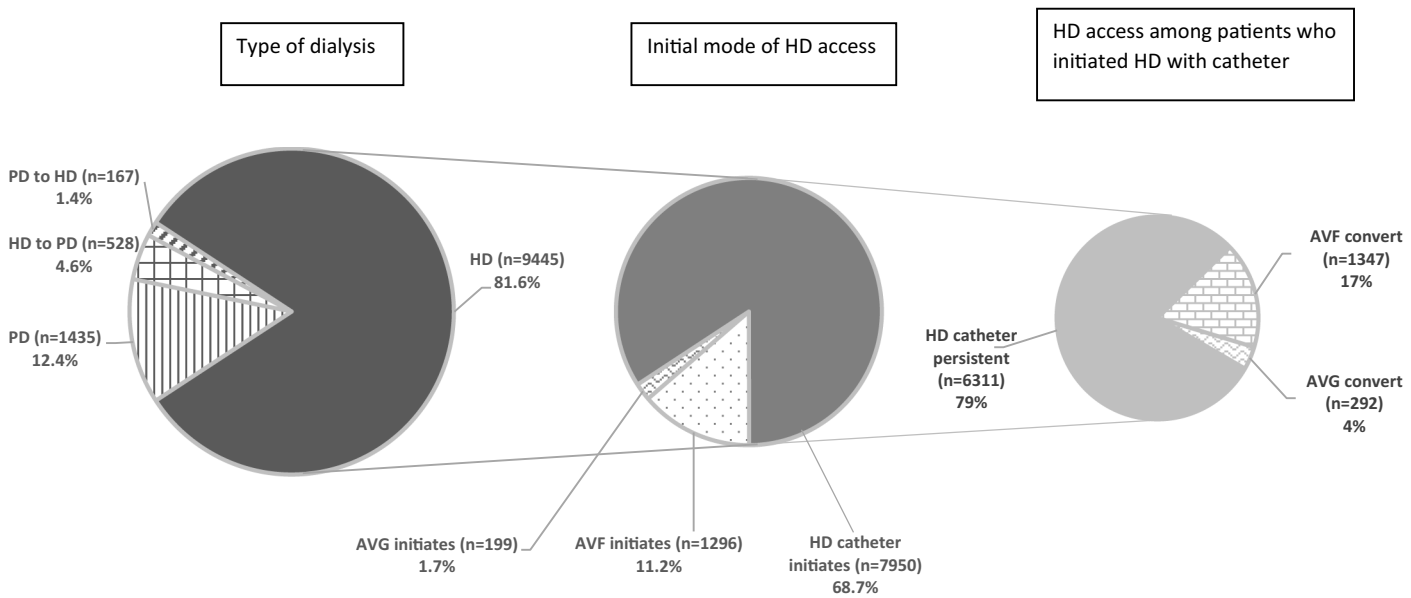

Fig. 1. Distribution of patients in study cohort and subcohorts. HD: hemodialysis; PD: peritoneal dialysis; HD to PD: patients who initiated renal replacement with HD but transitioned to PD over the study period; PD to HD: patients who initiated renal replacement with PD but transitioned to HD over the study period; AVF: arteriovenous fistula; AVG: arteriovenous graft; AVF initiates: patients who initiated HD with AVF; AVG initiates: patients who initiated HD with AVG; HD catheter initiates: patients who initiated HD with HD catheter; AVF convert: patients who initiated HD with catheter but converted to AVF during the study period; AVG convert: patients who initiated HD with catheter but converted to AVG during the study period; HD catheter persistent: patients who imitated HD with catheter and utilized same through the study period.

Table 1
Characteristics of pediatric patients who initiated renal replacement therapy via hemodialysis (HD), peritoneal dialysis (PD), conversion from hemodialysis to peritoneal dialysis (HD to PD) and converted from peritoneal dialysis to hemodialysis (PD to HD).

