TRANSPLANT INTERNATIONAL

Transplant International ISSN 0934-0874

ORIGINAL ARTICLE

Pancreas–Kidney transplantation: Impact of dialysis modality on the outcome

La Salete Martins,[1,2,3] Jorge Malheiro,[1,2] Sofia Pedroso,[1,2,3] Manuela Almeida,[1,2,3] Leonidio Dias,[1,3] António C. Henriques,[1,2,3] Donzília Silva,[3,4] José Davide,[3,4] António Cabrita,[1] Irene L Noronha[5] and Anabela Rodrigues[1,2]

1 Nephrology Department, Hospital Santo António, Centro Hospitalar do Porto, Porto, Portugal
2 Unit for Multidisciplinary Research in Biomedicine, Institute of Biomedical Sciences Abel Salazar and University Hospital de Santo António, University of Porto, Porto, Portugal
3 Transplantation Department, Hospital Santo António, Centro Hospitalar do Porto, Porto, Portugal
4 Surgery Department, Hospital Santo António, Centro Hospitalar do Porto, Porto, Portugal
5 Cellular and Molecular Nephrology Laboratory, Division of Nephrology, University of São Paulo, São Paulo, Brazil

Keywords
graft survival, intra-abdominal infection, peritoneal dialysis, simultaneous pancreas–kidney transplantation, type 1 diabetes, vascular thrombosis.

Correspondence
La Salete Martins, MD, Nephrology Department, Hospital Santo António, Centro Hospitalar do Porto, Largo Prof. Abel Salazar, 4099-001 Porto, Portugal.
Tel.: +351963035782;
fax: +351 222033189
e-mail: lasalet@gmail.com

Conflicts of interest
The authors of this manuscript have no conflict of interest to disclose. This research did not receive any specific grant from any funding agency in the public, commercial, or not-for-profit sector. Also, there were no personal relationships with other people or organizations that could inappropriately influence this work. This study has not been published previously, and it is not under consideration for publication elsewhere. It was presented as oral communication at the 2015 EPITA Winter Symposium.

This work was approved by the appropriate ethics committee. Therefore, it has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments; and in accordance with the Declaration of Istanbul.

Summary

It remains controversial whether dialysis modality prior to SPKT (simultaneous pancreas–kidney transplantation) affects the outcome. We analyzed outcomes in type 1 diabetic patients undergoing SPKT, comparing peritoneal dialysis (PD) and hemodialysis (HD) groups: 119 had been on HD; 39 on PD. They were comparable except regarding dialysis time, higher in HD patients (30 ± 23 vs. 21 ± 15 months, $P = 0.003$). Thrombosis-driven relaparotomy was more frequent in PD patients (12.8% vs. 1.7%, $P = 0.014$). Pancreas loss due to infection was higher in PD patients (12.8% vs. 3.4%, $P = 0.042$). Thrombosis-related kidney loss was more frequent in PD patients (5.1%, vs. 0% in HD patients, $P = 0.058$). Thirteen deaths occurred, more within the PD group (17.9% vs. 5%; $P = 0.011$), being infection the leading cause (13.5%, vs. 1.7% in HD patients, $P = 0.010$). Patient survival was inferior in PD patients. Besides PD, cardiovascular disease and graft failure were independent predictors of patient death. In conclusion, PD patients more frequently complicated with intra-abominal infection leading to pancreatic loss and with renal thrombosis, with adverse impact on survival. As a PD first strategy in end-stage renal disease patients is generally associated with good outcomes, these gloomier results after SPKT urge for careful adjustment of infection and thrombosis prophylactic protocols in PD patients.

Received: 17 November 2014
Revision requested: 31 December 2014
Accepted: 15 March 2015
Published online: 8 April 2015

doi:10.1111/tri.12565

Introduction

Several studies demonstrated that pre-emptive transplantation, defined as transplantation before chronic dialysis is required, improves patient and graft outcomes in renal transplant patients [1–3]. However, most patients have to start renal replacement by dialysis because the kidney graft is not immediately available.

Regarding dialysis modality, peritoneal dialysis (PD) or hemodialysis (HD), and its impact on transplant outcomes, there is no consensus on which is associated with better results [1,3–5], meaning that outcomes might be generally similar after adjusting for patient characteristics and center experience. The amount of time on dialysis may be the crucial factor with impact on outcome [1, 6], along with patient comorbidities [7]. Nevertheless, studies were focused mostly on renal transplantation only, and with inconclusive results related to several issues comparing previous dialysis modality: There are conflicting reports about an increased renal graft loss in PD patients [8], mainly due to renal vascular thrombosis (VT) [4,5,8–11], by unclear predisposing mechanisms [12]; and about an increased incidence of sepsis in these patients [13,14]. Early infection may be related to other factors, namely the length of hospitalization or more intense immunosuppression, as in cases of acute rejection [15].

