ORIGINAL ARTICLE



# Epidemiology of peritonitis following maintenance peritoneal dialysis catheter placement during infancy: a report of the SCOPE collaborative

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Received: 7 June 2017/Revised: 16 September 2017/Accepted: 10 October 2017/Published online: 17 November 2017 © IPNA 2017

#### Abstract

*Background* Maintenance peritoneal dialysis (PD) is the dialysis modality of choice for infants and young children. However, there are limited outcome data for those who undergo PD catheter insertion and initiate maintenance PD within the first year of life.

*Methods* Using data from the Children's Hospital Association's Standardizing Care to Improve Outcomes in Pediatric End Stage Renal Disease (ESRD) Collaborative (SCOPE), we examined peritonitis rates and patient survival in 156 infants from 29 North American pediatric dialysis centers who had a chronic PD catheter placed prior to their first birthday.

*Results* In-hospital and overall annualized rates of peritonitis were 1.73 and 0.76 episodes per patient-year, respectively. Polycystic kidney disease was the most frequent renal diagnosis and pulmonary hypoplasia the most common co-

See Acknowledgements for a full list of the centers/team leaders participating in the SCOPE Collaborative during the first 3 years.

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morbidity in infants with peritonitis. Multivariable regression models demonstrated that nephrectomy at or prior to PD catheter placement and G-tube insertion after catheter placement were associated with a nearly sixfold and nearly threefold increased risk of peritonitis, respectively. Infants with peritonitis had longer initial hospital stays and lower overall survival (86.3 vs. 95.6%, respectively; P < 0.02) than those without an episode of peritonitis.

*Conclusions* In this large cohort of infants with ESRD, the frequency of peritonitis was high and several risk factors associated with the development of peritonitis were identified. Given that peritonitis was associated with a longer duration of initial hospitalization and increased mortality, increased attention to the potentially modifiable risk factors for infection is needed.

**Keywords** Infant · Quality improvement · Peritonitis · Survival · Peritoneal dialysis

# Introduction

Although transplantation is the ideal renal replacement therapy (RRT) for children with end-stage renal disease (ESRD), technical aspects limit the feasibility of the procedure in the first year of life. Thus, dialysis is used as a bridge to successful early transplantation with peritoneal dialysis (PD), the dialytic modality of choice. Data from the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS) show that nearly 96% of children less than 2 years of age who receive long-term dialysis initiate therapy with PD [1]. However, there are limited outcome data from the time of PD catheter insertion for those patients who begin dialysis in the first year of life, especially for the newborn population, which has resulted in a lack of uniformity on the recommendation for long-term treatment [2]. Virtually all of the historical infant data have been based upon the outcome of infants following the initiation of home dialysis therapy, either from single-center studies utilizing retrospective analyses [3], or more recently from several reports obtained from either national or international reg-

istries [1, 4-8]. The Children's Hospital Association's Standardizing Care to Improve Outcomes in Pediatric End Stage Renal Disease (SCOPE) Collaborative is a multi-center quality transformation effort whose primary aim is to decrease peritonitis rates among pediatric maintenance PD patients [9, 10]. Using data from SCOPE, we have the unique opportunity to describe the outcome of 156 infants from 29 centers in North America from the time their PD catheter was placed for the initiation of chronic PD (CPD) prior to their first birthday. The information available from the dataset of this population includes follow-up information for up to 1-year post catheter insertion regarding both overall and in-hospital peritonitis rates, risk factors for infection and patient survival data. The identification of modifiable risk factors was sought in order to help future studies improve the course of these complex patients.

# Methods

# **SCOPE** collaborative

The design and structure of the SCOPE collaborative has been previously described in detail [9, 10]. To briefly summarize, the SCOPE collaborative was established to reduce peritonitis rates via implementation of three standardized PD catheter care bundles (catheter insertion bundle, patient and caregiver training bundle and follow-up care bundle). The components of the bundles were based on expert opinion and published guidelines. Unique to SCOPE, patients with ESRD were enrolled in the collaborative at the time of PD catheter placement, even if maintenance dialysis care had not yet been established on an outpatient basis. As such, the catheter may not have been used promptly at the time of enrollment or the patient may have initiated maintenance PD as an inpatient and remained hospitalized, in each case contributing data to SCOPE. Patients who had a PD catheter placed for temporary treatment of acute kidney injury were not enrolled into SCOPE. All catheters associated with patients enrolled during the study period, including prevalent catheters and new catheter insertions, were evaluated; therefore, a single patient could have contributed multiple catheters. Data on peritonitis episodes were collected prospectively. The Declaration of Helsinki was followed, and the collaborative protocol was approved by the Institutional Review Board at each participating center.