Characteristic	HD $n = 9445$ (81.6%)	PD $n = 1435$ (12.4%)	HD to PD converts $n = 528$ (4.6%)	PD to HD converts $n = 167$ (1.4%)	P value
Age in years: mean (SD/IQR)	14.6 (5.3/12–19)	12.2 (6.6/7–18)	14.7 (5.3/12–19)	14.4 (5.6/12–19)	<0.001
Female gender (%)	42.8	50.5	54.9	50.3	<0.001
Race:					
White (%)	55.9	57.6	57.0	53.3	
Black (%)	27.6	29.1	28.6	30.5	<0.001
Hispanic (%)	11.2	6.2	9.3	9.0	
Other (%)	5.3	7.1	5.1	7.2	
Diabetes mellitus (%)	2.9	1.8	2.5	0	0.017
Hypertension (%)	54.2	48.2	56.6	59.9	<0.001
Cancer (%)	1.7	1.0	1.0	0.6	0.094
Immobility (%)	1.7	2.2	0.6	1.8	0.11
Weight < 20 kg (%)	8.3	22.1	8.9	6.6	<0.001

HD: hemodialysis; PD: peritoneal dialysis; IQR: interquartile range.

Table 2
Characteristics of pediatric patients who initiated hemodialysis via AVF or AVG, converted to AVG or AVF after prior HD catheter use or persisted on catheter for hemodialysis.

Characteristic	AVF initiates $n = 1296$ (13.7%)	AVG initiates $n = 199$ (2.1%)	AVF converts $n = 1347$ (14.3%)	AVG converts $n = 292$ (3.1%)	HD catheter persistent $n = 6311$ (66.8%)	P value
Age in years: mean (SD/range)	15.3 (4.9/13–19)	14.4 (5.2/12–19)	15.3 (5.0/13–19)	14.9 (5.3/12–19)	14.3 (5.5/12–19)	<0.001
Female gender (%)	32.7	52.3	44.1	53.1	43.8	<0.001
Race:						
White (%)	61.7	50.3	51.8	44.5	56.2	<0.001
Black (%)	26.5	37.2	34.4	44.9	25.3	
Hispanic (%)	6.9	8.5	10.0	5.8	12.7	
Other (%)	4.9	4.0	3.9	4.8	5.7	
Diabetes mellitus (%)	2.2	3.5	2.8	3.1	3.0	0.62
Hypertension (%)	56.3	54.8	57.9	52.7	53.1	0.010
Cancer (%)	1.4	1.5	0.8	2.1	2.0	0.035
Immobility (%)	0.4	0.5	1.4	2.1	2.1	<0.001
Weight < 20 kg (%)	4.9	7.0	5.4	8.6	9.6	<0.001

AVF: arteriovenous fistula; AVG: arteriovenous graft; HD: hemodialysis.

mortality for patients who converted from PD to HD compared to those who utilized HD through the study period (aHR: 1.20; 95% CI: 0.81–1.79; P = 0.36). The association between dialysis type and mortality was modified by patients' age. Within the categories of patients 0–12 years, there was no significant difference in mortality between PD and HD (Table 5). However, there was a 73% and 76% increase in mortality for PD relative to HD among patients in the 13–17 (aHR: 1.73; 95% CI: 1.35–2.21; P < 0.001) and 18–20 (aHR: 1.76; 95% CI: 1.38–2.24; P < 0.001) age categories respectively (Table 5). On the continuous spectrum of age, the relative increase in mortality for PD relative to HD commenced at 13 years.

Comparing AVF initiates vs AVG initiates vs HD catheter persistent groups, unadjusted Kaplan Meier estimates of patient survival were highest for AVF and least for AVG at all time points: 97.5 vs 94.9 vs 94.2% at 1 year; 86 vs 77.8 vs 84% at 5 years and 81.3 vs 74.7 vs 80.4% at 7 years; P < 0.001 (Fig. 3, Table 6). Risk adjusted analyses demonstrated 78% increase in mortality with AVG compared to AVF (aHR: 1.78; 95% CI: 1.41–2.25; P < 0.001). When stratified according to persistent use and conversion types, initiation with an HD catheter and conversion to AVF were associated with 27% increase in mortality (aHR: 1.27; 95% CI: 1.01–1.61; P = 0.043), initiation with an HD catheter and conversion to AVG was associated with 2.2 fold increase in mortality (aHR: 2.19; 95% CI: 1.62–2.97; P < 0.001), while persistent use of HD catheters was associated with 29% increase in mortality (aHR: 1.29; 95% CI: 1.07–1.57; P = 0.009) compared to patients who initiated and persistently utilized AVF for HD. Adjusting for duration of HD catheter exposure, initiation of HD

Table 3
Distribution of patients in the age categories.

