Peritoneal Dialysis Modality Failure in a Middle-Income Country: A Retrospective Cohort Study

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Rationale & Objective: Technique failure in peritoneal dialysis (PD) remains one of the most critical challenges of this therapy and is associated with a significant increase in costs and morbidity. Our objective was to estimate the frequency of PD technique failure and identify factors associated with technique failure.

Study Design: A retrospective multicenter observational cohort study.

Setting & Participants: All adult patients initiating PD between January 1, 2010, and December 31, 2015, with follow-up until December 31, 2018, at the Renal Therapy Services network in Colombia.

Exposure & Predictors: PD modality (continuous ambulatory PD and automated PD) and demographic and clinical characteristics.

Outcomes: Technique failure, defined as a switch to hemodialysis lasting at least 30 days.

Analytical Approach: Sociodemographic and clinical characteristics of all patients were summarized descriptively according to modality. We estimated the cumulative incidence of technique failure, and a flexible parametric survival model with

A round 45 years have passed since Popovich et al¹ published their pioneering study of peritoneal dialysis (PD), and PD has evolved into a mature home therapy with continuously improving health outcomes.^{2,3} Despite these improvements, an observed characteristic over the years is that patients using PD experience greater technique failure compared with those treated by hemodialysis.^{4,5} The therapy outcomes have been improved step by step, incorporating developments such as the growth of automated PD, better connectology, new PD solutions, and continuous quality improvements in the processes of care, all of which have contributed to positive trends in the United States.^{6,7} Similar results have been observed in Canada, highlighting that peritonitis associated with PD remains a modifiable cause of technique failure.⁸

A limitation with PD is the lack of standardization of several health outcomes, particularly technique failure. To address this, the Peritoneal Dialysis Outcomes and Practice Patterns Study (PDOPPS) and the Australia and New Zea-land Dialysis and Transplant Registry (ANZDATA) recently published 2 articles that standardize the definition of technique failure.^{9,10} Additionally, the competing risk for death and transplantation has provided methodologic challenges with understanding technique failure.¹¹

competing risks was used to evaluate factors associated with this outcome.

Results: Among 6,452 patients meeting inclusion criteria, 67% were treated with continuous ambulatory PD. The cumulative incidence of technique failure within 1 year of PD initiation adjusting for competing risks was 6.9% (95% CI, 6.3%-7.6%); within 2 years, technique failure was 13.5% (95% CI, 12.6%-14.4%); and within 3 years, 19.6% (95% CI, 18.5%-20.7%). Female sex, larger center size, and higher Kt/V were associated with lower risk for modality change, whereas diabetes, history of major abdominal surgery, catheter implant technique (laparotomy and percutaneous techniques), obesity, and peritonitis were associated with a higher likelihood of technique failure.

Limitations: Variables of distance to the center, use of icodextrin, and measures of outcomes reported by patients were not included.

Conclusions: Technique failure is relatively uncommon in Colombia; catheter-related problems are the most frequent cause of technique failure. Best practices in catheter insertion could minimize the risk for this outcome.



Visual Abstract included

Complete author and article information provided before references.

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PD therapy results may vary according to geographies and health systems.^{12,13} In Colombia, a country with 28,417 patients receiving maintenance dialysis, 9,146 (32%) are treated with PD.¹⁴ The Colombian health system ensures access to kidney replacement therapy for 100% of the population, with a monthly reimbursement that is similar for hemodialysis and PD.¹⁵ The Renal Therapy Services (RTS) network in Colombia serves more than 4,000 PD patients across Colombia, representing \sim 40% of Colombia's dialysis population. Although Colombia is considered a middle-income country, its standardized clinical processes and procedures, a nephrologist to dialysis patient ratio of 1:125, a PD nurse to PD patient ratio of 1:50, and a consistent policy of continuous improvement have resulted in its dialysis therapy outcomes being comparable to more economically developed countries.¹⁶

In Colombia, PD patients have the opportunity to access either automated PD or continuous ambulatory PD (CAPD). Automated PD is more frequently offered to patients with fast peritoneal membrane transport, young people at work or who are academically active, and elderly patients who require caregiver support.

