



Pediatric kidney transplantation in China: an analysis from the IPNA Global Kidney Replacement Therapy Registry

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Abstract

Background The International Pediatric Nephrology Association (IPNA) Global Kidney Replacement Therapy (KRT) Registry was established to evaluate the incidence and outcomes of kidney replacement therapy (dialysis and transplantation) provided to children worldwide. Analysis of registry data for separate regions is feasible.

Methods Three centers located in Shanghai, Guangzhou, and Zhengzhou, which have the greatest number of pediatric kidney transplantation cases in China, participated in this analysis of transplant data. Data were registered by each center for patients under the age of 19 years who received a single-organ kidney transplant for the first time between 2011 and 2018.

Results In total, 415 patients (59.8% male) aged 1.4–18.7 (median 12.1) years were followed for 0.3–97.1 (median 27.7) months. The number of kidney transplants increased from a total of 129 during 2011–2014 to 286 cases during 2015–2018. 85.8% of patients received the transplanted kidney from a pediatric (age < 19 years) donor, and deceased donors accounted for 94% of all donors. 8.0% of grafts were lost. One and 5-year patient survival rates were 97.6% and 95.5%, respectively. The major cause of death was infection (7/14). Similar graft and patient survival rates were observed for organs from pediatric and adult donors in 6–11 and 12–18 year recipient age groups, whereas recipients < 6 years showed inferior patient and graft survival.

Conclusions Pediatric kidney transplantation shows favorable short-term and medium-term outcomes in China. Our experience supports use of pediatric donors in pediatric kidney transplantation, but attention directed to the outcome of recipients aged under 6 is necessary.

Keywords Kidney transplant · Children · Prognosis · China

Qian Shen and Xiaoyan Fang contributed equally to this work.

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Introduction

Kidney replacement therapy (KRT) for children with kidney failure includes peritoneal dialysis, hemodialysis, and kidney transplantation. After decades of innovation in the development of transplant surgery expertise and highly effective immunosuppressive drug regimens, accompanied by the expansion of donor resources, kidney transplantation has become the preferred KRT modality for children with kidney failure worldwide. In China, pediatric kidney transplantation has lagged behind the practice in developed countries, as there were only 717 pediatric kidney transplants conducted in China during the 28 year period of 1983 to 2010 [1]. In recent years, the improvements of medical technology and economic resources have led to major progress in pediatric kidney transplantation in China. In addition, subsequent to the establishment of a national system for organ donation and transplantation by the Ministry of Health and the Red Cross Society of China in 2010 [2], the donation after cardiac death (DCD) program has gradually matured and has played a pivotal role in the evolution both of pediatric and adult kidney transplantation in China. Moreover, with the growing awareness of the critical role of multidisciplinary teams comprising pediatric nephrologists, transplant surgeons, dialysis and transplant nurses and coordinators, pharmacists, dietitians, psychologists, social workers, and intensive care unit physicians, the “Chinese Pediatric Kidney Transplantation Management Collaboration Group” was established in 2016 to focus on and enhance pre-transplant preparation and post-transplant management to improve the long-term outcome and quality of life of pediatric kidney transplant recipients [3].

Endorsed by the International Pediatric Dialysis Network (IPDN), a national pediatric dialysis network and online registration platform, IPDN-China (www.pedpd.org.cn), was launched in 2012, while a national pediatric kidney transplantation registry was still unavailable. In 2017, the International Pediatric Nephrology Association (IPNA) launched the IPNA Global KRT Registry in an effort to collect information on the incidence and outcome of pediatric KRT worldwide. In addition, the IPNA registry created the opportunity for countries without a KRT registry to collect and analyze country-specific information as part of their goal to increase the quantity and quality of KRT care provided to their respective pediatric kidney failure populations. We, in turn, requested and received approval from IPNA to translate the registry’s data collection form into Chinese as a means by which we were able to contribute to the IPNA Global KRT Registry, in addition to creating a national registry for China. We then conducted an analysis of the submitted data to describe the current status of pediatric kidney transplants in

China and to explore factors associated with patient and graft survival.

Methods

Data source and study population

This study was approved by the Ethics Board of the Children’s Hospital of Fudan University. According to the principle of voluntary accession to data registration, the three centers which conduct the largest number of pediatric kidney transplants in China contributed data for this analysis. These three centers were Children’s Hospital of Fudan University (cooperated with Changhai Hospital, Shanghai Center), The First Affiliated Hospital of Sun Yat-sen University (Guangzhou Center), and The First Affiliated Hospital of Zhengzhou University (Zhengzhou Center).