Treatment type/Age group	0–5 years $n = 1217$ (10.5)	6–12 years $n = 2013$ (17.4)	13–17 years $n = 3961$ (34.2)	18–20 years $n = 4384$ (37.9)
Hemodialysis	70.8	78.5	83.1	84.7
Peritoneal dialysis	24.2	15.3	11.1	9.0
HD to PD converts	3.6	4.8	4.4	4.8
PD to HD converts	1.4	1.4	1.4	1.5

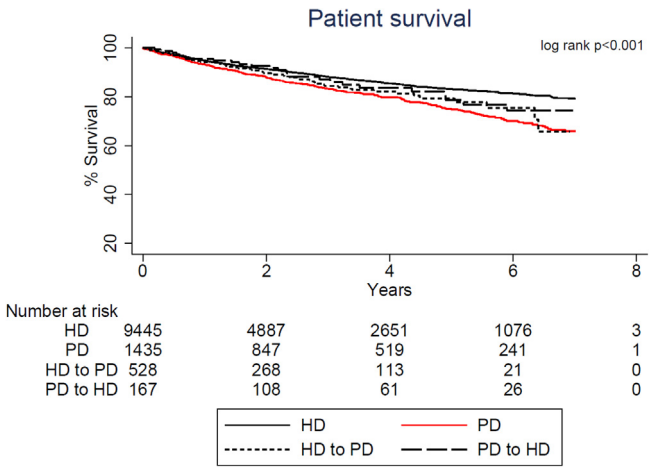

Fig. 2. Unadjusted Kaplan–Meier estimates of survival of HD, PD, HD to PD and PD to HD patients. Log rank p-value: comparing survival of all groups.

Table 4
Unadjusted Kaplan–Meier estimates of survival over time for hemodialysis (HD), peritoneal dialysis (PD), HD to PD converts and PD to HD converts.

Group	1 Year % (95% CI)	2 years % (95% CI)	3 years % (95% CI)	4 years % (95% CI)	5 years % (95% CI)	6 years % (95% CI)	7 years % (95% CI)	P-value
HD	94.9 (94.4–95.4)	91.4 (90.8–92.1)	88.2 (87.4–89.0)	85.5 (84.6–86.4)	83.2 (82.1–84.3)	81.3 (80.0–82.5)	79.3 (77.8–80.8)	<0.001
PD	93.3 (91.8–94.5)	88.0 (86.0–89.7)	83.4 (81.0–85.5)	79.8 (77.2–82.2)	75.0 (71.9–77.8)	70.2 (66.6–73.4)	66.0 (61.8–69.8)	
HD to PD	94.2 (91.6–96.0)	89.7 (86.3–92.4)	84.4 (79.9–88.0)	82.1 (77.2–86.1)	79.4 (73.5–84.2)	75.5 (67.1–82.0)	65.7 (49.5–77.8)	
PD to HD	95.6 (91.0–97.9)	92.7 (87.2–95.9)	87.1 (79.9–91.9)	83.8 (75.6–89.4)	78.8 (68.9–85.8)	74.3 (62.7–82.8)	74.3 (62.7–82.8)	

HD: hemodialysis; PD: peritoneal dialysis; CI: confidence interval.

Table 5
Relative hazards of mortality of PD relative to HD within the sub categories of age.

