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Impact of pretransplant dialysis on early graft function in pediatric kidney recipients*

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Summary

Delayed graft function (DGF) is a frequent complication of kidney transplantation (KT) that may affect both short- and long-term graft outcome. It has been reported that pretransplantation peritoneal dialysis was correlated with a better recovery of graft function than hemodialysis in adult kidney recipients. However, the effect of pretransplantation dialysis mode (PDM) seemed to be unclear on the early outcome of KT in pediatric recipients. In this study, the potential impact of PDM on early graft function was evaluated in 174 pediatric patients who underwent KT by using cadaveric donors. The primary outcome parameter was the time to reach a serum creatinine (SCr) level 50% of the pretransplantation value [$T_{1/2(SCr)}$], while DGF was defined as a $T_{1/2(SCr)}$ >3 days after KT ($n = 40$). By stratifying kidney recipients for normal function graft or DGF, this latter group showed a significantly higher body weight (BW) on the day of KT ($P = 0.014$), body surface area (BSA) ($P = 0.005$), warm ischemia time (WIT) ($P = 0.022$), early SCr on the day 1 after KT ($P < 0.001$), and $T_{1/2(SCr)}$ ($P < 0.001$), whereas lower urine volume (UV) collected in the first 24 h after KT ($P < 0.001$) and fluid load ($P < 0.001$) occurred. Univariate exponential correlation that was carried out between $T_{1/2(SCr)}$ and all the other variables had shown a better value than the linear correlation for BW ($R^2 = 0.28$ vs. $R^2 = 0.04$), BSA ($R^2 = 0.29$ vs. $R^2 = 0.03$), and SCr ($R^2 = 0.51$ vs. $R^2 = 0.28$). In a multivariate regression analysis performed by entering $T_{1/2(SCr)}$ as dependent variable and following a forward stepwise method, cold ischemia time (CIT) ($P = 0.027$) but not PDM ($P = 0.195$) reached significance. In a Cox regression analysis carried out with $T_{1/2(SCr)}$ as dependent variable, neither CIT nor PDM gained significance. This study suggests that PDM does not affect early graft function in pediatric kidney recipients.

Introduction

The need for dialysis and a delayed decrease of serum creatinine (SCr) are frequent complications of kidney transplantation (KT) [1,2]. A delay in recovery of graft function may persist for many months after KT, affecting graft survival [3,4]. Delayed graft function (DGF) may increase the risk for acute rejection (AR) in adult kidney recipients, and a combination of DGF and AR has been reported to cause a graft loss of up to 50% within the first year after KT [5]. Moreover, DGF is able to decrease long-term survival of transplanted kidneys [6,7], and its negative impact on graft survival may be predicted by the evolution of SCr rather than by the need for dialysis [6]. Thus, the effort to identify the potential risk factors that impair the incidence and severity of DGF seems to be a remarkable target [8].

It has been reported that pretransplantation peritoneal dialysis (PD) was correlated with a better recovery of renal function and overall short-term graft outcome than

hemodialysis (HD) in adult kidney recipients [8,9]. This finding may be related to a more stable fluid status observed in adults patients submitted to PD [8]. However, the impact of pretransplantation dialysis mode (PDM) on pediatric patients seemed to exert no clear effect on the graft outcome, suggesting the need for further investigation [10]. With this aim, in the present study the potential impact of PDM on the development of DGF was evaluated in a pediatric patient cohort.

Patients and methods

Patient selection criteria

In our department, 257 pediatric patients underwent a first KT from cadaveric donors between 1 June 1987 and 30 September 2001. For this study, we preliminarily considered only pediatric patients that were submitted to dialysis (PD or HD) for at least 3 months before KT, without switch from one dialysis modality to the other. Patient exclusion criteria were never-functioning grafts, acute renal failure (ARF) caused by vascular occlusion, obstructive nephropathy, biopsy-demonstrated hyperacute rejection, multiple-organ transplant, and incomplete pre- and/or post-transplantation data sets [8]. Following these criteria, clinical records of 174 pediatric patients (male/female = 97/77) were entered in the analyses. Kidney recipients were grouped for pretransplant dialysis (PD, $n = 79$; HD, $n = 95$) and early graft function.

Primary diseases

Pediatric kidney recipients enrolled in this study were in the following diagnostic categories: irreversible chronic renal failure ($n = 61$; 35.05%), hereditary nephropathies ($n = 32$; 18.39%), irreversible ARF ($n = 20$; 11.49%), congenital disorders ($n = 18$; 10.34%), metabolic disorders ($n = 7$; 4.02%), obstructive uropathies ($n = 3$; 1.72%), toxic nephropathies ($n = 2$; 1.14%), tumors requiring nephrectomy ($n = 1$; 0.57%), other indications ($n = 30$; 17.24%).