On the other hand, there is a lack of data about the preferable dialysis modality prior to simultaneous pancreas–kidney transplantation (SPKT). Option for PD or HD normally depends on patient condition, such as their own autonomy; comorbid situations; vascular and peritoneal conditions; dialysis-center factors; and patient convenience. Patient selection biases for each modality cannot be ruled out.

The purpose of this study was to analyze grafts and patient outcomes, in our type 1 diabetic (DM1) patients undergoing SPKT, comparing the subgroup that had been on PD with the other on HD.

Patients and methods

We conducted a retrospective longitudinal cohort study in adult SPKT performed at our unit. Among the 165 performed between May 2000 and December 2013, we studied 158 on dialysis prior to SPKT. Cases who received a pre-emptive transplant were not included in the comparative analysis because of the small number of patients ($n = 7$). PD was the dialysis modality in 39 patients, while 119 were on HD.

Systemic–enteric drainage was the technique used in all SPKT. Pancreas transplantation is performed using a side-to-side anastomosis between the donor′s duodenal arch and the recipient's jejunum, with pancreas head up. Vascular implantation normally does not require prior reconstruction. Donor′s aorta patch with the origin of the mesenteric superior artery and the splenic artery is anastomosed to the recipient′s common iliac artery and donor′s portal vein anastomosed to the recipient's common iliac vein. Kidney transplantation is performed through a second incision, on the left iliac fossae, with extraperitoneal graft placement, the usual practice for kidney transplantation alone. Peritoneal catheter is always removed during the surgery. Celsior is the preservation solution used for pancreas grafts. Immunosuppression comprised antithymocyte globulin, tacrolimus, mycophenolate, and steroids. Two abdominal drains are left for some days in the transplanted patient: one draining the abdominal cavity; the second draining the renal graft fossae. Drain removal depends on volume and drainage characteristics: They are removed after two consecutive days with decreasing exudate amylase level and drainage volume, combined with its leukocyte count and microbiological analysis revealing no signs of infection. All patients had one bladder catheter for at least 5 days; and one central venous catheter, usually for the 5 days of antithymocyte globulin administration. Antibiotic prophylaxis included vancomycin, flucanozole, and second-generation cephalosporin preoperatively and during the first few days while catheter and drains persist; cotrimoxazole, nystatin, and valgancyclovir were started after surgery. Before implantation, duodenal graft disinfection is always made using povidone–iodine, ampicillin, and fluconazole. Thrombosis prophylaxis was made with aspirin (100 mg/day) started before surgery and enoxaparin (from 20 to 40 mg/day, depending on patient weight and renal function recovery) started immediately after surgery, or when blood losses were considered to be not significant. Data were collected from patient file records, during the admission and after discharge, along with the outpatient follow-up.

Statistical analysis

Continuous data were described using mean (±standard deviation), and categorical data were expressed as number

(and percentages). Categorical data were compared using Pearson's χ^2 test or Fisher′s exact test and continuous variables were compared with Student's t-test or Mann–Whitney *U*-test, as appropriate. Patient survival was determined from the time of SPKT until death or end of follow-up. Death-censored kidney graft survival was determined from the time of SPKT until kidney failure (return to dialysis or retransplantation) or end of follow-up. Death-censored pancreas graft survival was determined from the time of SPKT until pancreas failure (permanent insulin requirement or retransplantation) or end of follow-up. Graft survival curves were performed using Kaplan–Meier method and compared by log-rank test. Multivariable Cox proportional hazards analysis was applied to assess independent predictors of patient death, including clinically relevant variables and/or those presenting $P \leq 0.15$ in univariable analysis: recipient gender and age, dialysis technique (HD vs. PD), time on dialysis, years of DM1, pretransplant glycated hemoglobin (HbA1c) $<$ or $\geq$ 9%, concomitant cardiovascular disease, and graft failure (kidney and/or pancreas).

A two-sided *P* value <0.05 was considered as statistically significant. Statistical analyses were performed using SPSS, version 20.0 (SPSS Inc., Chicago, IL, USA).