Treatment type/Age group	0–5 years HR (95% CI); p-value	6–12 years HR (95% CI); p-value	13–17 years HR (95% CI); p-value	18–20 years HR (95% CI); p-value
PD	1.36 (0.89–2.07); 0.15	1.05 (0.72–1.52); 0.8	**1.73** (1.35–2.21); <**0.001**	**1.76** (1.38–2.24); <**0.001**
HD to PD converts	0.73 (0.26–2.03); 0.55	0.69 (0.30–1.57); 0.37	1.42 (0.92–2.20); 0.11	**1.58** (1.11–2.25); **0.012**
PD to HD converts	0.63 (0.09–4.55); 0.65	0.28 (0.04–1.97); 0.20	1.41 (0.75–2.66); 0.29	1.57 (0.90–2.73); 0.11

HD: hemodialysis; PD: peritoneal dialysis; CI: confidence interval,

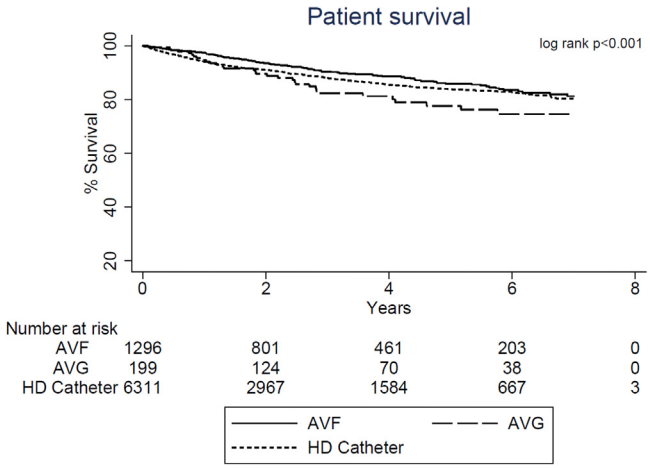

Fig. 3. Unadjusted Kaplan–Meier estimates of survival of patients who underwent HD via AVF, AVG and HD catheters. Log rank p-value: comparing survivor function of AVF, AVG and HD catheter groups.

with a catheter and conversion to AVF were associated with 66% decrease in mortality (aHR: 0.34; 95% CI: 0.28–0.40; P < 0.001), while conversion to AVG was associated with a 33% decrease in mortality (aHR: 0.67; 95% CI: 0.51–0.87; P < 0.001) compared to persistent HD catheter use. The predictors of mortality were female gender (aHR: 1.18; 95% CI: 1.06–1.32; P = 0.002), diabetes (aHR: 2.07; 95% CI: 1.63–2.63; P < .001), hypertension (aHR: 1.25; 95% CI: 1.12–1.40; P < .001), cancer (aHR: 3.14; 95% CI: 2.40–4.09; P < .001) and immobility (aHR: 3.64; 95% CI: 2.77–4.78; P < .001). Age was not a significant predictor of mortality (aHR: 1.00; 95% CI: 0.99–1.01; P = 0.55) and there was no difference in mortality comparing patients who were 6–12 years (aHR: 0.92; 95% CI: 0.74–1.15; P = 0.48), 13–17 years (aHR: 0.97; 95% CI: 0.79–1.18; P = 0.74) and 18–20 years (aHR: 1.02; 95% CI: 0.84–1.25; P = 0.81) relative to those who were 0–5 years.