#### **Data collection**

Data were collected from all infants who had a chronic PD catheter placed within the first year of life. These patients were followed for up to 1 year post catheter insertion for this analysis. Data pertaining to patient and catheter characteristics, along with peritonitis rates (annualized rate of episodes), causative organisms and outcomes (initial hospitalization duration and patient survival), were collected between October 1, 2011 and September 30, 2014 from 29 pediatric dialysis centers participating in the SCOPE collaborative. Peritonitis was defined as cloudy PD effluent with a white blood cell count of > 100/hpf and differential >50% polymorphonuclear cells/hpf, with or without a positive culture [9–11]. Treatment of peritonitis was according to each center's institutional practice, but centers were advised to follow International Society for Peritoneal Dialysis (ISPD) treatment recommendations [11].

#### Statistical analysis

Categorical variables were described using frequencies and percentages, whereas continuous variables were described using median and interquartile range (IQR) values. Patient characteristics, clinical characteristics and outcomes were compared using chi-square tests for categorical variables and a Wilcoxon rank-sum test for continuous variables. We fit a multivariable logistic regression model to assess the association of patient and clinical characteristics on the probability of developing peritonitis within the first year after PD catheter insertion. Covariates included in the initial model included race, sex, placement of the PD catheter prior to 30 days of life, hospital stay of > 30 days after catheter insertion, initiation of PD in the intensive care unit (ICU), placement of Gtube after placement of the PD catheter, presence of titanium adapter and history of nephrectomy. Due to the relatively small number of infections identified in the dataset and the presence of multicollinearity, we utilized a backwards selection approach to assess the association of the previous covariates with the probability of developing peritonitis. At each step in the backwards selection, covariates that failed to achieve a significance level of 0.10 were removed. The final model included history of nephrectomy and placement of Gtube after PD catheter insertion. All models included a random effect to account for clustering of insertions within the hospital. Cases with missing data, i.e. forms with missing or unknown information, were excluded from the denominator when percentages were calculated.

To assess the effect of nephrectomy and placement of a Gtube after PD catheter insertion on the time to peritonitis (peritonitis episodes that occurred after the two former surgeries were conducted), we performed two survival analyses based on Cox proportional hazards modeling after testing the proportional hazards assumption—one model for nephrectomy and a second for G-tube placement after PD catheter insertion. To account for the time between catheter insertion and enrollment in SCOPE, we left the data censored. Data for patients who had not developed peritonitis within 365 days of catheter placement were right censored.

All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC). P values of < 0.05 were considered to be statistically significant.

#### Results

## **Clinical characteristics**

Overall, of the 156 infants enrolled in the collaborative, 53% were less than 30 days of age at PD catheter insertion with a median day of life (DOL) at PD catheter insertion of 25 and a median weight of 3.3 kg (Table 1). The majority of infants had congenital abnormalities of the kidney and urinary tract (CAKUT) as their underlying etiology of ESRD.

 Table 1
 Clinical characteristics of the cohort

Clinical characteristics	Total cohort ( $N = 156$ )
DOL (at placement)	25 [8, 117]
DOL < 30 (at placement)	83 (53.2%)
GA (weeks)	36 [34, 38]
Male	102 (65.4%)
Weight (kg)	3.3 [2.6, 5.1]
Hospital time before placement (days)	4 [0, 14]
Anuric at placement,	36 (23.8%)
Primary disease	
CAKUT	95 (60.9%)
GN	2 (1.3%)
PKD	13 (8.3%)
Nephrotic syndrome/FSGS	2 (1.3%)
Ciliopathy	2 (1.3%)
Infarct	17 (10.9%)
Other	25 (16.0%)
Co-morbidity	
Pulmonary hypoplasia/CLD	39 (27.%5)
NEC	1 (0.7%)
Ocular	4 (2.9%)
Other	84 (57.5%)
Multiple	29 (19.6%)