Based on the IPNA registration and data collection form, a Chinese registration form was created. Data collected consisted of the following: patient date of birth, gender, primary kidney disease, dialysis history, date of kidney transplantation, donor type, donor age, survival status of graft and patient, and date and cause of death. Children under the age of 19 years who received their initial single-organ kidney transplant from Jan 1, 2011, to Dec 31, 2018, were included in the analysis. Data on patient and graft survival were collected up to January 2019.

Statistical analysis

Statistical analysis was performed using SPSS 21.0 for Macintosh (IBM SPSS, Chicago, IL). The mean \pm standard deviation or median interquartile range was used to describe the quantitative variables, such as age and duration of follow-up, depending on the distribution of the data. Frequency and percentage were used to describe categorical variables such as gender, primary kidney disease, donor type, donor age, dialysis before transplantation, graft loss, and mortality. Kaplan-Meier survival curves were used to calculate the patient survival rate. The chi-square test, Kruskal-Wallis test, Fisher’s exact test, and log-rank test were used to determine the differences in features by transplant center. The chi-square test, Wilcoxon rank-sum test, and Fisher’s exact test were used to determine the difference in characteristics by transplant era. Log-rank test was used to compare patient survival both in different donor-recipient age combinations and different recipient age groups. Binary logistic regression and Cox proportional hazards models were used to identify the risk factors for graft loss and patient mortality, respectively. *P* values < 0.05 were considered statistically significant.

Results

Patient and donor characteristics

A total of 415 patients were included in this study (Supplement 1 and Table 1); 143 from Shanghai Center, 126 from Guangzhou Center and 146 from Zhengzhou Center. Among the 415 patients, 248 (59.8%) were boys; age at transplantation ranged from 1.4 to 18.7 years (median age: 12.1 years old). Prior to transplantation, 337 patients (81.2%) received dialysis. The leading causes of kidney failure were congenital anomalies of the kidney and urinary tract (CAKUT, 32.1%) and steroid-resistant nephrotic syndrome (SRNS, 18.8%) in the 0–5 years and

6–11 years recipient age groups, respectively. In the adolescent age group (12–18 years), 64.5% of the cases had kidney failure secondary to an unknown etiology (Fig. 1). Deceased donors accounted for 94.2% of all donors, including 78.3% DCD donors and 15.9% donation after brain death (DBD) donors. The “pediatric to pediatric” matching policy (both recipient and donor < 19 years of age) was implemented in 85.8% of the patients.

Graft and patient survival

With a median follow-up time of 27.7 (11.4, 52.4) months, no patient was lost to follow-up. One hundred sixty-six and 76 patients reached the 3-year and 5-year follow-up, respectively.