Pediatric patient management

The PDM (HD or PD) was chosen by each nephrology unit that had originally under treatment the pediatric patients in agreement with the dialysis modality decision guide originally proposed by Hamburger *et al.* [11]. Strong indications for PD included patient aged 0–5 years and obligate situations such as vascular access failure, congestive heart failure, and social situations (family preference and living far from an in-center dialysis unit). The conditions where PD was preferred included age between 6 and 16 years, bleeding diathesis, labile diabetes, chronic infections, needle anxiety, and active lifestyle. PD was not preferred for patients with obesity, multiple hernias, severe backache, multiple abdominal surgeries, impaired manual dexterity, blindness, less-than-ideal home situation, and depression. Relative contraindications for PD included patients with severe malnutrition, multiple abdominal adhesions, ostomies, proteinuria >10 g/day, obstructive pulmonary disease, ascites, presence of a ventriculo-peritoneal shunt, upper limb amputation with no help at home, poor hygiene, and dementia. PD is contraindicated in patients with documented type II ultrafiltration failure, severe inflammatory bowel disease, active acute diverticulitis, abdominal abscess, active ischemic bowel disease, and severe active psychotic disorder/marked intellectual disability. PD and HD have been equally preferred in patients with polycystic kidney disease and diabetes mellitus [11].

Hemodialysis consisted of pressure–pressure monitored dialysis with bicarbonate dialysate. HD was carried out three times weekly, either with an unmodified cellulose membrane (cuprophane; Bellco-Sorin, Mirandola, Italy; Gambro 1.8L, Gambro, Lund, Sweden) or with a synthetic membrane (polysulfone; Bellco-Sorin). PD consisted in continuous exchanges of PD solution (at day: 1000–1100 ml/m^2; or at night, 1200–1400 ml/m^2 in automated PD). Patient hydratation during and immediately after KT was performed under guidance of central venous pressure and/or Swan-Ganz pulmonary wedge pressure. Furosemide was used to increase urine output if diuresis was below 1 ml/kg/h for more than 3 h. The immunosuppressive drugs used in several combinations were methylprednisolone (10 mg/kg on day 0, 8 mg/kg on day 1, 4 mg/kg on day 2, then prednisone 0.75 mg/kg on day 3), cyclosporine A (4 mg/kg), FK506 (0.15 mg/kg/b.i.d.), and, starting from 1998, mycophenolate mofetil (300/400 mg/m^2).

Parameters

The following patient-related parameters were considered: age, BW on the day of KT, body weight gain (BWG) as the difference between BW on the day of KT and on day 1 after KT, body mass index (BMI) calculated as [weight (kg)/height (m)^2], body surface area (BSA) calculated following the Mosteller formula [12], the total fluid administered during the first 72 h after KT, urine volume (UV) collected by an indwelling bladder catheter in the first 24 hr after KT, early SCr measured on the day 1 after KT, the mean of central venous pressure (CVP) values continuously measured in the first 24 h after KT. In addition, pediatric patients were evaluated about virological assessment (CMV, EBV, HCV, anti-HBs) and the performing of blood transfusions (≤5 transfusions with

≤2 units/transfusion) before KT. Cadaveric donor age, cold ischemia time (CIT), and warm ischemia time (WIT) were also collected. In view of the fact that actuarial graft and patients survival exceeded 90%, the primary outcome parameter was the days needed to reach a SCr level 50% below that before KT [$T_{1/2(SCr)}$] [8]. ARF was defined in the case of need for dialysis, while DGF was defined as a $T_{1/2(SCr)} > 3$ days after KT [8]. Patients undergoing dialysis after KT received HD even if they were on PD before KT. The need for post-transplant dialysis occurred in 21 patients with ARF, and in 10 patients with DGF. Thirty patients had isolated DGF, without need for dialysis.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation, median, confidence interval (CI), lower quartile (LQ), and upper quartile (UQ). Categorical variables are expressed as the number of observations in each category [13], and analyzed for the difference between proportions from independent samples (expressed as a percentage) by chi-square test with Yates' correction for continuity. Continuous variables were compared by the Mann–Whitney test, univariate Pearson's correlation and exponential regression. A series of multivariate regression analyses was carried out with $T_{1/2(SCr)}$ as dependent variable [8]. The forward stepwise method was used to evaluate the independent variables at each step, adding or deleting them from the models [14]. Survival analysis was carried out by using the Kaplan–Meier method, log-rank test for curve comparison, and Cox regression, assuming $T_{1/2(SCr)}$ as the 'time variable'. It should be noted that following this approach, relative risk (RR) >1 indicates a decreased risk for DGF, whereas RR <1 suggests an increased risk [8]. The statistical significance was assumed at $P < 0.05$ with a two-tailed null hypothesis. Statistical analyses were performed by using the software package STATISTICA 6.1 (StatSoft, Tulsa, OK, USA), MedCalc 7.5 (MedCalc Software, Mariakerke, Belgium), and a Cox regression calculator by John Pezzullo (in http://members.aol.com/johnp71/javastat.html).