Data are presented as the median with the interquartile range (IQR; Q1, Q3) given in square brackets, or as a number with the percentage in parenthesis

DOL, Day of life; GA, gestational age; CAKUT, congenital abnormalities of kidney and urinary tract; GN, glomerulonephritis; PKD, polycystic kidney disease; FSGS, focal segmental glomerulosclerosis; CLD, chronic lung disease; NEC, necrotizing enterocolitis

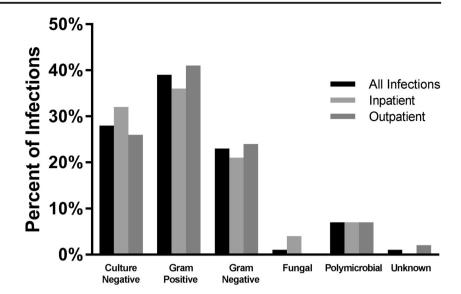
# Clinical and catheter-related characteristics associated with peritonitis

In-hospital and overall annualized peritonitis rates were 1.73 and 0.76 episodes per patient-year, respectively. Figure 1 shows the breakdown of peritonitis etiology for all peritonitis episodes, as well as for those episodes that arose during the initial hospitalization when the PD catheter was placed and those that occurred after home dialysis had been established, respectively. Overall, Gram-positive organisms accounted for the greatest percentage of infections, and culture-negative peritonitis accounted for 28% of peritonitis episodes. Four patients changed modalities due to peritonitis, two of which were inpatient peritonitis episodes and two of which occurred during outpatient care. The clinical characteristics of the cohort, subcategorized by history of peritonitis are presented in Table 2. Polycystic kidney disease was more common in those patients who experienced peritonitis than in those without peritonitis (16.9 vs. 2.2%, respectively; P < 0.05). Additionally, a history of pulmonary hypoplasia was present in a higher percentage of infants who developed peritonitis compared to those without infection (36.2 vs. 21.4%, respectively; P < 0.05).

The relationship between the occurrence of peritonitis and both catheter characteristics and additional procedures performed at or near the time of PD catheter insertion was also investigated (Table 3). The use of a curled PD catheter or plastic adaptor, nephrectomy prior to or concurrent with PD catheter insertion and G-tube insertion after catheter placement were more common in patients who experienced peritonitis (P < 0.05). Whereas the majority of all dialysis initiations took place in a private room within an acute care unit using the manual Dialy-Nate® system (sterile, pre-assembled and closed peritoneal dialysis system designed especially for neonatal and pediatric use; Utah Medical Products, Midvale, UT), there was no significant relationship noted between peritonitis and either the in-hospital location of dialysis initiation, the equipment used or the timing of PD initiation (< or > 14 days following catheter insertion) (Table 4).

### Peritonitis development during initial hospitalization

Sixty-five infants developed peritonitis, 23 of whom experienced their first episode during their initial hospitalization. Those with an episode of peritonitis during their initial hospitalization were younger at catheter placement (14 [IQR 8, 30] vs. 27 [IQR 8, 209] DOL; p < 0.04), were less likely to have CAKUT as their primary disease (30 vs. 61%; p < 0.05) and were more likely to have additional co-morbidities, including pulmonary hypoplasia (p < 0.05), than those who developed peritonitis only as an outpatient. Early catheter placement ( $\leq$ 30 days of age) versus later catheter placement was also more common in those who developed peritonitis during the initial Fig. 1 Peritonitis etiology. Description of microbiology for all peritonitis episodes and for those episodes that arose during the initial hospitalization versus those that occurred during outpatient peritoneal dialysis (PD) management. Gram-positive organisms accounted for the greatest percentage of all infections



hospital stay (29 vs. 9%; p < 0.01). As noted above, nephrectomy prior to or concurrent with PD catheter insertion, and Gtube insertion after catheter placement were more common in patients who experienced peritonitis, and of the 23 patients who developed peritonitis as an inpatient, only nine (39.1%) did not have a nephrectomy at or prior to PD catheter placement or G- tube insertion after catheter placement, compared with 60.9% of those who had outpatient peritonitis (p < 0.01). There were no differences in catheter characteristics/design (number of cuffs or shape), surgical site nor placement technique between those that did and did not develop peritonitis as an inpatient.