Table 1 General characteristics and comparison by transplant center

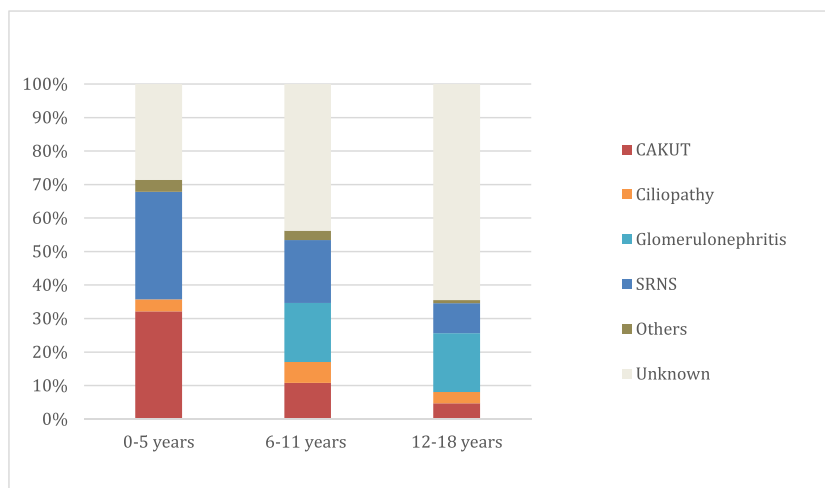
	All	Shanghai	Guangzhou	Zhengzhou	χ^2 value	P value
No.	415 (100%)	143 (34.5%)	126 (30.4%)	146 (35.2%)		
Gender (male)	248 (59.8%)	83 (58.0%)	71 (56.3%)	94 (64.4%)	2.083	0.352
Age(years)	12.1 (9.1, 15.1)	10.5 (4.0)	11.9 (9.0, 14.7)	14.5 (11.2, 16.4)	51.836	0.000
0–5	28 (6.7%)	13 (9.1%)	9 (7.1%)	6 (4.1%)	36.861	0.000
6–11	176 (42.4%)	82 (57.3%)	55 (43.7%)	39 (26.7%)		
12–18	211 (50.9%)	48 (33.6%)	62 (49.2%)	101 (69.2%)		
Follow-up(months)	27.7 (11.4, 52.4)	36.6 (13.9, 52.3)	25.2 (9.9, 47.2)	25.9 (11.6, 40.5)	7.775	0.021
Primary kidney disease					123.641	0.000
CAKUT	38 (9.2%)	28 (19.6%)	10 (7.9%)	0		
SRNS	61 (14.7%)	35 (24.5%)	22 (17.5%)	4 (2.7%)		
Glomerulonephritis	68 (16.4%)	23 (16.1%)	33 (26.2%)	12 (8.2%)		
Renal cystic ciliopathy	19 (4.6%)	11 (7.7%)	7 (5.6%)	1 (0.7%)		
Others	8 (1.9%)	3 (2.1%)	1 (0.8%)	4 (2.8%)		
Unknown	221 (53.3%)	43 (30.1%)	53 (42.1%)	125 (85.6%)		
Donor type					180.359	0.000
DCD	325 (78.3%)	142 (99.3%)	53 (42.1%)	130 (89.0%)		
DBD	66 (15.9%)	0	64 (50.8%)	2 (1.4%)		
LD	24 (5.8%)	1 (0.7%)	9 (7.1%)	14 (9.6%)		
Donor age (years)					13.530	0.001
< 19	356 (85.8%)	135 (94.4%)	101 (80.2%)	120 (82.2%)		
≥ 19	59 (14.2%)	8 (5.6%)	25 (19.8%)	26 (17.8%)		
Dialysis before transplantation	337 (81.2%)	140 (97.9%)	72 (57.1%)	125 (85.6%)	75.781	0.000
Graft loss	33 (8.0%)	11 (7.7%)	15 (11.9%)	7 (4.8%)	4.691	0.085
Mortality	14 (3.4%)	3 (2.1%)	3 (2.4%)	8 (5.5%)		0.280
Patient survival rate					3.553	0.169
1 year	97.6%	97.9%	98.9%	96.1%		
3 years	96.8%	97.9%	97.7%	94.9%		
5 years	95.5%	97.9%	97.7%	90.1%		

CAKUT, congenital anomalies of kidney and urinary tract; SRNS, steroid-resistant nephrotic syndrome; DCD, donation after cardiac death; DBD, donation after brain death; LD, living donor

N (%) for categorical variables and mean (SD) or median (IQR25, IQR75) for continuous variables

Kruskal-Wallis test was used to compare the mean/median age and follow-up period from different centers; Fisher exact test and log-rank test were used to compare the mortality rate and patient survival rate from different centers, respectively; the chi-square test was used for comparison for other features

Fig. 1 Primary kidney disease by different age groups. In the recipient age groups 0–5 years and 6–11 years, the leading cause of kidney failure was CAKUT (32.1%) and SRNS (18.8%), respectively. In the recipient age group 12–18 years, 64.5% of the cases had kidney failure secondary to an unknown etiology. CAKUT, congenital anomalies of kidney and urinary tract; SRNS, steroid-resistant nephrotic syndrome



The graft loss rate was 8.0%, and the 1-year, 3-year, and 5-year patient survival rates overall were 97.6%, 96.8%, and 95.5%, respectively. Fourteen of the 415 patients died. The median duration from transplantation to death was 7.0 (5.8, 17.7) months. The causes of death included infection (7 cases), cardiopulmonary failure (3 cases), cerebrovascular accident (1 case), malignancy (1 case), hepatic failure (1 case), and unknown reason (1 case).

Comparison by transplant center

Table 1 shows the detailed characteristics of the different transplant centers. The age at transplantation, duration of follow-up, distribution of primary kidney disease, donor type, donor age, and dialysis history differed significantly between the centers, whereas graft loss rate and mortality rates were similar.

Comparison by transplant era

The number of kidney transplantations increased significantly from 129 patients during 2011–2014 to 286 patients during 2015–2018. The comparison of patient characteristics in 2015–2018 and 2011–2014 revealed trends towards younger age at transplantation (11.9 (8.8, 14.8) vs. 12.5 (9.6, 16.1) years, $P=0.028$), more frequent pre-emptive transplantation (22.7% vs. 10.1%, $P=0.003$), higher utilization of pediatric donor organs (94.4% vs. 66.7%, $P<0.001$), and more DBD donors (23.1% vs. 0%, $P<0.001$). Graft survival and mortality did not differ significantly (Table 2).