2.3. Access patency and access survival

Maturation rate and median maturation interval for AVF vs AVG were 75% vs 80% (p = 0.82) and 56 vs 32 days (p = 0.37). Comparing AVF vs. AVG, primary patency was 54 vs 36% at 1 year, 31 vs 16% at 5 years and 27 vs 14% at 7 years (p < 0.001, Fig. 4, Table 7). Primary assisted patency was 62 vs 45% at 1 year, 42 vs 22% at 5 years and 36 vs 18% at 7 years (p < 0.001) (Fig. 5). Secondary patency was 68 vs 60% at 1 year, 53 vs 39% at 5 years and 48 vs 31% at 7 years (p < 0.001) (Fig. 6). The mean number of interventions required to achieve these patency rates was lower for AVF at 2.0 per fistula compared to 5.3 per AVG (P < .001). The proportion of patients requiring interventions was lower for AVF than AVG (35 vs 56%; P < .001). The majority of interventions were endovascular (70%) compared to open surgical interventions (30%). The risk adjusted analysis, showed 54% increase in primary patency (aHR: 1.54; 95% CI: 1.37–1.73, P < .001), 59% increase in primary assisted patency (aHR: 1.59; 95% CI: 1.40–1.80, P < .001) and 19% increase in secondary patency (aHR: 1.19; 95% CI: 1.04–1.37, P = 0.012) for AVF compared to AVG. AV access patency was 24% higher for males compared to females (aHR: 1.24; 95% CI: 1.13–1.54, P < 0.001); 26% higher for whites (aHR: 1.26; 95% CI: 1.14–1.39, P < 0.001) and 49% higher for Hispanics (aHR: 1.49; 95% CI: 1.24–1.79, P < 0.001) compared to Blacks. There was no difference in AV access patency comparing patients who were 6–12 years (aHR: 0.96; 95% CI: 0.78–1.19; P = 0.73), 13–17 years (aHR: 0.87; 95% CI: 0.72–1.06; P = 0.17) and 18–20 years (aHR: 0.88; 95% CI: 0.73–1.07; P = 0.20) relative to those who were 0–5 years.. Imaging studies performed were 1.2 per fistula per year (95% CI: 1.13–1.20) for AVF and 2.4 per graft per year (95% CI: 2.23–2.48) for AVG (p < 0.001). HD

Table 6
Unadjusted Kaplan–Meier estimates of survival over time for patients who initiated hemodialysis via AVF or AVG, converted to AVG or AVF after prior HD catheter use or persisted on catheter for hemodialysis.

Group	1 Year % (95% CI)	2 years % (95% CI)	3 years % (95% CI)	4 years % (95% CI)	5 years % (95% CI)	6 years % (95% CI)	7 years % (95% CI)	P-value
AVF Initiate	97.5 (96.5–98.3)	93.6 (92.0–95.0)	90.5 (88.4–92.2)	88.7 (86.4–90.7)	86.0 (83.2–88.3)	83.5 (80.2–86.4)	81.3 (77.3–84.7)	<0.001
AVG Initiate	94.9 (90.4–97.3)	89.6 (83.8–93.4)	82.4 (75.0–87.7)	81.4 (73.8–86.9)	77.8 (68.3–84.2)	74.7 (65.3–81.9)	74.7 (65.3–81.9)	
AVF convert	96.5 (95.3–97.4)	92.7 (91.0–94.1)	89.4 (87.2–91.1)	85.4 (82.8–87.6)	82.1 (79.0–84.7)	79.4 (75.7–82.5)	78.6 (74.7–82.0)	
AVG convert	90.4 (86.3–93.4)	84.1 (78.9–88.1)	80.0 (74.1–84.7)	75.2 (68.6–80.7)	68.9 (60.9–75.7)	64.2 (54.9–72.1)	61.1 (50.3–70.3)	
HD catheter persistent	94.2 (93.6–94.8)	91.1 (90.3–91.9)	88.2 (87.1–89.1)	85.6 (84.4–86.8)	84.0 (82.7–85.3)	82.7 (81.2–84.1)	80.4 (78.5–82.2)	

AVF: arteriovenous fistula; AVG: arteriovenous graft; HD: hemodialysis; CI: confidence interval.

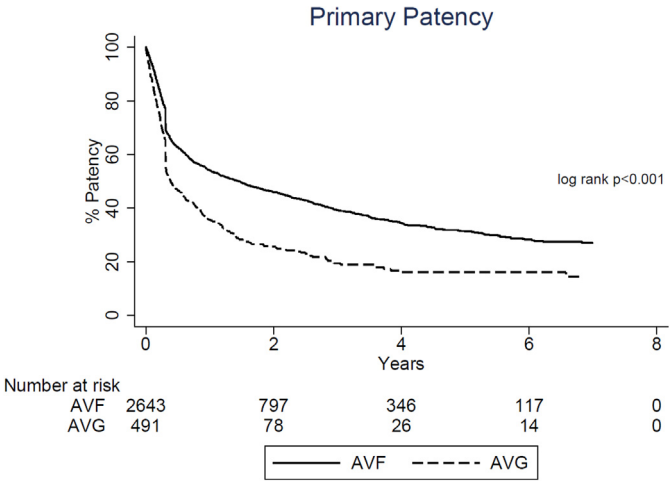

Fig. 4. Unadjusted Kaplan–Meier estimates of primary patency of AVF and AVG in pediatric patients. Log rank p-value: comparing primary patency of AVF and AVG groups.