The objective of the present study is to estimate the frequency of PD technique failure and identify factors that

PLAIN-LANGUAGE SUMMARY

Technique failure is a key performance indicator of peritoneal dialysis (PD) therapy quality. In our study, we examined the frequency of technique failure in a cohort of incident patients receiving PD, adjusting for the presence of competing risks, including death and kidney transplantation. The presence of diabetes, lower Kt/V, an episode of peritonitis during follow-up, or the catheter implant technique through major abdominal surgery were risk factors for technique failure. These data from a large cohort allow us to identify sensitive points in PD therapy to seek improvements in the quality of care and patients' quality of life.

are associated with technique failure using survival analysis with competing risks.

METHODS

Study Design and Patients

A retrospective multicenter cohort study of incident patients undergoing PD in Colombia was conducted between January 1, 2010, and December 31, 2015, with follow-up until December 31, 2018, at the RTS network in Colombia. Inclusion criteria were patients older than 18 years with a kidney failure diagnosis who initiated dialysis using PD. Exclusion criteria were current pregnancy and nonkidney indications for dialysis, such as congestive heart failure and liver cirrhosis. Patients used 1 of 2 PD modalities: (1) CAPD using Baxter systems – Twin Bag system, and (2) automated PD using Home Choice with the Ambuflex bag system.

The study protocol was approved by the clinical research ethics committee of RTS Colombia (June 13, 2019, Minute, item number 030), which exempted the use of informed consent because this study does not contain identifiable information and is an observational study.

Data Source and Analysis Baseline Patient Characteristics

Baseline demographic and disease characteristic variables including age, sex, history of diabetes mellitus, history of hypertension, history of cardiovascular disease, history of major abdominal surgery, end-stage kidney disease comorbidity index,¹⁷ obesity, presence of a caregiver, socioeconomic level, school level, center size (determined by the number of incident patients per year >48),¹⁸ peritoneal equilibration test (PET), uncontrolled blood pressure, hemoglobin level, phosphorus level, albumin level, Kt/V, urine output, peritonitis episode, implant technique (percutaneous: placement of catheters by percutaneous puncture with or without image guidance; laparotomy: open surgical insertion performed by surgeon; and mini laparotomy: open small laparotomy performed by nephrologist), location of the catheter, and days at first use. All data were retrospectively collected from patients' electronic medical records. The main exposure variable was PD modality (automated PD or CAPD).

Study Outcomes

The outcome was technique failure. The definition of technique failure was applied when a patient was switched to hemodialysis for at least 30 days. Competing-risks events were death and kidney transplantation. During follow-up, patients were censored for events of kidney function recovery, withdrawal or suspension of therapy, and change of provider.

Statistical Analysis

We used descriptive statistics to report population characteristics by PD modality using median and interguartile range for non-normal distributed variables. No data imputation procedure was performed because the models were built on patients with complete information. We followed the Royston-Parmar approach to fitting a flexible parametric survival model with competing risks, in which the baseline hazard function is modeled as a restricted cubic spline function of log time.^{19,20} This method allows one to model all the functions of accumulated incidence by specific cause simultaneously, as well as the survival times censored on the right, and the assumption of proportionality is not required. The flexible parametric survival model incorporating competing risk for death and kidney transplantation included the following variables: time to technique failure; PD modality; age; sex; caregiver; center size; history of diabetes mellitus, hypertension, cardiovascular disease, and major abdominal surgery; ESKD comorbidity index; obesity; socioeconomic level; education; PET; uncontrolled blood pressure; hemoglobin, phosphorus, and albumin levels; Kt/V; urine output; peritonitis episode; and catheter implant technique and location and days in place at first use. Backward regression was applied to yield a more parsimonious model. To assess the consistency of the estimates, sensitivity analysis was performed on the number of knots chosen for the spline. The best model was selected considering the Akaike and Bayesian information criteria. The model was constructed using 3 df, locating the knots at the 0, 33, 67, and 100 centiles of the baseline distribution.