Results

The overall pattern of continuous variables related to kidney recipients is shown in Table 1. The mean age of pediatric recipients was 14.47 ± 5.35 (Table 1), whereas the mean age of cadaveric donors was 13.84 ± 10.8 years (median 11.5; 95% CI from 12.22 to 15.46; LQ 7; UQ 17). In 108 patients (62.06%), $T_{1/2(SCr)}$ was reached within the first 3 days after KT. DGF was observed in 40 patients (22.98%), and ARF in 26 patients (14.94%). No significance was found in order to primary diseases of pediatric kidney recipients grouped for PDM (Table 2), as well as for virological assessment and the performing of blood transfusions before KT (Table 3). In the patients who received blood transfusions before KT, both DGF and ARF occurred in five cases each.

After comparison of kidney recipients grouped for DGF, patients with DGF showed a significantly higher BW ($P = 0.014$), BSA ($P = 0.005$), WIT ($P = 0.022$), early post-transplant SCr ($P < 0.001$), and $T_{1/2(SCr)}$ ($P < 0.001$), whereas lower UV ($P < 0.001$) and fluid load ($P < 0.001$) occurred (Table 4). No significance was noted for BMI, CIT, BWG, and CVP (Table 4), as well as for residual renal function before KT expressed as creatinine clearance (data not shown). In the ARF group ($n = 26$), higher values than in the normal kidney function group were found for SCr ($P < 0.0001$) and $T_{1/2(SCr)}$

Table 1. Overall pattern of the pediatric kidney recipient-related continuous variables.

Variable	Mean	Median	–95% CI	+95% CI	LQ	UQ
Patient age (years)	14.47 ± 5.35	15	13.67	15.27	11	18
BW (kg)	38.61 ± 16.29	39.5	36.14	41.08	24.5	50.2
BSA (m^2)	1.2 ± 0.36	1.24	1.15	1.26	0.91	1.48
BMI (kg/m^2)	19.43 ± 5.47	18.5	18.58	20.28	16.4	21.2
CIT (h)	15.23 ± 3.57	15	14.7	15.77	13	18
WIT (min)	46.97 ± 9.71	47.5	45.49	48.45	40	54
SCr D1 (mg/dl)	6.69 ± 3.42	6.4	6.17	7.21	4.2	9.3
BWG (g/24 h)	1812 ± 2481	1000	1440	2184	300	2200
CVP (mmHg)	5.87 ± 2.82	6	5.41	6.34	4	8
UV (ml/24 h)	2692 ± 2547	2160	2308	3075	1014	3620
Fluid load (ml/h)	129 ± 107	109	113	146	59	169
$T_{1/2(SCr)}$ (days)	5.02 ± 5.64	3	4.15	5.89	2	5

CI, confidence interval; LQ, lower quartile; UQ, upper quartile; BW, body weight; BSA, body surface area; BMI, body mass index; CIT, cold ischemia time; WIT, warm ischemia time; SCr, serum creatinine on day 1; BWG, body weight gain; CVP, central venous pressure; UV, urinary volume; $T_{1/2(SCr)}$, days to reach a serum creatinine level 50% below that before transplantation.

Table 2. Diagnostic categories and primary diseases in pediatric kidney recipients grouped for pretransplant dialysis mode.