Results

The relevant demographic and clinical data of the study population are presented in Table 1. PD and HD patients were similar for the majority of their pretransplant characteristics: age; gender; duration of diabetes; HbA1c; body mass index (BMI); percent of patients chronically taking aspirin; percent of patients with previously known cardiovascular disease (CVD); and value of hemoglobin (Hb) before surgery. Time on dialysis was the single distinguishable parameter, being inferior to the PD group (20.7 ± 14.6 months, vs. 32.0 ± 22.1 months in the HD group, $P = 0.003$). On the contrary, time on the waiting list for transplantation was undistinguishable (14 months for PD vs. 16 months for HD patients, $P = 0.137$). Regarding donor characteristics, the proportion of grafts from donors with traumatic brain death (74.4% for PD; 74.8% for HD) and length of donor′s admission in the intensive care unit (2.6 days for PD; 2.8 days for HD) as well as donor's age (28 years for both groups) were similar between PD and HD patients. Other factors, such as the number of HLA mismatches; cold ischemia time; acute rejection rate; and length of admission, did not differ between both groups. There was a trend toward a lower rate of delayed renal graft function in PD patients. In those cases of dialysis need after SPKT, HD was always used.

The global relaparotomy rate was similar in PD and HD patients. However, when we analyzed the reasons for re-intervention, thrombosis predominated (12.8%) among all causes for reoperation in PD patients (28.2%), being significantly higher when compared to HD patients (12.8% vs. 1.7%, $P = 0.014$). A nonsignificant higher proportion of HD patients (7.6%, vs. 2.6% in PD patients) underwent bleeding-driven relaparotomy. To exclude a possible effect

Table 1. Demographic and clinical characteristics of the study population

	Total (*n* = 165)	Pre-emptive (*n* = 7)	HD (*n* = 119)	PD (*n* = 39)	*P* value HD vs. PD
Recipient age (years)	34.8 ± 6.0	33.6 ± 7.5	35.2 ± 6.3	33.9 ± 4.8	0.167
Female gender (R)	87 (52.7%)	2 (28.6%)	57 (47.9%)	25 (64.1%)	0.079
Time of diabetes (years)	23.87 ± 5.98	24.4 ± 9.2	23.6 ± 6.2	24.7 ± 4.5	0.285
Time on dialysis (months)	29.2 ± 21.0	–	32.0 ± 22.1	20.7 ± 14.6	0.003
HbA1c pre-SPKT (%)	9.0 ± 6.9	7.8 ± 1.5	9.4 ± 7.8	8.0 ± 1.4	0.130
HbA1c pre-SPKT≥9%	52 (37.4%)	2 (33.3%)	42 (40%)	8 (28.6%)	0.267
BMI (kg/m^2)	22.3 ± 2.1	21.7 ± 2.8	22.2 ± 2.9	22.5 ± 2.4	0.637
Cardiovascular disease (*n*/%)	31 (18.8%)	2 (28.6%)	24 (20.2%)	5 (12.8%)	0.304
Taking aspirin pre-SPKT	120 (72.7%)	5 (71.4%)	86 (72.3%)	29 (74.4%)	0.799
Hb pre-SPKT (g/dl)	10.9 ± 1.2	11.1 ± 0.9	10.9 ± 1.3	10.9 ± 0.7	0.943
Hospital stay (days)	25 ± 19	16 ± 6	25 ± 17	27 ± 26	0.718
Donor age (years)	28.2 ± 10.6	28.7 ± 15.3	28.3 ± 10.4	28.0 ± 10.7	0.248
HLA mismatches (total)	4.53 ± 1.08	4.86 ± 1.07	4.55 ± 1.04	4.42 ± 1.20	0.566
Cold ischemia time (hours)	11.3 ± 4.0	9.3 ± 3.2	11.6 ± 5.1	10.9 ± 4.4	0.786
Delayed (renal) graft function	24 (14.5%)	1 (14.3%)	21 (17.6%)	2 (5.1%)	0.067
Acute rejection (*n*/%)	26 (15.8%)	1 (14.3%)	21 (17.6%)	4 (10.3%)	0.272
SPKT with relaparotomy	42 (25.5%)	1 (14.3%)	30 (25.2%)	11 (28.2%)	0.711
Causes					
Infection	20 (12.1%)	0	16 (13.4%)	4 (10.3%)	1.0
Bleeding	10 (6.1%)	0	9 (7.6%)	1 (2.6%)	0.453
Thrombosis	8 (4.8%)	1 (14.3%)	2 (1.7%)	5 (12.8%)	0.014
Others	4 (2.4%)	0	3 (2.5%)	1 (2.6%)	1.0

of era and cumulative experience on the rate of infection and thrombosis complications, the rate of such events was explored in each year of the SPKT program and it was seen that the events were distributed similarly along the time course of the SPKT program.