Multivariable analyses were conducted to assess the effect of demographic, clinical, and laboratory variables on risk for technique failure over time, and peritonitis was assessed as a time-dependent variable. Variables that after univariate regression had probability ≤ 0.2 were included in the multivariable model, as well as those with recognized clinical importance. The backward regression method was applied to have a more parsimonious model. We fitted models varying the number of interior knots from 1 to 6 and inspected the Akaike and Bayesian information criteria to determine the optimal fit. Additionally, we estimated the technique failure cumulative



Figure 1. Flow chart of peritoneal dialysis (PD) patients in the study. Of the 6,673 originally recruited patients (corresponds to the total number of incident adult patients receiving PD at Renal Therapy Services network in Colombia), 221 did not meet the eligibility criteria and 583 patients finished the study without presenting an outcome or censure events.

incidence adjusting for competing-risk events, and Pepe and Mori's statistical test was used to compare the equality of the cumulative incidence functions by modality. STATA 14 (StataCorp LLC) was used in statistical analyses.

RESULTS

Patients

A total of 6,452 patients met participation criteria and were included in the analysis (Fig 1). Sociodemographic and clinical characteristics of all patients are summarized descriptively by PD modality in Table 1. Median age was 61 years, 54% were men, 54% had a history of diabetes, and 67% were treated with CAPD.

Outcomes

There were 1,462 technique failure events with a rate of 10.6 (95% CI, 10.1-11.2) events/100 patient-years. The cumulative incidence functions of technique failure adjusting for competing risks at the end of the first year were 6.9% (95% CI, 6.3%-7.6%); second year, 13.5% (95% CI, 12.6%-14.4%); and third year, 19.6% (95% CI, 18.5%-20.7%). We compared the cumulative incidence function of CAPD and automated PD and did not observe a

statistically significant difference when adjusting for death (P = 0.66) or kidney transplantation (P = 0.72; Fig 2).

Regarding the hazard function, we observed an instantaneous potential for technique failure that increased in the first 40 days followed by a slight decrease until 1 year and a further downward trend thereafter (Fig 3). The most common reasons for technique failure were catheter complications (catheter obstruction due to fibrin, omentum, adhesions, or catheter out of place), peritonitis, and psychosocial/medical indications (Table 2).

Flexible Parametric Survival Model With Competing Risks

Multivariable analyses were conducted to assess the effect of demographic, clinical, and laboratory variables on risk for technique failure, adjusting for the competing risks of death and kidney transplantation over 3 years of follow-up. Our results indicate that the PD modality does not have a statistically significant effect on risk for technique failure when controlled for confounding variables. We also observed that for every 10-year age increase, female sex, center size, and Kt/V reduced the risk for failure. Factors related to higher risk for technique failure were diabetes, history of major abdominal