Diagnostic category/primary disease	HD ($n = 95$)	PD ($n = 79$)	χ^2	*P*-value
ICRF ($n = 61$)	37 (38.95%)*	24 (30.38%)*	1.04	0.307
Vesico-ureteral reflux ($n = 32$)	19 (20%)	13 (16.46%)	0.163	0.685
Focal glomerulorosclerosis ($n = 18$)	12 (12.63%)	6 (7.59%)	0.701	0.402
Chronic glomerulonephritis ($n = 5$)	3 (3.16%)	2 (2.53%)	0.043	0.835
IgA-nephropathy ($n = 3$)	2 (2.11%)	1 (1.27%)	0.026	0.871
Nephrosic syndrome ($n = 2$)	1 (1.05%)	1 (1.27%)	0.335	0.562
Hypertensive nephrosclerosis ($n = 1$)	–	1	–	–
IARF ($n = 20$)	11 (11.58%)	9 (11.39%)	0.04	0.841
Acute and subacute glomerulonephritis ($n = 15$)	8 (8.42%)	7 (8.86%)	0.028	0.866
Hemolytic–uremic syndrome ($n = 3$)	2 (2.11%)	1 (1.27%)	0.026	0.872
Anaphylactoid purpura ($n = 2$)	1 (1.05%)	1 (1.27%)	0.335	0.562
Hereditary nephropathies ($n = 32$)	16 (16.84%)	16 (20.25%)	0.146	0.702
Medullary cystic disease ($n = 19$)	7 (7.37%)	12 (15.19%)	1.967	0.160
Alport syndrome ($n = 5$)	4 (4.21%)	1 (1.27%)	0.49	0.484
Polycystic kidney disease ($n = 3$)	2 (2.11%)	1 (1.27%)	0.026	0.872
Joubert syndrome ($n = 3$)	2 (2.11%)	1 (1.27%)	0.026	0.872
Prune Belly syndrome ($n = 1$)	–	1	–	–
Alstrom syndrome ($n = 1$)	1	–	–	–
Congenital disorders ($n = 18$)	11 (11.58%)	7 (8.86%)	0.113	0.736
Dysplasia ($n = 14$)	9 (9.47%)	5 (6.33%)	0.229	0.632
Hypoplasia ($n = 3$)	2 (2.11%)	1 (1.27%)	0.026	0.872
Toxic nephropathies ($n = 2$)	1 (1.05%)	1 (1.27%)	0.335	0.562
Tumors requiring nephrectomies ($n = 1$)	–	1	–	–
Other indications ($n = 30$)	15 (15.79%)	15 (18.99%)	0.126	0.722
Etiology unknown† ($n = 26$)	12 (12.63%)	14 (17.72%)	0.499	0.479
Vasculitis ($n = 4$)	3 (3.16%)	1 (1.27%)	0.102	0.748

*% within overall dialysis group.
†Documented chronic renal failure of at least 6–8 weeks duration.
HD, hemodialysis; PD, peritoneal dialysis; ICRF, irreversible chronic renal failure; IARF, irreversible acute renal failure.

Table 3. Virological assessment and carrying out of blood transfusions before transplantation in pediatric kidney recipients grouped for pretransplant dialysis mode.

Parameter	HD ($n = 95$)	PD ($n = 79$)	χ^2	*P*-value
CMV+ (no. patients)	93 (97.89%)*	75 (94.94%)*	0.415	0.519
EBV+ (no. patients)	93 (97.89%)	76 (96.20%)	0.043	0.834
HCV+ (no. patients)	4 (4.21%)	1 (1.27%)	0.49	0.484
Anti-Hbs+ (no. patients)	–	–	–	–
Blood transfusions (no. patients)	8 (8.42%)	9 (11.39%)	0.415	0.519

*% within overall dialysis group.
HD, hemodialysis; PD, peritoneal dialysis; EBV, Epstein–Barr virus; CMV, cytomegalovirus; HCV, hepatitis C virus.

($P < 0.0001$), whereas lower values occurred for WIT ($P = 0.047$), UV ($P < 0.0001$), and fluid load ($P < 0.0001$). After comparison of DGF *vs.* ARF group, this latter revealed higher values for SCr ($P = 0.038$) and $T_{1/2(SCr)}$ ($P < 0.0001$), while lower values were found for UV ($P < 0.0001$) and fluid load ($P < 0.0001$). By stratifying continuous variables for PDM, in HD group were observed significantly higher patient age, BW, BSA ($P < 0.001$), and BMI ($P = 0.009$), as well as a lower early SCr after KT ($P = 0.008$) (Table 4). DGF occurred in 21 HD *vs.* 19 PD patients ($P = 0.994$), while ARF was observed in 11 HD *vs.* 15 PD patients ($P = 0.705$).

The results of the univariate correlation analysis for the kidney recipient-related continuous variables are summarized in Table 5. Univariate exponential correlation was carried out between $T_{1/2(SCr)}$ and all the other variables included in Table 5. The exponential correlation showed a better value than the linear correlation for BW ($R^2 = 0.28$ vs. $R^2 = 0.04$), BSA ($R^2 = 0.29$ vs. $R^2 = 0.03$), and SCr ($R^2 = 0.51$ vs. $R^2 = 0.28$) (Fig. 1). The cut-off of the

Table 4. Comparison of continuous variables in pediatric kidney recipients grouped for DGF and type of dialysis.