Table 2 summarizes complications leading to each graft loss and patient death, in both groups. Death-censored pancreas graft loss was not significantly different in both groups (28.2% for PD, vs. 19.3% for HD patients). However, we registered more pancreas losses due to infection among PD patients (12.8%, vs. 3.4% among HD patients, $P = 0.042$). There was a trend toward a higher rate of global pancreas failure (death-censored) at month 1 in PD patients (15.4%, vs. 6.7% in HD patients, $P = 0.099$), but thereafter this difference disappeared. Additionally, we verified that the permanence of the abdominal drain after surgery was almost double in PD patients (means of 4.7 ± 1.5 days, vs. 2.6 ± 1.2 days in HD patients, $P < 0.001$).

We analyzed past peritonitis in PD patients and also intra-abdominal complications observed in this group. From the 39 PD patients, only ten have had peritonitis: These experienced 14 peritonitis episodes— four patients with two episodes. The isolated microbiological agents were gram positive in all but one: *Staphylococcus Epidermidis* (6 cases); *Staphylococcus Aureus* (3 cases); *Streptococcus Viridans* (2 cases); *Enterococcus Faecalis* (2 cases); and *Pseudomonas Aeruginosa* (1 case). The latter was efficiently treated with antibiotics and the patient had an uneventful recovery more than 1 year before SPKT, not needing catheter substitution. This patient did not present abdominal complications after SPKT. Only one of five the patients who complicated with intra-abdominal infection had in the past a gram-positive peritonitis (*Staph Epidermidis*, 11 months ago), and the intra-abdominal agents after SPKT were distinct: *E. Coli* and *Klebsiella Pneumoniae*. Similarly, only one of the four who complicated with pancreas thrombosis had a *Staphylococcus Aureus* peritonitis, 8 months before SPKT. Microbiological agents identified in the five patients with intra-abdominal infection were almost exclusively gram negative: *E. Coli*+ *Klebsiella*; *Enterobacter Aerogenes*; *Pseudomonas* (2 cases); and *Klebsiella*+ vancomycin-resistant *Enterococcus Faecium*.

As a note, from the single 3 patients who were on PD > 40 months, only one had a peritonitis in the past, but none of these 3 suffered intra-abdominal complications after SPKT. Plastic peritonitis and obstruction were not registered. Additionally, none was switched to HD due to lack of ultrafiltration or PD efficacy. One single patient was switched from PD to HD, due to visual impairment, 13 months before SPKT and was accounted as an HD patient in this study. Excluding the 3 cases who started renal replacement by HD, for a few weeks, waiting for conditions for PD catheter utilization, none was switched from HD to PD.

As to the renal graft, death-censored graft failure was also not different in both groups (12.8% for PD, vs. 5.9% for HD patients). Analyzing the causes of renal loss, we noted a similar acute rejection rate in both groups, but a tendency

Table 2. Graft failure and patient death occurrence and its causes.

	Total ($n = 165$)	Pre-emptive ($n = 7$)	HD ($n = 119$)	PD ($n = 39$)	*P* value HD vs. PD
Pancreas (Px) failure*	35 (21.2%)	1 (14.3%)	23 (19.3%)	11 (28.2%)	0.242
Rejection	8 (4.8%)	1 (14.3%)	5 (4.2%)	2 (5.1%)	0.659
Thrombosis	11 (6.7%)	0	7 (5.9%)	4 (10.3%)	0.290
Bleeding	3 (1.8%)	0	3 (2.5%)	0	1.0
Infection	9 (5.5%)	0	4 (3.4%)	5 (12.8%)	0.042
Other causes	4 (2.4%)	0	4 (3.4%)	0	0.576
>1 month			15 (13.5%)	5 (15.2%)	0.811
Px Failure_global	41 (24.8%)	1 (14.3%)	28 (23.5%)	12 (30.8%)	0.367
Px Failure_1 month*	14 (8.5%)	0	8 (6.7%)	6 (15.4%)	0.099
Kidney (Kx) failure*	13 (7.9%)	1 (14.3%)	7 (5.9%)	5 (12.8%)	0.156
Rejection	9 (5.5%)	0	7 (5.9%)	2 (5.1%)	1.0
Thrombosis	3 (1.8%)	1 (14.3%)	0	2 (5.1%)	0.058
Infection	1 (0.6%)	0	0	1 (2.6%)	0.238
>1 month			7 (5.9%)	3 (8.1%)	0.629
Kx Failure_global	20 (12.1%)	1 (14.3%)	11 (9.2%)	8 (20.5%)	0.060
Kx Failure_1 month*	3 (1.8%)	1 (14.3%)	0	2 (5.1%)	0.060
Patient death	13 (7.9%)	0	6 (5.0%)	7 (17.9%)	0.011
Cardiovascular	4 (2.4%)	0	4 (3.4%)	0	0.578
Infection	7 (4.2%)	0	2 (1.7%)	5 (13.5%)	0.010
Other causes	2 (1.2%)	0	0	2 (5.9%)	0.052
Follow-up (years)	5.87 ± 3.64	5.89 ± 3.77	6.30 ± 3.48	4.55 ± 3.88	0.015