Clinical characteristics	No peritonitis $(N = 91 \text{ patients})$	Peritonitis $(N = 65 \text{ patients})$	P value
DOL (At placement)	32 [9, 129]	21 [8, 88]	0.40
DOL <30 (At placement)	43 (47.3%)	40 (61.5%)	0.89
GA (weeks)	36 [34, 38]	37 [34, 38.5]	0.23
Male	59 (64.8%)	43 (66.2%)	0.87
Weight (kg)	3.3 [2.6, 5.2]	3.3 [2.6, 4.6]	0.95
Hosp time before PD catheter placement (days)	4 [0, 14]	4.5 [0, 14]	0.81
Anuric at PD catheter placement	17 (19.1%)	19 (30.6%)	0.10
Primary disease			0.04
CAKUT	62 (68.1%)	33 (50.8%)	-
GN	2 (2.2%)	0 (0.0%)	-
PKD	2 (2.2%)	11 (16.9%)	-
Nephrotic syndrome/FSGS	1 (1.1%)	1 (1.5%)	-
Ciliopathy	1 (1.1%)	1 (1.5%)	-
Infarct	9 (9.9%)	8 (12.3%)	-
Other	14 (15.4%)	11 (16.9%)	-
Co-morbidity, N(%)			-
Pulmonary hypoplasia/CLD	18 (21.4%)	21 (36.2%)	0.05
NEC	0 (0.0%)	1 (1.8%)	0.41
Ocular	2 (2.4%)	2 (3.6%)	1.00
Other	46 (54.1%)	38 (62.3%)	0.32
Multiple	13 (15.1%)	16 (25.8%)	0.11

Data are presented as the median with the IQR (Q1, Q3) given in square brackets, or as a number with the percentage in parenthesis

DOL day of life, GA gestational age, PD peritoneal dialysis, GN glomerulonephritis, PKD polycystic kidney disease, CLD chronig lung disease, NEC necrotizing enterocolitis

Table 2Clinical characteristicsassociated with peritonitis

**Table 3** Catheter and placementcharacteristics according topresence or not of peritonitis

Catheter and placement characteristics	No peritonitis ( $N = 91$ catheters)	Peritonitis ( $N = 66$ catheters)	P value
Type of catheter			0.02
Curled	70 (82.4)	57 (95.0)	
Straight	15 (17.6)	3 (5.0)	
Number of cuffs			0.14
1	29 (33.0)	27 (45.0)	
2	59 (67.0)	33 (55.0)	
Configuration			0.36
Swan neck	46 (54.8)	37 (62.7)	
Straight	36 (42.9)	21 (35.6)	
Other	2 (2.4)	1 (1.7)	
Adaptor			0.05
Titanium	58 (67.4)	32 (51.6)	
Plastic	28 (32.6)	30 (48.4)	
Surgical placement			0.60
Laparoscopic	38 (44.7)	29 (49.2)	
Open	47 (55.3)	30 (50.8)	
Exit site orientation			1.00
Lateral/downward	80 (92.0)	57 (91.9)	
Upward	7 (8.0)	5 (8.1)	
G-tube placement timing			0.04
N/A	40 (44.0)	21 (31.8)	
Before/same time	30 (33.0)	17 (25.8)	
After	21 (23.1)	28 (42.4)	
Prophylactic antimicrobial with/ G-tube placement			0.89
None	6 (16.2)	3 (8.8)	
Antifungal	2 (5.4)	2 (5.9)	
Antibiotic	18 (48.7)	17 (50.0)	
Antifungal +Ab	11 (29.7)	12 (35.3)	
PD catheter placement in setting of G-tube			0.84
Right	31 (64.6)	29 (65.9)	
Left	13 (27.1)	13 (29.5)	
Midline	4 (8.3)	2 (4.5)	
Additional procedures prior or at the time of	of PD catheter placement		
Acute PD catheter	9 (10.3)	4 (6.3)	0.39
Vesicostomy	5 (6.0)	5 (8.6)	0.74
Ureterostomy	4 (4.7)	2 (3.4)	0.71
Urinary stoma	0 (0.0)	0 (0.0)	1.00
Colostomy	2 (2.4)	3 (5.1)	0.40
Nephrectomy <sup>a</sup>	3 (3.6)	11 (18.6)	0.003
Omentectomy	52 (61.2)	35 (56.5)	0.57