	DGF ($n = 40$)	No DGF ($n = 108$)	*P*-value	HD ($n = 95$)	PD ($n = 79$)	*P*-value
Patient age (years)	14.75 ± 5.92	14.54 ± 5.21	0.416	16.67 ± 4.66	11.82 ± 4.93	<0.001
BW (kg)	44.80 ± 19.74	36.94 ± 13.95	0.014	43.15 ± 14.69	32.99 ± 16.51	<0.001
BSA (m^2)	1.34 ± 0.43	1.17 ± 0.31	0.005	1.31 ± 0.31	1.08 ± 0.37	<0.001
BMI (kg/m^2)	21.44 ± 7.62	19.01 ± 4.68	0.060	20.04 ± 4.77	18.72 ± 6.15	0.009
CIT (h)	15.87 ± 4.35	15 ± 3.16	0.474	15.04 ± 3.34	15.46 ± 3.83	0.668
WIT (min)	49.76 ± 9.79	45.31 ± 9.5	0.022	45.77 ± 9.58	48.52 ± 9.72	0.086
SCr D1 (mg/dl)	8.14 ± 3.29	5.4 ± 2.68	<0.001	5.97 ± 3	7.53 ± 3.69	0.008
BWG (g/24 h)	2116 ± 2205	1729 ± 2563	0.126	1879 ± 2172	1730 ± 2824	0.053
CVP (mmHg)	5.56 ± 3.19	6.16 ± 2.62	0.419	5.59 ± 3.04	6.25 ± 2.47	0.156
UV (ml/24 h)	1774 ± 1181	3613 ± 2731	<0.001	2644 ± 1960	2749 ± 3124	0.306
Fluid load (ml/h)	91 ± 50	167 ± 115	<0.001	128 ± 82	131 ± 132	0.26
$T_{1/2(SCr)}$ (days)	7.76 ± 4.76	2.09 ± 1.14	<0.001	4.55 ± 4.65	5.62 ± 6.7	0.722

DGF, delayed graft function; HD, hemodialysis; PD, peritoneal dialysis; BW, body weight; BSA, body surface area; BMI, body mass index; CIT, cold ischemia time; WIT, warm ischemia time; SCr, serum creatinine on day 1; BWG, body weight gain; CVP, central venous pressure; UV, urinary volume; $T_{1/2(SCr)}$, days to reach a serum creatinine level 50% below that before transplantation.

Table 5. Univariate correlation analysis for the pediatric kidney recipient-related continuous variables (*R* values).

	Age	BW	BSA	BMI	CIT	WIT	SCr	BWG	CVP	UV	Fluid load	$T_{1/2(SCr)}$
Age												
BW	0.70**											
BSA	0.71***	0.98***										
BMI	0.23**	0.53***	0.25***									
CIT	−0.04	−0.04	−0.06	0								
WIT	−0.15	−0.06	−0.09	0.02	0.13							
SCr D1	0.12	0.31***	0.34***	0.15	0.11	0.18*						
BWG	0.11	0.01	0.01	−0.07	−0.07	−0.06	−0.07					
CVP	−0.1	−0.2*	−0.16	0.03	0.03	−0.02	−0.08	−0.12				
UV	0.13	0.15	0.17*	−0.03	−0.01	−0.21**	−0.21	−0.02	0.04			
Fluid load	0.08	0.17*	0.19*	−0.02	0	−0.21**	−0.2*	−0.01	0.04	0.99***		
$T_{1/2(SCr)}$	0.05	0.21*	0.16*	0.04	0.17*	0.15	0.46***	0	−0.21**	−0.39***	−0.38***	

*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.

BW, body weight; BSA, body surface area; BMI, body mass index; CIT, cold ischemia time; WIT, warm ischemia time; SCr, serum creatinine on day 1; BWG, body weight gain; CVP, central venous pressure; UV, urine volume; $T_{1/2(SCr)}$, days to reach a serum creatinine level 50% below that before transplantation.

slope for BW, BSA, and SCr was around 53, 1.5, and 4 respectively.

A multivariate regression analysis was performed by entering $T_{1/2(SCr)}$ as dependent variable, and an organ preservation-related variable (CIT), the volume-related parameters (BWG, UV, fluid load), and PDM as independent variables, following a forward stepwise method (Table 6). In model A ($R^2 = 0.174$; $P < 0.001$), in which CIT and the volume-related parameters were included, only CIT reached a statistical significance ($\beta = 0.16$; $P = 0.022$). When PDM was entered in the model, a slight increase in R^2 was observed (0.182 vs. 0.174), although no significance was noted for this variable ($P = 0.195$). The β for CIT and dialysis mode did not show substantial changes when alternatively one of the three volume-related parameters was excluded from the model (Table 6, model C without UV; model D without BWG; model E without fluid load). In each model, CIT but not PDM reached statistical significance, suggesting that only CIT was a predictor for $T_{1/2(SCr)}$, independently of volume-related parameters. Conversely, although fluid load and UV reached respectively statistical significance when the either variable was alternatively excluded (model C and E, $P < 0.0001$), they lost any significance when simultaneously included in the other models. No statistical significance was observed by testing other regression models that included volume-related parameters and variables such as BW, BSA, and WIT (data not shown).