Donor-recipient age combination and comparison of survival

In the recipient age groups 0–5 years and 6–11 years, 100% and 94.3% of patients, respectively received a pediatric donor kidney. In the adolescent age group, 76.8% of recipients

received a kidney from a pediatric donor ($P=0.000$). Both in the recipient age groups 6–11 years and 12–18 years, organs from pediatric and adult donors showed similar graft loss (OR 0.577 (95% CI 0.066–5.016) in 6–11 years group, OR 2.398 (95% CI 0.529–10.871) in 12–18 years group), and mortality did not differ (Fig. 2).

Risk factors for graft loss and mortality

Variables included age at transplantation, gender, primary kidney disease, dialysis history, donor type, donor age, transplant center, and transplant era. Transplant age 0–5 years was associated with a higher risk both of graft loss (6–11 years: OR 0.159 (95% CI 0.044–0.576), 12–18 years: OR 0.227 (95% CI 0.064–0.811)) and mortality (6–11 years: HR 0.180 (95% CI 0.040–0.811), 12–18 years: HR 0.216 (95% CI 0.052–0.905)) (Fig. 3).

Discussion

We report 415 first kidney transplants which took place at the three most active pediatric transplant centers in China from 2011 to 2018, accounting for 33.5% of all pediatric kidney transplants during that 8-year period according to the Chinese Scientific Registry of Kidney Transplantation (CSRKT, www.csrkt.org). The number of kidney transplantations at these three centers increased more than two-fold from 2011–2014 to 2015–2018, and increasingly younger children underwent transplantation with time. However, prior data showed that only 717 pediatric kidney transplants were performed at 102 different transplantation centers during the period of 1983 to 2010 in China. The mean age at transplantation was 15.4 ± 2.5 years during that period of time [1]. Our study shows deceased donors accounted for 94.2% of all donors and the “pediatric to pediatric” matching policy was implemented in 85.8% of the patients. Favorable short-term and medium-

Table 2 Comparison by transplant era

	2011–2014	2015–2018	χ^2/Z value	<i>P</i> value
No.	129	286		
Gender (male)	74 (57.4%)	174 (60.8%)	0.446	0.518
Age(years)	12.5 (9.6, 16.1)	11.9 (8.8, 14.8)	-2.204	0.028
0–5	5 (3.9%)	23 (8.0%)	2.731	0.253
6–11	54 (41.9%)	122 (42.7%)		
12–18	70 (54.2%)	141 (49.3%)		
Follow-up(months)	63.0 (53.9, 72.1)	18.1 (8.2, 30.3)	-15.787	0.000
Primary kidney disease				0.650
CAKUT	12 (9.3%)	26 (9.1%)		
SRNS	20 (15.5%)	41 (14.3%)		
Glomerulonephritis	18 (14.0%)	50 (17.5%)		
Renal cystic ciliopathy	8 (6.2%)	11 (3.8%)		
Others	4 (3.2%)	4 (1.4%)		
Unknown	67 (51.9%)	154 (53.8%)		
Donor type			49.201	0.000
DCD	112 (86.8%)	213 (74.5%)		
DBD	0	66 (23.1%)		
LD	17 (13.2%)	7 (2.4%)		
Donor age (years)				
< 19	86 (66.7%)	270 (94.4%)	56.089	0.000
≥ 19	43 (33.3%)	16 (5.6%)		
Dialysis before transplantation	116 (89.9%)	221 (77.3%)	9.321	0.003
Graft loss	14 (3.4%)	19 (4.6%)	2.152	0.170
Mortality	6 (1.4%)	8 (1.9%)	0.455	0.500

CAKUT, congenital anomalies of kidney and urinary tract; SRNS, steroid-resistant nephrotic syndrome; DCD, donation after cardiac death; DBD, donation after brain death; LD, living donor

N (%) for categorical variables and median (IQR25, IQR75) for continuous variables

Wilcoxon rank-sum test was used to compare the median age and follow-up period between different transplant eras; Fisher exact test was used to compare the etiology of kidney failure between different transplant eras; the chi-square test was used for comparison for other features

term outcomes with respect to graft and patient survival are observed, whereas recipients younger than 6 years demonstrate inferior patient and graft survival.