Data are presented as a number with the percentage in parenthesis

PD peritoneal dialysis

<sup>a</sup> Of the 14 nephrectomies, ten were in patients with autosomal recessive polycystic disease

# Multivariable regression model

A multivariable regression model was subsequently used to identify factors independently associated with an increased risk for developing peritonitis as both an inpatient and outpatient. Nephrectomy at or prior to PD catheter placement and G-tube insertion after catheter placement were associated with a nearly sixfold [odds ratio (OR) 5.93, 95% confidence

**Table 4** Catheter usagecharacteristics according topresence or not of peritonitis

Catheter usage characteristics	No peritonitis ( $N = 91$ catheters)	Peritonitis ( $N = 66$ catheters)	P value
Dialysis initiation location			0.072
General floor	16 (17.8%)	11 (16.7%)	
Neonate intensive care unit	39 (43.3%)	41 (62.1%)	
Pediatric intensive care unit	18 (20.0%)	9 (13.6%)	
Other	17 (18.9%)	5 (7.6%)	
Dialysis initiation in private room			0.409
Yes	48 (71.6%)	43 (78.2%)	
No	19 (28.4%)	12 (21.8%)	
Planned dressing changes			0.739
Dialysis nurse	51 (59.3%)	35 (53.0%)	
Bedside nurse	15 (17.4%)	13 (19.7%)	
Both	20 (23.3%)	18 (27.3%)	
Dialy-Nate® system used			0.207
Yes	36 (53.7%)	37 (64.9%)	
No	31 (46.3%)	20 (35.1%)	
Dialy-Nate® tubing change (days)	3 [1, 3]	3 [1, 3]	0.426
Dialy-Nate® bag change (days)	1 [1, 1]	1 [1, 1]	0.263
Use of dialysis within 14 days	32 (52.5%)	30 (62.5%)	0.293
Days before use of dialysis within 14 days	2 [1, 5]	1 [1, 2]	0.317

Data are presented as the median with the IQR (Q1, Q3) given in square brackets, or as a number with the percentage in parenthesis

interval (CI) 1.51, 23.27; p < 0.01] and a nearly threefold [OR 2.81, 95% CI 1.31, 6.01; p < 0.01] increased risk of peritonitis, respectively. Only patients undergoing nephrectomy at or prior to PD catheter placement had a higher overall annualized peritonitis rate (2.55 episodes per patient-year) than the inhospital rate (1.73 episodes per patient-year) (p < 0.01). The associated Kaplan–Meier survivor analysis describing the shorter time to peritonitis in those who underwent nephrectomy is noted in Fig. 2a, along with the time to peritonitis in patients who underwent G-tube insertion after catheter placement (Fig. 2b).