Comparison of the Kaplan–Meier curves between PD versus HD for $T_{1/2(SCr)}$ assumed as the time variable

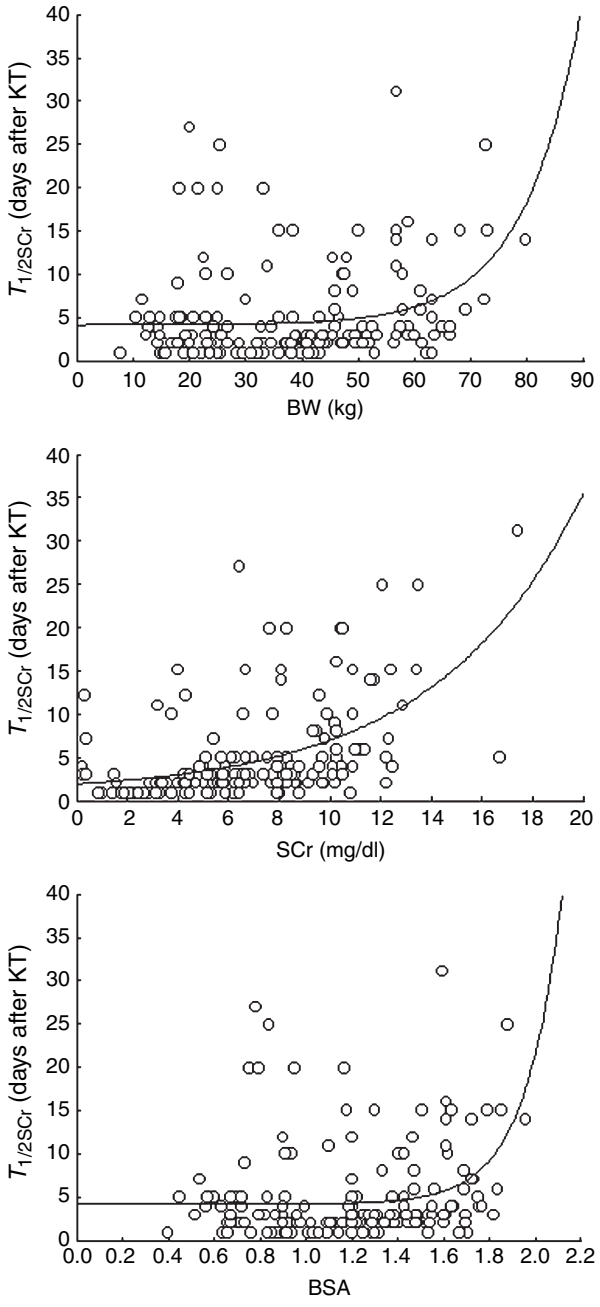

Figure 1 Exponential regression between $T_{1/2(SCr)}$ and BW $y = 4.21 + \exp[-5.12 + (0.097) * x]$, $R^2 = 0.28$; $T_{1/2(SCr)}$ and BSA $y = 4.26 + \exp[-9.46 + (6.15) * x]$, $R^2 = 0.29$; $T_{1/2(SCr)}$ and SCr $y = 0.93 + \exp[0.064 + (0.17) * x]$, $R^2 = 0.28$.

Table 6. Multiple regression forward analysis for $T_{1/2(SCr)}$ (days to reach a serum creatinine level 50% below that before transplantation) as dependent variable.

Model	β	β SE	*P*-value
Model A ($R^2 = 0.174$; $P < 0.001$)			
CIT (h)	0.16	0.07	0.022
BWG (g/24 h)	0.004	0.07	0.946
UV (ml/24 h)	−0.54	0.67	0.424
Fluid load (ml/h)	0.16	0.67	0.811
Model B ($R^2 = 0.182$; $P < 0.001$)			
PDM	−0.09	0.07	0.195
CIT (h)	0.15	0.07	0.027
BWG (g/24 h)	0.006	0.07	0.922
UV (ml/24 h)	−0.59	0.67	0.382
Fluid load (ml/h)	0.20	0.67	0.757
Model C ($R^2 = 0.179$; $P < 0.001$)			
PDM	−0.08	0.06	0.212
CIT (h)	0.16	0.07	0.023
BWG (g/24 h)	0.008	0.06	0.902
Fluid load (ml/h)	−0.37	0.06	<0.0001
Model D ($R^2 = 0.182$; $P < 0.001$)			
PDM	−0.09	0.06	0.181
CIT (h)	0.15	0.06	0.026
UV (ml/24 h)	−0.59	0.67	0.379
Fluid load (ml/h)	0.21	0.67	0.754
Model E ($R^2 = 0.182$; $P < 0.001$)			
PDM	−0.08	0.06	0.199
CIT (h)	0.15	0.06	0.025
BWG (g/24 h)	0.007	0.07	0.915
UV (ml/24 h)	−0.38	0.69	<0.0001

SE, standard error; PDM, pretransplantation dialysis mode; CIT, cold ischemia time; UV, urinary volume; BWG, body weight gain.