As we know, kidney transplantation is widely recognized as being the preferred KRT option for children with kidney

failure, offering optimal patient survival probabilities, as well as superior cognitive development, quality of life, and growth compared with dialysis [4, 5]. The United Kingdom Transplant Registry data on 3236 pediatric kidney transplants performed between 1 January 1992 and 31 December 2016

Fig. 2 Patient survival by donor-recipient age combination. Both in the recipient age groups 6–11 years and 12–18 years, pediatric donors and adult donors showed similar patient survival rate ($Z = 1.779$, $P = 0.620$)

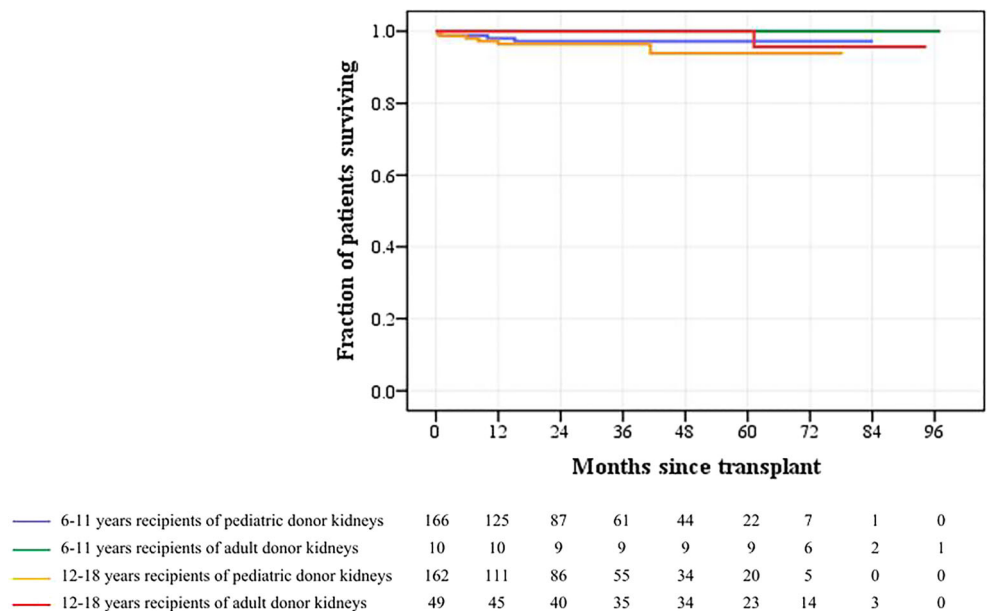
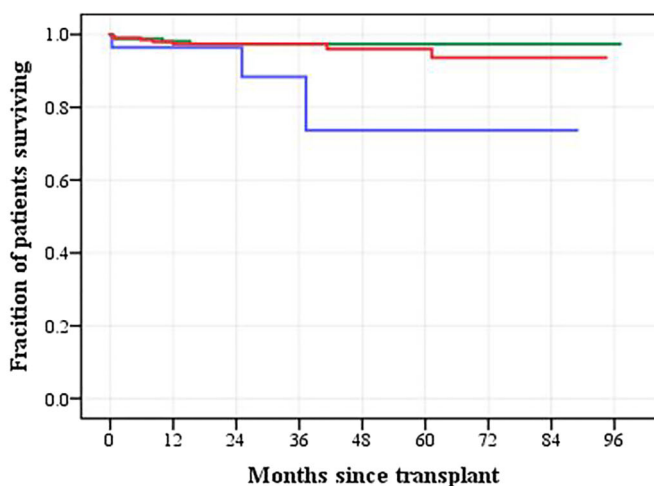


Fig. 3 Patient survival by recipient age. Compared with the recipient age groups 6–11 years and 12–18 years, patient survival rate was lower in patients transplanted at 0–5 years of age ($Z = 7.028$, $P = 0.030$)



— 0-5 years recipients	28	17	14	6	3	2	1	1	0
— 6-11 years recipients	176	135	96	70	53	31	13	3	1
— 12-18 years recipients	211	156	126	90	68	43	19	3	0

showed 25-year patient survival reached 79% and 86% in deceased donor transplant and living donor transplant, and the half-lives for living donor and deceased donor kidneys were 14 and 15 years, respectively [6]. Since the establishment of a new national system for organ donation and transplantation by the Ministry of Health and the Red Cross Society of China in 2010 [2], pediatric kidney transplantation in China has developed relatively rapidly in recent years. The establishment of the Chinese Pediatric Kidney Transplantation Management Collaboration Group in 2016 has also proven to be exceedingly important. This national collaboration group has focused on pre-transplant preparation (vaccinations for preventable diseases, diagnosis of primary kidney disease, effective dialysis and nutrition, attention to cognitive delays, social-psychological assessment) and post-transplant management (regular evaluation and follow-up, nutrition and growth, financial support) [3]. In our study, the 1-year and 5-year patient survival rates were 97.6% and 95.5%, respectively, well comparable to the data from the 2018 report of the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS) [7], which demonstrated 5-year patient survival rates of 98.10% and 97.95% in living donor and deceased donor transplant recipients, respectively during the transplant period of 2007 to 2017.