catheter survival was 82.4% (81.4–83.4) at 1 year, 77.4% (76.2–78.6) at 2 years and 74.8% (73.5–76.1) at 3 years. PD catheter survival was 73.2% (70.7–75.5) at 1 year, 62.6% (59.7–65.3) at 2 years and 52.9% (49.8–55.9) at 3 years. 12% of PD catheters underwent revisions to achieve these survival rates.

2.4. Renal transplantation

There were 3423 (30%) patients in the HD and PD cohort who received a renal transplant within the study period. The proportion of patients who received renal transplants was 30% for HD, 30% for PD, 24% for those who converted from HD to PD and 26% for those who converted from PD to HD ($p = 0.026$). Within the subcohort of HD patients, prevalence of renal transplantation was 17% for AVF initiates, 17% for AVG initiates, 24% for AVF converts, 12% for AVG converts and 35% for patients who persistently dialyzed via HD catheter ($p < .001$). The median time to renal transplantation from date of dialysis access creation was 12 (IQR: 6.0–23.2) months. Renal transplantation was associated with a 7-fold increase in patient survival (aHR: 6.89; 95% CI: 5.05–9.38, $P < 0.001$).

3. Discussion

End stage renal disease portends a significant burden in children and adolescents because these patients will rely on renal replacement therapy for many years of their lives. Dialysis serves a critical role in patients unable to receive a renal transplant, prior to renal transplantation and in those with failed transplants. The average life expectancy for the HD dependent pediatric population is greater than 30 years [25,26]. This places a high premium on interventions that augment survival and preserve vascular access options for future use. The results from this study show that more than 70% of the patients in this study did not receive a renal transplant for the duration under review.

In this study, age was not a significant predictor of mortality; however, age modified the association between dialysis type and mortality. In the overall cohort, PD was associated with higher risk adjusted mortality compared to HD. However, when considered within categories of age, the was no significant difference between PD and HD in the younger patients, while PD was associated with higher mortality in the patients 13 years and older. Remote studies of small sample of patients comparing HD and PD have shown conflicting results [27,28]. Lower hospitalization rates owing to dialysis related complications have also been reported for HD relative to PD in children [29]. We acknowledge that several factors including age, quality of life and health facility access may contribute to choice of mode of dialysis. The population based relative mortality risk that we have reported should be considered when choosing a modality for renal replacement therapy in children.

Within the subcohort of HD patients, the majority (84%) of children and adolescents initiated HD with a catheter and 67% persisted on catheters for HD. The incidence and prevalence of HD catheter use in pediatric patients exceed those in the adult population [30,31]. This is likely owing to the anticipation of renal transplantation in these young patients or their small body size. Although the highest proportion of patients less than 20 kg in weight (9.6%) was in the HD catheter persistent group, this does not account for the high proportion of incident (84%) and prevalent (67%) HD catheter use. The results of this study show that initiation of HD with AVF is associated with better survival after adjusting for renal transplantation and comorbidities. The risk adjusted analyses controlling for demographic, clinical factors, renal transplantation and duration of HD catheter usage also revealed a two-thirds decrease in mortality when patients convert from HD catheter to AVF (66%) and one-thirds decrease with conversion to AVG (33%) when compared to continuous HD catheter use. This benefit was unraveled only after adjusting for duration for HD catheter use. This implies that, for patients with similar duration of HD catheter exposure, conversion to AVF or AVG is associated with better survival relative to persistent catheter use. These findings negate the contemporary practice of primary or temporary HD catheter use prior to renal transplantation. The balance tilts further in favor of arteriovenous access when the potential for central venous stenosis with prolonged HD catheter use is taken into consideration. Central venous stenosis in these young patients significantly interferes with future options for HD access and confers life and organ threatening risks in the long term [21].