Table 1. Baseline Characteristics of the Study Population According to Modality

	Total	CAPD	APD	
Characteristics	(N = 6,452)	(n = 4,342)	(n = 2,110)	
Sociodemographics				
Male sex	3,505 (54.3%)	2,276 (52.4%)	1,229 (58.3%)	
Age, y	61.0 [50-71]	61.0 [50-71]	61.0 [50-70]	
Socioeconomic level				
Low	2,908 (45.1%)	2,076 (47.8%)	832 (39.4%)	
Medium	2,996 (46.4%)	1,851 (42.6%)	1,145 (54.3%)	
High	448 (7.0%)	345 (8.0%)	103 (4.9%)	
Data not available	100 (1.5%)	70 (1.6%)	30 (1.4%)	
Education level				
Elementary school or none	4,090 (63.4%)	2,842 (65.5%)	1,248 (59.2%)	
High school	2,000 (31.0%)	1,312 (30.2%)	688 (32.6%)	
University degree	362 (5.6%)	188 (4.3%)	174 (8.3%)	
Caregiver: yes	4,358 (67.5%)	2,912 (67.1%)	1,446 (68.5%)	
Kidney Clinic & Peritoneal Catheter	· · · ·		, <u> </u>	
Center size > 48 patients ^a	653 (10.1%)	406 (9.4%)	247 (11.7%)	
Catheter used in first 7 db	3,566 (55.3%)	2,290 (52.7%)	1,276 (60.5%)	
Technique of catheter implant			<u>, </u>	
Mini laparotomy	1,214 (18.8%)	870 (20.0%)	344 (16.3%)	
Percutaneous	1,810 (28.1%)	936 (21.6%)	874 (41.4%)	
Laparotomy	2,787 (43.2%)	1,989 (45.8%)	798 (37.8%)	
Data not available	641 (9.9%)	547 (12.6%)	94 (4.5%)	
Peritoneal catheter location				
Hemiabdomen left/lateral	2,062 (32.0%)	1,593 (36.7%)	469 (22.2%)	
Hemiabdomen left/down	1,064 (16.5%)	620 (14.3%)	444 (21.0%)	
Hemiabdomen left/up	288 (4.5%)	231 (5.3%)	57 (2.7%)	
Hemiabdomen right/lateral	1,465 (22.7%)	822 (18.9%)	643 (30.5%)	
Hemiabdomen right/down	609 (9.4%)	331 (7.6%)	278 (13.2%)	
Hemiabdomen right/up	362 (5.6%)	225 (5.2%)	137 (6.5%)	
Data not available	602 (9.3%)	520 (12.0%)	82 (3.9%)	
Clinical Characteristics				
Diabetes history	3,465 (53.7%)	2,329 (53.6%)	1,136 (53.8%)	
Hypertension history	5,500 (85.2%)	3,696 (85.1%)	1,804 (85.5%)	
Cardiovascular disease history	211 (3.3%)	136 (3.1%)	75 (3.6%)	
ESKD comorbidity index	2.0 [0-3]	2.0 [0-3]	2.0 [0-3]	
Major abdominal surgery history	349 (5.4%)	227 (5.2%)	122 (5.8%)	
Obesity ^c	838 (13.0%)	549 (12.7%)	289 (13.7%)	
Uncontrolled blood pressure ^d	2,784 (43.2%)	1,838 (42.3%)	946 (44.8%)	
Urine output, >100 mL/d	5,601 (86.8%)	3,746 (86.3%)	1,855 (87.9%)	
PET				
Low	1,485 (23.0%)	888 (20.5%)	597 (28.3%)	
Average	3,711 (57.5%)	2,585 (59.5%)	1,126 (53.4%)	
Fast	315 (4.9%)	245 (5.6%)	70 (3.3%)	
Data not available	941 (14.6%)	624 (14.4%)	317 (15.0%)	
Peritonitis during follow-up	1,867 (28.9%)	1,291 (29.7%)	576 (27.3%)	
Laboratory Values				
Kt/V ^e	2.3 [1.9-2.9]	2.3 [1.9-2.9]	2.4 [1.9-2.9]	
Hemoglobin, g/dL	10.1 [8.9-11.3]	10.0 [8.8-11.2]	10.2 [8.9-11.5]	
Albumin, g/dL	3.6 [3.2-3.9]	3.6 [3.2-3.9]	3.6 [3.2-4.0]	
Phosphorus; mg/dL	4.9 [4.1-6.0]	4.9 [4.0-5.9]	5.0 [4.1-6.1]	

Note: Values expressed as median [interquartile range] or number (percent). Abbreviations: APD, automated peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis; ESKD, end-stage kidney disease; PET, peritoneal equilibration test. ^aCenter size was determined by the number of incident patients per year.

^bData not available for 551. ^cObesity was determined by body mass index \geq 30 kg/m².

^dDetermined by systolic blood pressure > 140 mm Hg and/or diastolic blood pressure > 90 mm Hg.

^eData not available for 642.



Figure 2. Cumulative incidence functions of each outcome (technique failure, death, and renal transplantation) according to modality. Abbreviations: APD, automated peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis.

surgery, catheter implant technique, obesity, and peritonitis (Tables 3, S1, and S2).

DISCUSSION

In an extended network of home dialysis clinics in Colombia, the incidence rate of technique failure, a key indicator of the effectiveness and safety of a PD program that is associated with high mortality and morbidity,²¹ was approximately 10 events/100 patient-years at risk.

This rate, although high, is lower than that in many prior reports.²²⁻²⁵ Following adjustment for the competing risks for death and kidney transplantation, we obtained cumulative incidences of 7%, 13%, and 20% in the first, second, and third year, respectively. Our favorable results could be explained by the PD model offered by the extended network of RTS in Colombia, which has relevant characteristics such as national coverage, high-quality standards, specific training for health professionals, monthly comprehensive evaluation, monitoring of key performance indicators per site, and the development of quality improvement plans.¹⁶ Additionally, conditions of the Colombian geography, with remote areas difficult to

access, could influence modality selection such that that clinical teams work more proactively to return patients to the PD program as soon as possible.