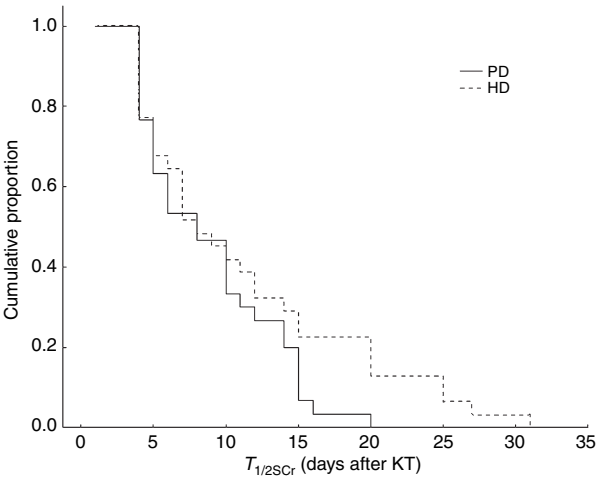

Figure 2 Comparison of the Kaplan–Meier curves between pediatric kidney recipients who underwent pretransplantation PD or HD for $T_{1/2(SCr)}$ assumed as the time variable ($P = 0.149$).

showed no significant difference at the log-rank test ($P = 0.149$), although PD reached a better end-point than HD (Fig. 2). Cox proportional hazard regression analysis was performed by entering the same variables included in the multivariate model of Table 6. In model A ($\chi^2 = 9.26$; $P = 0.098$), where all variables were included, no statistical significance was observed. CIT ($\beta = -0.05$; $P = 0.093$) and UV ($\beta = 0.00$; $P = 0.091$) were the variables more near to significance (Table 7).

Table 7. Cox regression analysis for $T_{1/2(SCr)}$ (days to reach a serum creatinine level 50% below that before transplantation) assumed as the time variable.

Model	β	β SE	RR	*P*-value
Model A ($\chi^2 = 9.26$; $P = 0.098$)				
PDM	0.18	0.30	1.20	0.548
CIT (h)	−0.05	0.03	0.94	0.093
UV (ml/24 h)	0.00	0.00	1.00	0.091
BWG (g/24 h)	−0.00	0.00	1.00	0.726
Fluid load (ml/h)	−0.06	0.04	0.93	0.116
Model B ($\chi^2 = 6.60$; $P = 0.158$)				
PDM	0.17	0.30	1.19	0.573
CIT (h)	−0.04	0.03	0.96	0.192
BWG (g/24 h)	−0.00	0.00	1.00	0.829
Fluid load (ml/h)	0.0	0.00	1.00	0.037

SE, standard error; RR, relative risk; PDM, pretransplantation dialysis mode; CIT, cold ischemia time; UV, urinary volume; BWG, body weight gain.

Conversely, PDM was far from statistical significance (β =0.18; $P = 0.548$), although RR >1 was noted. In model B ($\chi^2 = 6.60$; $P = 0.158$), in which the UV was left out, CIT showed an increased *P*-value ($P = 0.192$), with only a minimal change in β (−0.05 vs. −0.04). In the other models, no significance was found for CIT or volume-related parameters when one of these latter was left out (data not shown).