*death-censored.

to a higher rate of losses due to thrombosis in PD patients (5.1%, vs. 0% in HD patients, $P = 0.058$). There was a trend toward an increased first-month renal graft failure in PD patients (5.1%, vs. 0% in HD patients, $P = 0.060$), and we observed that this tendency persisted after this period, when accounting for the total number of renal losses during follow-up (20.5%, vs. 9.2% among HD patients, $P = 0.060$).

We also analyzed other factors prior to SPKT that might have influenced thrombosis rate, leading or not to graft loss: The rate of patients taking aspirin as chronic medication; the level of Hb; and pre-existent CVD were similar in patients with and without thrombosis. On the contrary, patients who complicated with thrombosis more often were under PD (6/39 vs. 7/119, $P = 0.061$). The same analysis was made for pre-existent conditions predisposing to bleeding, needing surgery or even leading to graft loss. None of the studied factors (chronic medication with aspirin, Hb level, previous CVD, and dialysis modality) were associated with a higher incidence of bleeding. Among those who complicated with bleeding, 11 of 12 were on HD, but this was not statistically significant ($P = 0.296$).

Patient death was significantly higher in the PD group: 17.9% ($n = 7$), compared with 5.0% ($n = 6$) in the HD group, $P = 0.011$. Infection, as a cause of death, predominated in PD patients (13.5%, vs. 1.7% in HD patients, $P = 0.010$). CVD-related death was registered only in HD group (4 cases, or 3.4%), although not statistically different from the PD group.

Four-year and 8-year survival rates are presented in Table 3. Death-censored survival rates for pancreas graft were similar in HD and PD patients, irrespective of first-month losses inclusion or not. Death-censored survival rates for the renal graft were similar in HD and PD patients when first-month losses were excluded. If these early losses were also considered, then renal survival was inferior in PD patients. Lower patient survival was observed in the PD group (87.0% and 71.2% vs. 98.1% and 95.2% in HD group, at 4 and 8 years, respectively, $P = 0.003$).

On multivariate analysis, graft failure (one or both grafts), the modality of dialysis, and concomitant CVD were confirmed as independent predictors of patient death (Table 4). The likelihood of death was 8.76 times higher if at least one graft failed; 6.23 times higher if PD was the dialysis modality prior to SPKT; and 4.05 times higher when they have had clinically significant CVD. Figure 1 illustrates patient survival curves.

Table 3. Four-year and 8-year survival rates (log-rank test) of HD and PD patients

	4-years	8-years	
Pancreas graft survival (death-censored)			
HD	82.3%	78.9%	
DP	79.5%	57.7%	$P = 0.128$
Pancreas graft survival (death-censored) —excluding 1st-month losses			
HD	88.2%	84.5%	
DP	93.9%	68.1%	$P = 0.561$
Kidney graft survival (death-censored)			
HD	98.1%	92.4%	
DP	88.1%	82.9%	$P = 0.048$
Kidney graft survival (death-censored) —excluding 1st-month losses			
HD	98.1%	92.4%	
DP	92.5%	87.4%	$P = 0.333$
Patient survival			
HD	98.1%	95.2%	
DP	87.0%	71.2%	$P = 0.003$

Discussion

Results from published studies about the relationship between dialysis modality and the outcome of transplant are not concordant. PD has been associated with poorer transplant outcomes by some authors [8–11], but others did not report any detrimental effect of PD [4,5]. However, most of these results came from kidney transplantation alone (KTA).