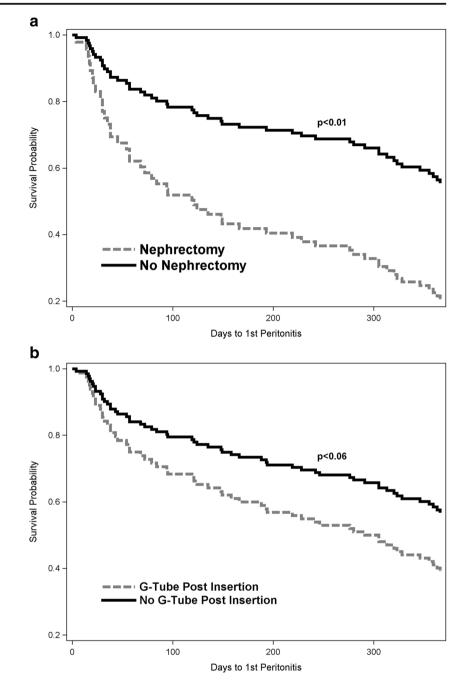
### Outcomes

Overall, infants who experienced peritonitis had a significantly longer duration of initial hospitalization than those who never had peritonitis, with median (IQR) values of 82 (48, 128) versus 60 (21, 90) days, respectively (p < 0.05). This was largely the result of initial hospital stays being longer in those with a history of inpatient peritonitis than in those who developed peritonitis as an outpatient, with median (IQR) values of 116 (105, 196) versus 59 (24, 91) days, respectively (p < 0.01). In addition, of the 23 patients who developed inpatient peritonitis, the nine who did not undergo nephrectomy at or prior to PD catheter placement and did not have a Gtube inserted after catheter placement had a significantly shorter initial hospital duration than the 14 infants who had either nephrectomy at or prior to PD catheter placement or Gtube insertion after catheter placement, with median (IQR) hospitalizations of 95 (53, 116) versus 154 (113, 197) days, respectively (p < 0.15).

Although overall patient survival was excellent, infants with a history of peritonitis experienced lower overall survival (86.3 vs. 95.6%, respectively; p < 0.05) than those patients with no history of peritonitis. The collaborative only recorded the cause of death if it was the result of infection; one such death occurred. Survival during the initial hospitalization was significantly lower in those who developed peritonitis as an inpatient versus those who only developed peritonitis as an outpatient (75 vs. 95.2%, respectively; p < 0.02). A similar trend was noted in the difference for overall survival through the 1-year post-PD catheter insertion follow-up between those who developed peritonitis as an inpatient versus those an inpatient versus those who only developed peritonities as an inpatient versus those who only developed peritonities as an inpatient versus those who only developed peritonities as an inpatient versus those who only developed peritonities as an inpatient versus those who only developed peritonities as an inpatient versus those who only developed peritonities as an inpatient versus those who only developed peritonities as an outpatient (75 vs. 92.9%; p < 0.06).

# Discussion

Given that chronic PD is the most commonly used dialysis modality in infants, there is a need for better patient and technique outcome data, in part because of the ethical considerations that still exist pertaining to the use of RRT in this complex patient population. In the past, very high rates of Fig. 2 Peritonitis Kaplan–Meier survivor analysis. The associated Kaplan–Meier survivor analysis for peritonitis in patients who underwent nephrectomy at or prior to peritoneal dialysis (PD) catheter placement (**a**) and G-tube insertion after catheter placement (**b**)



morbidity and mortality have been reported in infants receiving CPD, although the data have often arisen from a relatively small number of patients and single-center studies, limiting its general applicability. While recent publications have provided data from larger cohorts, including those from national and international collaboratives [1, 4–7], the vast majority of published information has been restricted to chronic care experiences in the outpatient setting with little, if any, information pertaining to the infant patient's initial inpatient experience when the severity and complex nature of a patient's illness can have a significant impact on outcome. One more recent report did note a higher risk of access revision in this young

age group, but did not include any peritonitis data [7, 12]. Thus, the unique nature of our analysis is the inclusion of infection-related data from a substantial number of infants immediately following PD catheter placement during their initial hospitalization. These data complement the home CPD-related data, and together these data provide critical information on peritonitis rates, peritonitis risk factors and patient outcomes, all of which can help inform management decisions.

As expected, peritonitis rates were relatively high in this cohort, with an overall annualized rate of 0.76 episodes per patient-year compared with a rate of 0.46 in older children from the SCOPE collaborative [13], and an annualized rate

of 0.6 episodes per patient-year in children more than 2 years of age in the NAPRTCS [14]. The only other study with a comparable large cohort of infants who started PD at <1 year of age reported an annualized rate of 0.58 in 84 infants [6].

In contrast to the overall peritonitis rate, we found that the annualized peritonitis rate experienced during the hospitalization when the PD catheter was placed was extremely high at 1.73. The exact reasons for such a high rate are unknown, and there were no substantial differences between inpatient and outpatient peritonitis in terms of the microbiological etiology of the infections. Clearly, the performance of a nephrectomy at or prior to PD catheter placement or G-tube insertion after catheter placement contributed to the higher rate of peritonitis seen during the initial hospitalization (see below). The high rate is likely also related to the severity of illness overall as inpatient peritonitis was more common in those with multiple co-morbidities and those who had a PD catheter inserted in the first month of life. Whereas the high inpatient rate of peritonitis may, in part, be related to the use of manual PD techniques by relatively untrained personnel as it relates to the provision of dialysis in the ICU or hospital ward, arguing against this is our finding that the use of the Dialy-Nate® system did not emerge as a risk factor for peritonitis. A similar but alternative argument is that the difference between the inpatient and outpatient rates may be due to the outpatient care being overseen by trained staff and parents using the SCOPE treatment bundles which have already been shown to be associated with a decrease in the rate of peritonitis [10].