Discussion

A delay in functional recovery of transplanted kidneys may negatively affected short- and long-term graft outcome [3,4,7]. Pretransplantation PD was reported to influence positively the recovery of renal function after KT in adult recipients [8,9], and it was hypothesized that fluid status might be implicated in this finding [8]. On the contrary, in patients over 60 years of age the long-term use of PD (>2 years) has been associated with increased mortality rates, irrespective of diabetic status or gender [15]. In pediatric patients, PD is strongly indicated for children aged 0–5 years, and should be preferred for those aged 6–16 years [11,16]. However, pretransplantation dialysis resulted to exert no clear effect on the graft outcome in pediatric kidney recipients [10], suggesting the need for further investigation. Theoretically, the most suitable approach to evaluate the effect of PDM on KT outcomes would be a prospective study. However, as Termorshuizen *et al.* [15] argued, conducting such a study in patients with end-stage renal diseases could be regarded as extremely difficult, because of advantages and disadvantages associated with PDM choice for individual patients. Therefore, we retrospectively analysed pretransplantation PDM to evaluate its potential effects on early graft function in a cohort of pediatric patients, following rigorous patient selection criteria. HD or PD was chosen by each nephrology unit that had originally under treatment the pediatric patients, in agreement with the dialysis modality decision guide proposed by Hamburger *et al.* [11]. Although PD is the preferred dialysis treatment for children, a cross-sectional survey study has demonstrated that specialization of clinicians is able to influence treatment recommendations for children and adolescents with end-stage renal disease, being pediatric nephrologists more likely than adult nephrologists to recommend PD for identical patients [17]. In our patients, a strict link between pediatrics, nephrologists and surgeons has allowed the optimization of dialysis choice. Patients that switched from one dialysis modality to the other before KT were excluded from this study, differently from other series that enrolled patients treated with both PD and HD [18]. We adopted this exclusion criteria to obtain a more rigorous comparison between PD and HD. Considering that in our series both patient and graft survival exceeded 90%, $T_{1/2(SCr)}$ was assumed as the primary outcome parameter, in agreement with Van Biesen *et al.* [8]. Differently from the study performed by Van Biesen's group on adult kidney recipients [8], we made specific evaluation in pediatric patients for primary diseases, virological assessment and blood transfusions before KT. We did not find significant differences by grouping these parameters for PDM. Notably, almost all of our patients were EBV+, CMV+, and HCV−, without occurrence of anti-HBs+. Although blood transfusions before KT might have a positive effect in pediatric patients who received ≤5 transfusions [19], in our series only 17 patients received blood transfusions before KT, according to conservative transfusion policy adopted in southern Europe during the last decade [20].

In our series, although $T_{1/2(SCr)}$ was reached relatively earlier in pediatric patients who underwent PD, no significant difference was observed after comparison of this time variable for PDM, in contrast with previous findings in adult kidney recipients [6,8]. As expected, in both ARF and DGF patients an unfavourable difference for UV, fluid load, SCr, and $T_{1/2(SCr)}$ was noted by comparing them with patients who had no impaired post-transplant outcomes. The univariate correlation analysis for the continuous variables showed no significant relationship between fluid load and BWG or CVP, as previously reported for adult kidney recipients [8]. By performing exponential correlation between $T_{1/2(SCr)}$ and all the other continuous variables, we found a better value than the linear correlation for BW, BSA, and SCr. Interestingly, we did not observe significance in the exponential correlation for CIT, in contrast with previ-

ous findings in adult kidney recipients [8]. However, in a multivariate regression analysis that we carried out following a forward stepwise method, CIT resulted in all models as a predictor for $T_{1/2(SCr)}$, independently from volume-related parameters. Conversely, although in some regression models UV and fluid load contributed to $T_{1/2(SCr)}$, these variables were intermutually related, as resulted by the lack of significance when both UV and fluid load were entered in the same regression models. Notably, PDM did not reach statistical significance in any multivariate regression model, suggesting a poor impact of this parameter on DGF in pediatric kidney recipients. On the contrary, we did not find significance neither by a simple comparison of the PD versus HD patients within ARF or DGF groups, differently from a significantly higher rate of DGF reported in HD adult patients [18]. Finally, in the Cox regression analysis UV and fluid load confirmed their intermutual relationship, whereas CIT did not reach significance.

Our findings in pediatric patients did not confirm the results reported by Van Biesen *et al.* [8] in adult kidney recipients, where PDM revealed to be an independent predictor for $T_{1/2(SCr)}$. In that study, performed on 119 patients, the incidence of DGF was lower, and the authors suggested that their finding may be the result of a short CIT, being CIT median and UQ values in DGF and no-DGF group 22 and 30 h versus 19 and 23 h, respectively [8]. However, these CIT values, that did not reach full statistical significance after intergroup comparison [8], do not seem to diverge from those reported in a study population carried out on the United States Renal Data System (USRDS), in which an overall CIT of 20.4 ± 8.5 h was observed in 13 486 adult renal transplant recipients [21]. In our series, the overall CIT value (15.23 ± 3.57 h) was lower than in the USRDS, and no significant difference for this parameter occurred between DGF and no-DGF group. Although earlier studies demonstrated that CIT may play a critical role on transplanted kidney outcome [22,23], and even if we found that CIT resulted in multivariate regression models as an independent predictor for $T_{1/2(SCr)}$, we failed to confirm a statistical significance for CIT in both exponential correlation and Cox regression models. Our short CIT supported these findings, differently from the results of Van Biesen *et al.* [8], where their longer CIT had a strong impact on the graft outcome in all analyses. Considering that a high incidence of DGF may be a product of long CIT [8], our results seem to substantiate that the evaluation of PDM impact on graft outcome has not been overwhelmed. Otherwise from findings reported in adult patients, this study suggests that PDM does not affect early graft function in pediatric kidney recipients.

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