In SPKT, infection [16–20], thrombosis [21,22], and bleeding [21], leading to subsequent relaparotomy [20,21,23], are feared complications, as they have been associated with lower graft survival.

There are several classical and well-recognized risk factors for VT, such as multiple vessels, technical problems during anastomosis, very young pediatric donors or elderly donors, thrombocytosis, hemoconcentration, hypotension, and the existence of a previous transplant [9]. Obviously, hypercoagulable states substantially increase the rate of thrombosis [9,21]. Diabetes, itself, has been considered an additional risk factor for thrombosis [9], and prothrombotic disorders may be frequent in DM1 patients undergoing SPKT [24].

Though controversies still exist, PD may predispose to a thrombophilic state by several mechanisms [9] that are not

Table 4. Multivariable Cox proportional analysis of predictors of patient death

	HR	IC 95%	*P*
Concomitant cardiovascular disease	4.051	1.091–15.041	0.037
Graft failure (kidney and/or pancreas)	8.764	2.198–34.950	0.002
Dialysis modality (PD vs. HD)	6.231	1.460–26.591	0.013
Recipient age	1.055	0.939–1.186	0.367
Recipient gender (M vs. F)	1.987	0.508–7.773	0.324
Months on dialysis	0.941	0.962–1.037	0.941
Years of diabetes evolution	1.089	0.946–1.253	0.235
Pretransplant HbA1c (<vs. ≥9%)	0.243	0.053–1.126	0.071

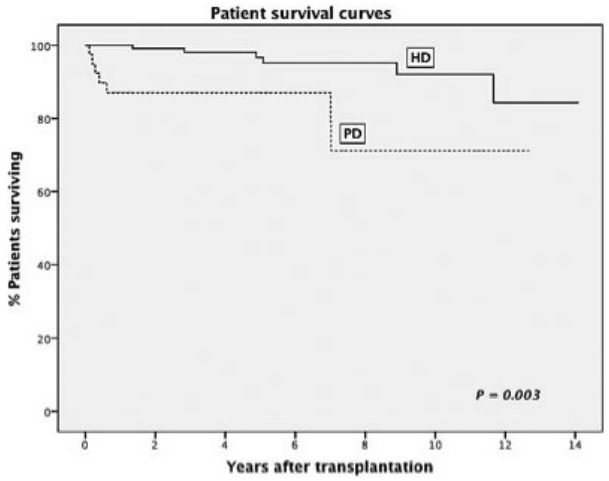

Figure 1 Patient survival curves (Kaplan–Meier method).

completely clear. Enhanced plasmatic activities of procoagulant factors [25] and hemoconcentration [26] were mentioned as being more likely to occur in PD than in HD patients. Robertson *et al.* [12] showed that the addition of low-dose aspirin was beneficial in reducing the rate of VT in KTA patients. Additionally, impaired fibrinolysis caused by increased plasma plasminogen activator inhibitor-1 (PAI-1) levels is linked with insulin resistance that occurs with uremia and might be exacerbated in certain PD patients [27].

Concerning the prevention of pancreas graft thrombosis, one recent study reported potential beneficial effects with low-dose heparin started in the early postoperative period (in association with aspirin), at the expense of a higher number of relaparotomies [21]. Others have found better results using lower molecular-weight heparin and concluded that this prophylaxis strategy might not be inferior to the one using dose-adjusted intravenous unfractionated heparin [22].

PD population usually includes patients with vascular access problems, possibly due to a pre-existing prothrombotic state in some of them—a selection bias that may help to explain higher rates of renal VT in PD patients [9]. The transplant center volume and professional skill can additionally influence the results. Our transplant team for SPKT is restricted and has remained stable over the years, rendering a bias from different technical skills of multiple surgeons very unlikely.

In this study, we observed a higher relaparotomy rate due to thrombosis and a near significant higher rate of renal graft loss secondary to thrombosis, in PD patients. Only 2 patients had a previous renal transplant and none complicated with VT, albeit repeated transplantation is an established risk factor [9]; Hb level and chronic medication with aspirin were comparable in PD and HD patients. However, we have to be cautious in interpreting these results, given the small number of renal thrombosis (2 cases). Future results from larger series including PD patients may bring more consistent data regarding the association between PD and thrombosis in SPKT patients who are normally under thrombosis prophylaxis.

A distinct approach, with more aggressive anticoagulation prophylaxis, has been suggested in PD patients, but it is not definitely established. Yet, the bleeding risk must be weighed. More studies clarifying the predisposing factors to thrombotic events in PD patients are needed, in order to design an effective prophylaxis against thrombosis.