Currently, infection is still the dominant cause of pediatric hospitalizations and death after kidney transplant [5, 7]. In our study, infections accounted for 50% and cardiopulmonary failure for 21% of deaths after transplantation. In the 2018 NAPRTCS report, infection and cardiopulmonary failure were responsible for 25.0% and 13.9% of deaths, respectively [7]. In the Australian and New Zealand Dialysis and Transplant Registry following 1810 children and adolescents from 1970 to 2015, 5-year patient survival increased from

85% in 1970–1985 to 99% in 2005–2015, predominantly because of marked reductions in cardiovascular and infection-related deaths [8]. Preventive measures (vaccinations for preventable diseases, prophylactic antibiotics/antiviral therapy) and monitoring and management of infection in pediatric kidney transplantation still need to be strengthened in China.

Our previous studies have demonstrated that the use of grafts from deceased pediatric donors is a potential approach to expand the donor pool and thus minimize waiting time [9, 10]. Shortages in donor kidneys along with improvements in surgical technique have led to an increased popularity of using young donor kidneys for transplantation. There is also a potential benefit for the family of the deceased child, as many families desire to donate their child's organs to provide an opportunity for another human to survive [11]. In this study, comparing the data of 2015–2018 with those of 2011–2014, more children received pediatric donor organs, which is in line with an increase in the percentage of pre-emptive transplantation. Although earlier reports have shown a higher risk of graft loss in recipients of (very) young donors due to surgical complications, high rates of graft thrombosis, early rejection, and hyper-filtration injury, there has been an expansion in the practice of deceased pediatric donors recently, and there is emerging evidence that good outcomes can be achieved [12]. In addition, the “pediatric to pediatric” matching policy (both recipient and donor < 19 years of age) has been implemented in many parts of the world, although the percentage of pediatric to pediatric transplants varies by country. In Europe, among deceased donor transplant recipients, an average of 61.4% children received pediatric donor kidneys, ranging from 16.7% in Belarus to 73.2% in France [13]. This “pediatric to pediatric” matching policy potentially eliminates the cardiovascular complications of graft-recipient size mismatch

and can reduce the risk of hypo-perfusion and graft non-function [14]. Grafts from pediatric donors have also shown superior long-term kidney function compared with grafts from adult donors [15, 16]. The relative glomerular filtration rate of allografts from pediatric donors was significantly higher than those from adult deceased or living-related donors after at least 4 years of follow-up in a cohort of pediatric kidney allograft recipients [15]. Pediatric donor allografts also tend to adapt to the growing child by maintaining and even increasing glomerular filtration rate over many years after transplantation, as opposed to an adult donor allograft, which will initially adapt to the pediatric recipient following transplantation but thereafter will not increase its filtration function to correlate with the increasing size and filtration demand of the growing child [14]. Data from the Scientific Registry of Transplant Recipients (SRTR) showed that among children (< 10 years) and adolescent (10–18 years) recipients, outcomes using either an ideal kidney from deceased donors aged between 15 and 35 years or split kidney from small pediatric donors (aged ≤ 8 years and weight < 30 kg) were very similar. In turn, the authors concluded that pediatric kidneys could augment the kidney donor pool and should not be considered expanded criteria donor kidneys [17]. To that end, deceased donors accounted for 94.2% of our kidney transplants, and 85.8% of all donors were pediatric donors (< 19 years). With a median follow-up time of 27.7 months, the graft loss rate was 8%, indicating good graft outcomes from the use of pediatric donor kidneys in pediatric recipients. However, the numbers of pediatric to pediatric transplants in children in China and worldwide are relatively limited, and the duration of follow-up is limited. Thus, ongoing data collection by the IPNA KRT registry will be crucial to provide long-term data on graft survival, as well as outcomes such as proteinuria, so as to address concerns regarding issues such as glomerulomegaly and hyper-filtration.