The most frequent causes of technique failure were catheter related, highlighting an area for improvement because at least some of these episodes could be avoidable with different surgical techniques and the development of better diagnostic and treatment strategies for identifying and addressing catheter malfunction. Additional common causes included peritonitis and psychosocial factors (social support, patient choice/"burn out") that may be modifiable with patient and caregiver education and support and potentially modifications in patient selection for PD.^{12,25}

It is important to note that the hazard function shows there is increased risk for technique failure within the first 40 days. Thus, patient care and prevention of problems with the catheter and infectious complications should be emphasized at this early stage.

The cumulative incidence technique failure was not different for patients who started with CAPD compared with automated PD. This result was corroborated in the multivariable analysis, in which this factor was not statistically significant. This finding differs slightly from reports



Figure 3. Technique failure hazard function. The smoothed hazard estimates show that there is some increased risk in the first 40 days, which attenuates after the early failures have occurred.Outcome and censure events, 5869 (90.96) n (%) Technique failure events, 1462 (22.66) Competing risks events, 2406 (37.29)-Death, 1955 (30.30) -Transplant, 451 (6.99) Censure events, 2001 (31.01) - Kidney function recovery, 262 (4.06) - Therapy withdrawal/suspension, 449 (6.96) - Change of provider , 1290 (19.99)End of study, n (%) 583 patients (9.04) 6452 eligible patients 6673 patients 221 patients did not meet eligibility criteria

in the literature that suggest that the automated PD modality confers a slight increase in risk for technique failure.^{12,13} This could be because in our study, the

Table 2.	Reasons	for F	D Tech	nique	Failure
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populations using the 2 modalities are very similar and the selection is very balanced, depending largely on patient preference. Of note, it is important to highlight that factors such as socioeconomic level and educational level were not related to technique failure, similar to previous reports.^{21,26} This result is of great value given that Colombia is a country with economic inequity, a substantial proportion of the population below the poverty line, and limited access to high-quality education.

Our study found several factors, similar to the prior literature, associated with lower risk for technique failure, such as older age, female sex, larger center size defined by the number of incident patients per year, and higher Kt/V.^{12,13,18,25,27} The size of the center could be an indirect indicator of expertise and training of PD teams.¹⁸

Traditionally, peritonitis is one of the most important causes of technique failure. We found in this cohort that having at least 1 event of peritonitis during the follow-up period increased the risk for technique failure 2-fold compared with those without a history of peritonitis; our data are consistent with other reports.²⁸ Likewise, we observed that a history of diabetes and history of major abdominal surgery, obesity, and catheter implant technique were associated with higher risk for technique failure, also similar to that seen in other reports.^{18,26,29,30} Surgical implantation technique was also associated with higher risk for PD technique failure; this likely is related to the fact that open abdominal surgery is indicated in patients with some type of pathology of the abdominal wall,