While some authors reported similar abdominal infection rates in PD and HD patients [16,17], there are several others reporting higher incidence of peritonitis in PD patients [18,19,28]. Manipulation of the peritoneal catheter, communicating with the skin and the external environment, is the major cause for peritonitis in PD patients. Whether this catheter remains colonized by microbial agents due to biofilm formation, even without overt infection, is a real possibility [16]. However, the cultured agents from the drainage are frequently diverse (gram negative) from those more often cultured during peritonitis episodes (gram positive) in PD patients [16], as we also observed. In SPKT, there are other confounding factors, such as the surgery procedure itself and the opening of the small bowel to perform duodenal anastomosis.

Fluid collections, as well as vascular catheters or surgical drains, contribute to the risk of infection. Some degree of persistent ascites after PD catheter removal is frequently observed, representing chronic and remarkable changes in peritoneal membrane [29]. Important volume drainage leads to the maintenance of the surgical drain for more days, as we observed in our PD group, again increasing the risk of infection. In our practice, PD catheter is always removed at the beginning of SPKT procedure and residual ascites cultured. The abdominal drainage is repeatedly cultured while it remains important and the drain maintained, being removed as soon as possible when drainage amylase decreases and microbiological analysis is sterile. However, prophylactic antibiotics may need to be extended in patients with more prolonged drain patency.

Fibrosis and peritoneal thickening following PD [30] may adversely affect peritoneal and intestinal healing after the surgery, contributing to increased technical difficulty and to the rate of leak and infection [16]. Graft pancreatitis and duodenal leak are of paramount importance for abdominal cavity infection occurrence [31]. Abdominal surgical re-exploration, in immunosuppressed patients, represents another risk factor for infectious complications and for adverse graft outcomes [23], leading to an enhanced rate of transplantectomy [20].

More intense immunosuppression used in SPKT, compared with KTA, also augments patient susceptibility for several types of infections. Our results demonstrated an increased rate of pancreas loss due to infection in PD patients. The length of admission and the acute rejection incidence, possible contributors to infection [15], cannot explain the higher infection rate in this group, given that they were similar between HD and PD patients.

Other relevant clinical variables explaining our worse outcomes in PD patients were not identified: both groups had similar age, time of diabetes, acute rejection, and delayed graft function rates as well as comorbidities such as CVD. On the contrary, PD patients had a mean time on dialysis lower than HD patients, meaning they were early referred to SPKT, which is a positive aspect. Additionally, more patients were referred from PD centers in the more recent years, which explains the shorter follow-up after SPKT in the PD group. It has been reported that PD patients are more likely to receive a renal transplant [8], and less likely to evolve with delayed kidney graft function [8], a tendency also observed in our study.

CVD and graft loss are unquestionable risk factors for patient death [32]. In our study, PD was a predictor of death, mainly due to infection and thrombosis. Should these results be confirmed in further studies, then HD might be preferable for SPKT candidates, to optimize transplant outcome. Focused investigation is utterly needed as the risk of these complications after SPKT may be potentially modifiable with adjusted per-operatory infection and thrombosis prophylactic protocols.

Authorship

LSM: designed the study, performed research, analyzed data, contributed to discussion, and wrote the manuscript. ACH and DS: performed research and contributed to discussion. JM: analyzed data and contributed to discussion. AC, SP, MA, LD, and JD: contributed to discussion and interpretation of data. ASR and ILN: contributed to discussion and edited the manuscript. All the authors reviewed and approved the final version of the manuscript.