Prior studies have reported primary patency rates that range from 43 to 100% and secondary patency in the range of 64–100% at 1 year [10,12,13,16,17,19,32]. These studies were largely limited by their relatively small sample sizes and nonuse of the standard reporting terms [16–18,33,34]. However, we acknowledge the efforts of the preceding investigators in evaluating this unique and often understudied category of patients. The patency rates for AVF and AVG in the current study exceed those from the adult and elderly population of patients [31,35–37]. However, the higher patency of AVF relative to AVG, better survival among AVF initiates compared to the other groups and improved

Table 7
unadjusted Kaplan–Meier estimates of AVF and AVG patency.

Patency	1 Year % (95% CI)	2 years % (95% CI)	3 years % (95% CI)	4 years % (95% CI)	5 years % (95% CI)	6 years % (95% CI)	7 years % (95% CI)	P-value
Primary								
AVF	54.1 (52.1–56.0)	46.1 (44.0–48.1)	39.2 (37.1–41.4)	34.4 (32.2–36.6)	31.3 (29.0–33.6)	28.2 (25.8–30.7)	27.0 (24.4–29.7)	<0.001
AVG	35.6 (31.2–40.0)	25.6 (21.5–29.9)	19.4 (15.4–23.8)	16.0 (12.0–20.6)	16.0 (12.0–20.6)	16.0 (12.0–20.6)	14.4 (10.0–19.7)	
Primary assisted								
AVF	62.0 (60.0–63.8)	55.7 (53.6–57.6)	49.6 (47.5–51.7)	45.2 (42.9–47.4)	42.2 (39.7–44.5)	38.6 (35.9–41.3)	36.2 (33.2–39.3)	<0.001
AVG	45.0 (40.3–49.5)	35.0 (30.4–39.6)	26.8 (22.2–31.6)	23.1 (18.5–28.0)	22.4 (17.8–27.4)	20.3 (15.7–25.5)	18.5 (13.2–24.5)	
Secondary								
AVF	68.2 (66.4–70.0)	63.8 (61.8–65.7)	59.3 (57.2–61.4)	55.4 (53.2–57.6)	53.3 (51.0–55.7)	50.0 (47.3–52.6)	48.2 (45.2–51.2)	<0.001
AVG	59.8 (55.2–64.1)	51.9 (47.0–56.5)	44.6 (39.5–49.6)	40.2 (34.8–45.5)	38.8 (33.3–44.3)	34.5 (28.5–40.6)	30.8 (23.7–38.2)	

AVF: arteriovenous fistula; AVG: arteriovenous graft; HD: hemodialysis; CI: confidence interval.

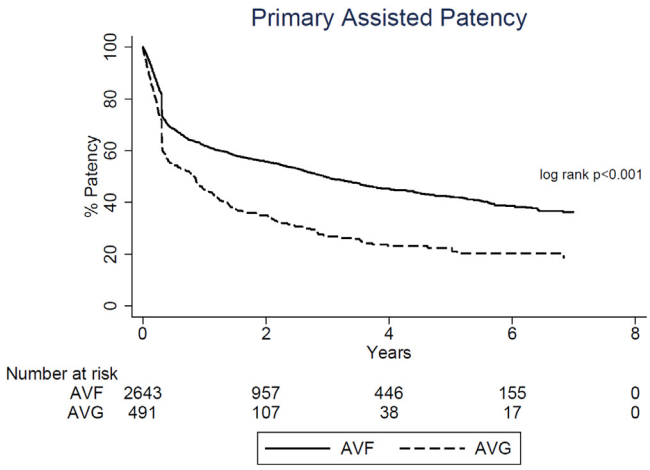

Fig. 5. Unadjusted Kaplan–Meier estimates of primary assisted patency of AVF and AVG in pediatric patients. Log rank p-value: comparing primary patency of AVF and AVG groups.

functional outcomes such as urea clearance, hemoglobin concentration and serum albumin that have been reported with AVF use support the fistula first approach in pediatric patients [6,9].