The relatively large sample size of this study population and the extensive collection of patient-related data allowed us to perform a multivariable analysis to determine independent risk factors associated with the development of peritonitis, both as an inpatient and outpatient. Several of the factors identified in the univariate analysis did not remain significant after inclusion in the multivariable model. One example was the finding of an association between the use of a curled catheter and an increased risk of peritonitis. Similarly, in another study [5] the use of a straight catheter was associated with poor postperitonitis sequela. However, in both studies, the multivariate analysis did not demonstrate any relationship between catheter properties/configuration and peritonitis risk. In contrast, two factors that did remain significant in the multivariable model were nephrectomy at or prior to PD catheter placement and Gtube insertion after catheter placement; these were associated with a nearly sixfold and nearly threefold increased risk of peritonitis, respectively. The risk of infection associated with G-tube insertion after PD catheter placement has previously been described [15, 16] and has resulted in the recommendation for G-tube placement to preferentially occur prior to or at the time of PD catheter placement, along with the judicious use of antibiotic and antifungal prophylaxis [11]. Although the SCOPE collaborative has not incorporated prophylaxis as part of the treatment bundles, centers were encouraged to follow the ISPD guidelines as mentioned above.

The identification of nephrectomy as an independent risk factor for peritonitis in the pediatric PD population is likely due to the disturbance of the potential peritoneal space that occurs with nephrectomy which may, in turn, delay healing and predispose to the development of peritonitis. Alternatively, nephrectomy may be a surrogate for the diagnosis of autosomal recessive polycystic kidney disease (ARPKD), a disorder previously reported to be associated with a higher risk of infection, as well as mortality [17]. Indeed, previous reports on the outcome of infants with ARPKD have noted a high rate of peritonitis associated with transient peritoneal leaks [18]. Supporting this association, ARPKD and nephrectomy were found to be highly co-linear (when two or more predictor variables in a multiple regression model are highly correlated) in our analysis, which is not surprising since infants with ARPKD often require nephrectomy to relieve increased abdominal pressure and pulmonary embarrassment.

Fortunately, patient survival rates were relatively high in our population overall, an outcome that likely reflects improvements in the global care of this population that have taken place over time. Whereas experiencing an episode of peritonitis lowered patient survival to approximately 87%, this was highly influenced by the much lower survival (75%) of those who developed peritonitis as an inpatient. Having an episode of peritonitis as an outpatient did not affect overall survival, as reflected by a survival rate in these patients of nearly 93%. Since the collaborative only recorded the cause of death if it was the result of infection-and there was one such death-we were unable to perform a further analysis looking for associations between either patient or catheter characteristics with cause of death. Carey et al. [1], using NAPRTCS data from 2000 to 2012, reported the overall survival of 98 neonates and 182 infants at 3 years after dialysis initiation to be 78.6 and 84.6%, respectively, which is an improvement compared to the 1992-1999 NAPRTCS experience. Van Stralen et al. [5], using data derived from four large national and international registries, reported a 2-year patient survival rate of 81% for 242 patients who initiated CPD as neonates. In view of the fact that the data collected by Carey et al. [1] and Van Stralen et al. [5] were only collected from patients who had progressed to home dialysis, it should not be surprising that our patients who experienced peritonitis during their initial hospitalization had lower survival rates when compared to those two patient cohorts. Additionally, the hospital stays of our patients were significantly longer in those who developed peritonitis during their initial hospitalization when the PD catheter was placed. This study thus provides further evidence that there is increased morbidity and mortality in association with peritonitis when it occurs early in the course of ESRD care, a characteristic that now appears to define a particularly vulnerable population.