Of course, recipient and donor age are both known to affect graft survival. Graft failure was highest in the youngest and adolescent transplant recipients [13]. In adolescents, poor graft survival was attributed to poor adherence with immunosuppression regimens [18]. Recipients less than 5 years of age showed a higher risk of graft failure, especially during the first 3 months post-transplant, most likely reflecting the surgical difficulties associated with transplantation in the youngest patients [19]. Similar results were demonstrated both in the United Kingdom Transplant Registry data and the 2014 NAPRTCS report [6, 20]. The former indicated recipients under the age of 6 years had lower 1-year kidney allograft survival than recipients aged 6 years and over and this difference was maintained up to 10 years, and the latter showed the poorest graft survival in deceased donor recipients less than 2 years of age, especially during the initial post-transplant period. The European Society for Paediatric Nephrology/European Renal Association-European Dialysis and

Transplantation Association (ESPN/ERA-EDTA) registry study also demonstrated that graft survival varied by recipient age. Compared with the recipient age group 6–11 years, graft failure risk was higher in patients transplanted at 0–5 years of age and during adolescence (12–19 years). In addition, the youngest deceased donor age group (0–5 years) showed the highest risk of graft failure [13]. In our study, 100%, 94.3%, and 76.8% of recipients aged 0–5 years, 6–11 years, and 12–18 years received pediatric donor kidneys, respectively. Transplant age under 6 years showed a higher risk both in graft loss and mortality compared with transplants performed with children aged 6–11 years and 12–18 years. In both of the latter patient cohorts, recipients of pediatric donor and adult donor kidneys showed similar graft loss rates and mortality risks. Therefore, additional data will be required to better determine whether recipient age under 6 years is an independent risk factor for graft failure and mortality or whether the pediatric donor-youngest recipient (0–5 years) combination is most predictive of a poor outcome in the Chinese pediatric kidney transplantation cohort.

Some limitations of our study need to be acknowledged. First, the exact age of the graft, as well as the date and cause of graft failure, were not included in the registry, which could further help differentiate early from long-term graft failure and optimal donor-recipient age combination. Second, the issue of unmeasured donor and recipient variables, such as the number of human leucocyte antigen mismatches, the percentage of panel reactive antibodies, the ischemia time, and immunosuppression regimens, might lead to residual confounding. Third, in this study, more than 50% of the cases had kidney failure from unknown etiology. Fourth, the median follow-up time in this study was 27.7 months. Only 166 and 76 patients reached the 3-year and 5-year follow-up, respectively. Therefore, the outcome results should be interpreted accordingly. Finally, only the three most active centers in terms of number of pediatric kidney transplants performed were enrolled in this study. Our results are hardly generalizable to the rest of China and should stimulate additional data collection from transplant centers throughout China.

Conclusion

The number of pediatric kidney transplantations has increased, and kidney transplantation shows favorable short-term and medium-term outcome with respect to graft and patient survival in the three largest pediatric kidney transplant centers in China. Our limited experience provides evidence that the use of pediatric donor kidneys can result in successful transplant outcomes. In order to decrease the graft loss and mortality in the youngest recipients, not only are additional multidisciplinary efforts required, but also further granular data collection in regard to pediatric donor kidneys and

different donor-recipient age combinations are needed to better identify the risk factors. In July 2018, the National Health Commission of the People's Republic of China announced an updated organ allocation and sharing policy [21]. This current allocation scheme preferentially allocates pediatric deceased donor kidneys to children on the transplant waitlist. We believe the new strategy for implementation increases the organ allocation priority for children and will promote the further development of pediatric kidney transplantation in China.

Authors' contributions Each author has participated sufficiently in the work to take public responsibility for the content. Hong Xu and Qian Shen participated in the conception and design of the study; Qian Shen, Xiaoyan Fang, Xinyue Man, Yihui Zhai, Longshan Liu, Changxi Wang, Wenjun Shang, Guiwen Feng, Lei Zhang, and Li Zeng conducted data acquisition, analysis, and interpretation; Qian Shen and Xiaoyan Fang drafted the article and provided intellectual content of critical importance to the work described; Hong Xu, Bradley A Warady, Franz Schaefer, Youhua Zhu, Jing Chen, and Jia Rao revised the article. All authors have final approval of the version to be published.

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Data availability All data generated or analyzed during this study are included in this paper.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethics approval This study was approved by the Ethics Board of the Children's Hospital of Fudan University.