0-90 d	91 d-1 y	>1-2 y	>2-3 y	>3-8 y	Total
56 (42.4%)	96 (34.5%)	89 (26.8%)	84 (30.7%)	74 (16.6%)	399 (27.3%)
5 (3.8%)	33 (11.9%)	69 (20.8%)	72 (26.3%)	192 (43.0%)	371 (25.4%)
51 (38.6%)	73 (26.3%)	67 (20.2%)	50 (18.2%)	60 (13.5%)	301 (20.6%)
0 (0.0%)	3 (1.1%)	1 (0.3%)	5 (1.8%)	8 (1.8%)	17 (1.2%)
0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.4%)	0 (0.0%)	1 (0.1%)
0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (0.1%)
6 (4.5%)	5 (1.8%)	12 (3.6%)	1 (0.4%)	8 (1.8%)	32 (2.2%)
45 (34.1%)	61 (21.9%)	49 (14.8%)	39 (14.2%)	26 (5.8%)	220 (15.0%)
0 (0.0%)	1 (0.4%)	2 (0.6%)	0 (0.0%)	3 (0.7%)	6 (0.4%)
0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (0.7%)	3 (0.2%)
0 (0.0%)	3 (1.1%)	3 (0.9%)	4 (1.5%)	11(2.5%)	21 (1.4%)
12 (9.1%)	45 (16.2%)	43 (13.0%)	32 (11.7%)	37 (8.3%)	169 (11.6%)
0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.4%)	2 (0.1%)
12 (9.1%)	42 (15.1%)	40 (12.0%)	26 (9.5%)	26 (5.8%)	146 (10.0%)
0 (0.0%)	3 (1.1%)	3 (0.9%)	6 (2.2%)	9 (2.0%)	21 (1.4%)
6 (4.5%)	26 (9.4%)	55 (16.6%)	28 (10.2%)	51 (11.4%)	166 (11.4%)
0 (0.0%)	0 (0.0%)	1 (0.3%)	1 (0.4%)	4 (0.9%)	6 (0.4%)
6 (4.5%)	26 (9.4%)	54 (16.3%)	25 (9.1%)	45 (10.1%)	156 (10.7%)
0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.7%)	2 (0.4%)	4 (0.3%)
2 (1.5%)	5 (1.8%)	6 (1.8%)	5 (1.8%)	18 (4.0%)	36 (2.5%)
2 (1.5%)	2 (0.7%)	0 (0.0%)	0 (0.0%)	6 (1.3%)	10 (0.7%)
0 (0.0%)	3 (1.1%)	6 (1.8%)	5 (1.8%)	12 (2.7%)	26 (1.8%)
0 (0.0%)	0 (0.0%)	3 (0.9%)	3 (1.1%)	14 (3.1%)	20 (1.4%)
132 (100%)	278 (100%)	332 (100%)	274 (100%)	446 (100%)	1,462 (100%)
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Abbreviation: PD, peritoneal dialysis.

 Table 3. Flexible Parametric Survival Model With Competing Risks

	Hazard		
Characteristics	Ratio	Ρ	95% CI
Automated PD ^a	1.12	0.15	0.96-1.30
Age, per 10 y ^b	0.90	0.01	0.86-0.94
Female sex ^c	0.81	0.01	0.69-0.94
Center size > 48 ^d	0.54	0.01	0.39-0.75
History of diabetes	1.18	0.03	1.01-1.39
History of major abdominal surgery	1.78	0.01	1.35-2.34
Percutaneous implant technique ^e	1.41	0.01	1.13-1.76
Laparotomy implant technique ^e	1.70	0.01	1.40-2.05
Obesity ^f	1.52	0.01	1.26-1.84
Kt/V	0.91	0.03	0.83-0.99
Peritonitis during follow-up	1.81	0.01	1.53-2.14

^aReference, continuous anbulatory peritoneal dialysis.

^bFor every 10 years of age increase.

^cReference, male sex.

^dCenter size was determined by the number of incident patients per year.

^eReference, mini laparotomy.

^fBody mass index \geq 30 kg/m².

significant obesity, history of surgeries, or suspected peritoneal adherences, which may lead to confounding by indication. In contrast to several other studies, several key factors were not associated with technique failure, including urine output and PET results.^{26,29,31-34}

In summary, catheter-related problems, peritonitis, and treatment in smaller PD centers are critical factors associated with technique failure, and addressing these, particularly catheter issues early in the PD course and potentially the ability of staff to troubleshoot and expertise in training patients and their caregivers, may result in improved PD outcomes.

Strengths of this study include the substantial number of patients; detailed clinical data for patients, including PD adequacy, residual kidney function, PET results, and PD catheter surgical placement data; and incorporation of both facility and patient data into models. In addition, robust statistical methodologies were used with multivariable adjustment, including accounting for competing risks for death and kidney transplantation, thereby limiting confounding.

Limitations of this study are that the variables of distance to the dialysis center and the use of icodextrin were not included, as well as the absence of data for patientreported outcome measures.

In conclusion, rates of technique failure were relatively low in a generalizable population from Colombia, with catheter-related problems the main cause of technique failure. Strategies to diagnose and address catheter-related problems expeditiously could be very influential to enhance PD success.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

 Table S1. Flexible parametric survival univariate regression with competing risks

Table S2. Sensitivity analysis with variability in the number of knots

ARTICLE INFORMATION

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