Among patients who inevitably have to initiate HD with a catheter, conversion to AVF is a rational approach to limiting prolonged HD catheter exposure and the associated risks that we have shown. In view of these findings, the low incidence and prevalence of AVF's relative to HD catheters attract the need for urgent national redress to improve pediatric AVF rates. Multidisciplinary collaborations targeting prompt and durable AVF placement have been shown to be effective in improving AVF uptake in the pediatric population [15,16]. This leaves room for reorientation and implementation across the US. From a surgical perspective, optimum preoperative planning including vein mapping, specialized and meticulous operative techniques and close postoperative surveillance serve as prime targets for AVF outcomes improvement. These approaches have been utilized by specialty centers that report better patency rates than the national average contained in this study [11,14–16,32]. The higher patency rates from those centers indicate goals of what can be achieved at provider, facility and regional levels.

The proportion of patients who received a renal transplant in this study reflects those who commenced treatment for ESRD via HD or PD and subsequently received a renal transplant. It excludes those who received renal transplants ab initio as well as those who commenced ESRD treatment prior to the study period. This study is limited in its retrospective nature and it does not offer a randomized comparison of HD versus PD and the HD access alternatives under review. We minimized selection bias by adjusting for baseline characteristics, renal transplantation and stratifying patients who converted from one mode of dialysis to another. Under the presumption that some patients remain on HD catheters because they are too sick to undergo AVF or AVG placement, subsequent conversion to AVF or AVG implies that these patients were later deemed well enough to receive permanent access, thus approximating the clinical state of patients who initiated hemodialysis with an AVF or AVG. Owing to data coding constraints, we are unable to identify HD and PD catheter related infections or HD catheter revisions that did not result in removal/replacement. The study is limited in the granularity of clinical details available in the USRDS. As such, we cannot account for factors that might impact patency such as conduit size and location, medication use and biologic or synthetic graft subtypes. Strengths of this study include its robust sample size, as well as the longitudinal nature of the data. These population-based outcomes of HD access heighten the need for preemptive AVF creation in the pediatric population and prompt conversion from HD catheter to AVF irrespective of the potential for renal transplantation. These outcomes should inform the expectations of patients and their care providers when considering options for dialysis access in children and adolescents.

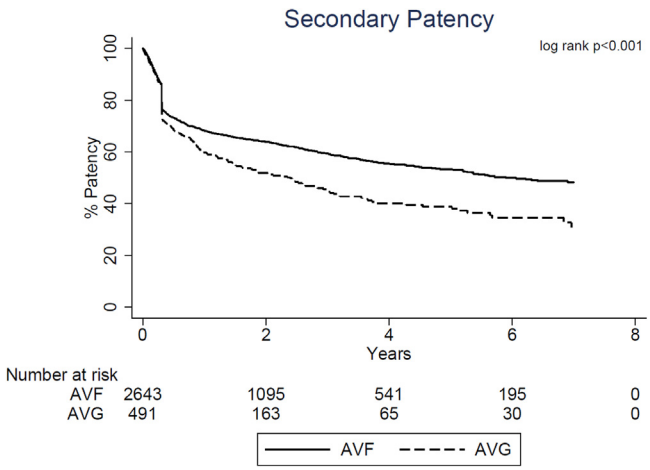

Fig. 6. Unadjusted Kaplan–Meier estimates of secondary patency of AVF and AVG in pediatric patients. Log rank p-value: comparing secondary patency of AVF and AVG groups.

4. Conclusion

There was no difference in risk adjusted mortality between HD and PD in children less than 13 years. PD is associated with higher mortality compared to HD in adolescents. Initiation of HD with AVF is associated with better patency and patient survival relative to AVG and persistent use of HD catheters in pediatric patients irrespective of transplant potential. Conversion from HD catheter to AVF or AVG in patients who inevitably initiate HD with a catheter is associated with better survival compared to persistent HD catheter use as a bridge to renal transplantation. National reorientation and multidisciplinary collaborations are needed to improve AVF utilization at incident HD and reverse the extremely high utilization of HD catheters in these young patients.

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