Consent to participate Not applicable

Code availability Not applicable

References

- Liu L, Zhang H, Fu Q, Chen L, Sun C, Xiong Y, Shi B, Wang C (2014) Current status of pediatric kidney transplantation in China: data analysis of Chinese Scientific Registry of Kidney Transplantation. *Chin Med J* 127:506–510
- China Organ Donation Administrative Center (2010) China organ donation pilot program. <http://www.rcscod.cn/cstatute/cdonationdocuments/20100301/699052.htm> Accessed 10 April 2020
- Shen Q, Jiaojiao L, Yihui Z, Jing C, Xiaoyan F, Jia R, Lin F, Xiaoshan T, Jialu L, Yunli B, Wu B, Lei Z, Zhu Y, Xu M, Zhu T, Li Z, Hong X (2020) Multi-disciplinary management of pediatric renal transplantation. *J Nephrol Dialy Transplant* 29:20–25 (article in Chinese)
- Winterberg PD, Garro R (2019) Long-term outcomes of kidney transplantation in children. *Pediatr Clin N Am* 66:269–280
- Vergheze PS (2017) Pediatric kidney transplantation: a historical review. *Pediatr Res* 81:259–264
- Mumford L, Maxwell H, Ahmad N, Marks SD, Tizard J (2019) The impact of changing practice on improved outcomes of paediatric renal transplantation in the United Kingdom: a 25 years review. *Transpl Int* 32:751–761
- Chua A, Cramer C, Moudgil A, Martz K, Smith J, Blydt-Hansen T, Neu A, Dharmidharka VR, NAPRTCS investigators (2019) Kidney transplant practice patterns and outcome benchmarks over 30 years: the 2018 report of the NAPRTCS. *Pediatr Transplant* 23:e13597
- Francis A, Johnson DW, Melk A, Foster BJ, Blazek K, Craig JC, Wong G (2020) Survival after kidney transplantation during childhood and adolescence. *Clin J Am Soc Nephrol* 15:392–400
- Zhao WY, Zhang L, Zhu YH, Zhu FY, Chen Y, Shen Q, Xu H, Zeng L (2014) Single kidneys transplanted from small pediatric donors less than 15 kilograms into pediatric recipients. *Transplantation* 98:e97–e100
- Zhao WY, Zhang L, Zhu YH, Chen Y, Zhu FY, Shen Q, Xu H, Zeng L (2014) En bloc kidneys transplanted from infant donors less than 5 kg into pediatric recipients. *Transplantation* 97:555–558
- Sung RS (2010) Transplantation: pediatric kidney donation after cardiac death. *Nat Rev Nephrol* 6:387–388
- Marlais M, Callaghan C, Marks SD (2016) Kidney donation after circulatory death: current evidence and opportunities for pediatric recipients. *Pediatr Nephrol* 31:1039–1045
- Chesnaye NC, van Stralen KJ, Bonthuis M, Groothoff JW, Harambat J, Schaefer F, Canpolat N, Garnier A, Heaf J, de Jong H, Schwartz Sørensen S, Tönshoff B, Jager KJ (2017) The association of donor and recipient age with graft survival in paediatric renal transplant recipients in a European Society for Paediatric Nephrology/European Renal Association-European Dialysis and Transplantation Association Registry study. *Nephrol Dial Transplant* 32:1949–1956
- Chaudhuri A, Grimm P, Concepcion W (2016) Small pediatric deceased donors for pediatric renal transplant recipients. *Pediatr Transplant* 20:7–10
- Dubourg L, Cochat P, Hadj-Aïssa A, Tydén G, Berg UB (2002) Better long-term functional adaptation to the child's size with pediatric compared to adult kidney donors. *Kidney Int* 62:1454–1460
- Pape L, Hoppe J, Becker T, Ehrich JH, Neipp M, Ahlenstiel T, Offner G (2006) Superior long-term graft function and better growth of grafts in children receiving kidneys from paediatric compared with adult donors. *Nephrol Dial Transplant* 21:2596–2600
- Suneja M, Kuppachi S, Katz D, Hunsicker L (2019) Small split pediatric kidneys to expand the donor pool: an analysis of Scientific Registry of Transplant Recipients (SRTR) data. *Transplantation* 103:2549–2557
- Van Arendonk KJ, King EA, Orandi BJ, James NT, Smith JM, Colombani PM, Magee JC, Segev DL (2015) Loss of pediatric kidney grafts during the 'high-risk age window': insights from pediatric liver and simultaneous liver-kidney recipients. *Am J Transplant* 15:445–452
- Arbus GS, Rochon J, Thompson D (1991) Survival of cadaveric renal transplant grafts from young donors and in young recipients. *Pediatr Nephrol* 5:152–157
- North American Pediatric Renal Trials and Collaborative Studies (2014) NAPRTCS 2014 Annual Transplant Report. <https://web.emmes.com/study/ped/annrept/annualrept2014.pdf>. Accessed 31 December 2017
- National Health Commission of the People's Republic of China (2018) China organ allocation and sharing policy. <http://www.nhc.gov.cn/zyygj/s3586/201808/d35d96f2db82403e2ba41f2c583896.shtml>. Accessed 10 April 2020

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