There are several limitations to this study. First, given that centers voluntarily enroll patients in the SCOPE database, selection bias is possible. However, since centers enter the collaborative to improve their practice, each center had the incentive to enter all patients, unless the family refused consent. Also, since there are a substantial number of patients and a wide range of centers within the collaborative, we believe that the data are generalizable to at least the North American infant PD population. Second, and as noted above, although centers in the collaborative were advised to follow previously published international guidelines for the diagnosis and treatment of peritonitis [11], it is possible that peritonitis rates were affected by center to center variation in the criteria that were used to diagnose an episode of peritonitis. The high rate of culture-negative peritonitis reported in this study in particular, may be a reflection of a failure to rigorously adhere to such diagnostic or culture technique-related guidelines. Potentially, this could have led to an overestimation of the peritonitis rate, although the rate of culture-negative peritonitis in the study is in line with previous reports. Finally, the very nature of being in a collaborative focused on reducing peritonitis rates may have altered peritonitis rates and overall outcomes, limiting extrapolation to centers outside of the collaborative.

In summary, this large cohort of infants who underwent PD catheter placement and initiated CPD during their first year of life provides unique data on risk factors associated with the development of peritonitis, helping to reinforce current ISPD guidelines, especially as to the timing of G-tube placement when a PD catheter is needed. Additionally, it is one of the first studies to demonstrate a high rate of peritonitis in infants during the inpatient stay associated with PD catheter placement. Clearly, additional study of the peritonitis risk factors identified in this analysis is warranted in order to help improve PD-related outcomes and patient survival in this high-risk patient population.

Acknowledgements The following centers/team Leaders participated in the SCOPE Collaborative during the first 3 years:

AI DuPont Hospital for Children: Joshua Zaristky, Susan Kieffner; American Family Children's Hospital: Allison Redpath Mahon, Dawn Foster; Lurie Children's Hospital of Chicago: Mahima Keswani, Nancy Majkowski; Arkansas Children's Hospital: Richard Blaszak, Christine Blaszak; Boston Children's Hospital: Michael Somers, Theresa Pak; Children's Hospital New Orleans: Diego Aviles, Evie Jenkins; Children's Hospital Los Angeles: Rachel Lestz, Alice Sanchez; Children's Hospital of Wisconsin: Cynthia Pan, Jackie Dake; Children's Medical Center Dallas, Raymond Quigley, Haridas Thankappan; Children's Mercy Hospital: Bradley Warady, JoLyn Grimes; Children's National Medical Center: Kirtida Mistry, Jennifer Carver; Cincinnati Children's Hospital Medical Center: Rene Van De Voorde, Ellen Irvin; Driscoll Children's Hospital: Samhar Al-Akash, Britt Stone; Mavnard Children's Hospital at Vidant Medical Center: Guillermo Hidalgo, Malinda Harrington; Johns Hopkins Children's Center: Alicia Neu, Barbara Case; Kosair Children's Hospital: Sushil Gupta, Andrea Baker; Levine Children's Hospital: Jack Weaver, Annabelle Chua; Lucile Packard Children's Hospital at Stanford: Cynthia Wong, Brandy Begin; Mattel Children's Hospital UCLA: Isidro Salusky, Barbara Gales; Nationwide Children's Hospital: Hiren Patel, Beth Smith; Phoenix Children's Hospital: Mark Joseph, Deb Haskins; Rainbow Babies Hospital: David Kenagy, Beth Vogt; Seattle Children's Hospital: Coral Hanevold, Nancy McAfee; St. Louis Children's Hospital: Ann Beck, Meg Shea; Cohen Children's Medical Center of New York: Christine Sethna, Myung Cho; Texas Children's Hospital: Sarah Scwartz, Helen Currier; The Children's Hospital at Montefiore: Amy Skversky, Maureen Eisele; The Children's Hospital of Philadelphia: Madhura Pradhan, Christine Breen; UCSF Benioff Children's Hospital: Paul Brakeman, Lina Campopiano; University of Iowa Children's Hospital: Jennifer Jetton, Jennifer Ehrlich; Upstate Golisano Children's Hospital: Lawrence Shoemaker, Nancy Zacharek.

**Compliance with ethical standards** The Declaration of Helsinki was followed and the collaborative protocol was approved by the Institutional Review Board at each participating center. Consent was obtained for all subjects enrolled when required by the Institutional Review Board at each participating center.

**Conflict of interest** We declare that the results presented in this paper have not been published previously in whole or part, except in abstract format.

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