References

1. Meier-Kriesche HU, Port FK, Ojo AO, *et al.* Effect of waiting time on renal transplant outcome. *Kidney Int* 2000; **58**: 1311.
2. Kasiske BL, Snyder JJ, Matas AJ, Ellison MD, Gill JS, Kausz AT. Preemptive kidney transplantation: the advantage and the advantaged. *J Am Soc Nephrol* 2002; **13**: 1358.
3. Gill JS, Tonelli M, Johnson N, Pereira BJ. Why do preemptive kidney transplant recipients have an allograft survival advantage? *Transplantation* 2004; **78**: 873.
4. Molnar MZ, Mehrotra R, Duong U, *et al.* Dialysis modality and outcomes in kidney transplant recipients. *Clin J Am Soc Nephrol* 2012; **7**: 332.
5. Kramer A, Jager KJ, Fogarty DG, *et al.* Association between pre-transplant dialysis modality and patient and graft survival after kidney transplantation. *Nephrol Dial Transplant* 2012; **27**: 4473.
6. Goldfarb-Rumyantzev A, Hurdle JF, *et al.* Duration of end-stage renal disease and kidney transplant outcome. *Nephrol Dial Transplant* 2005; **20**: 167.
7. Wu C, Evans I, Joseph R, *et al.* Comorbid conditions in kidney transplantation: association with graft and patient survival. *J Am Soc Nephrol* 2005; **16**: 3437.
8. Snyder JJ, Kasiske BL, Gilbertson DT, Collins AJ. A comparison of transplant outcomes in peritoneal and hemodialysis patients. *Kidney Int* 2002; **62**: 1423.
9. Ojo AO, Hanson JA, Wolfe RA, *et al.* Dialysis modality and the risk of allograft thrombosis in adult renal transplant recipients. *Kidney Int* 1999; **55**: 1952.
10. Murphy BG, Hill CM, Middleton D, *et al.* Increased renal allograft thrombosis in CAPD patients. *Nephrol Dial Transplant* 1994; **9**: 1166.
11. van der Vliet JA, Barendregt WB, Hoitsma AJ, Buskens FG. Increased incidence of renal allograft thrombosis after continuous ambulatory peritoneal dialysis. *Clin Transplant* 1996; **10**: 51.
12. Robertson AJ, Nargund V, Gray DW, Morris PJ. Low dose aspirin as prophylaxis against renal-vein thrombosis in renal-transplant recipients. *Nephrol Dial Transplant* 2000; **15**: 1865.
13. Binaut R, Hazzan M, Pruvot FR, Dracon M, Lelièvre G, Noël C. Comparative study of chronic ambulatory peritoneal dialysis versus hemodialysis patients after kidney transplantation: clinical and financial assessment. *Transplant Proc* 1997; **29**: 2428.
14. Vanholder R, Heering P, Loo AV, *et al.* Reduced incidence of acute renal graft failure in patients treated with peritoneal dialysis compared with hemodialysis. *Am J Kidney Dis* 1999; **33**: 934.
15. Passalacqua JA, Wiland AM, Fink JC, Bartlett ST, Evans DA, Keay S. Increased incidence of postoperative infections associated with peritoneal dialysis in renal transplant recipients. *Transplantation* 1999; **68**: 535.
16. Kim RD, Oreopoulos DG, Qiu K, *et al.* Impact of mode of dialysis on intra-abdominal infection after simultaneous pancreas-kidney transplantation. *Transplantation* 2005; **80**: 339.
17. Papalois BE, Troppmann C, Gruessner AC, Benedetti E, Sutherland DE, Gruessner RW. Long-term peritoneal dialysis before transplantation and intra-abdominal infection after simultaneous pancreas-kidney transplantations. *Arch Surg* 1996; **131**: 761.
18. Malaise J, Squifflet JP, Van Ophem, D; EUROSPK Study Group. Influence of the type of renal replacement therapy on peritonitis rate after simultaneous pancreas kidney transplantation. *Transplant Proc* 2002; **34**: 2823.

19. Padillo-Ruiz J, Arjona-Sánchez A, Muñoz-Casares C, Ruiz-Rabelo J, Navarro MD, Regueiro JC. Impact of peritoneal dialysis versus hemodialysis on incidence of intra-abdominal infection after simultaneous pancreas-kidney transplant. *World J Surg* 2010; **34**: 1684.
20. Jimenez C, Manrique A, Morales JM, *et al.* Influence of dialysis modality on complications and patient and graft survival after pancreas-kidney transplantation. *Transplant Proc* 2008; **40**: 2999.
21. Scheffert JL, Taber DJ, Pilch NA, Chavin KD, Baliga PK, Bratton CF. Clinical outcomes associated with the early postoperative use of heparin in pancreas transplantation. *Transplantation* 2014; **97**: 681.
22. Schenker P, Vonend O, Ertas N, *et al.* Incidence of pancreas graft thrombosis using low-molecular-weight heparin. *Clin Transplant* 2009; **23**: 407.
23. Perez-Saez MJ, Toledo K, Navarro MD, *et al.* Long-term survival of simultaneous pancreas-kidney transplantation: influence of early posttransplantation complications. *Transplant Proc* 2011; **43**: 2160.
24. Wullstein C, Woeste G, Zapletal C, Trobisch H, Bechstein WO. Prothrombotic disorders in uremic type-1 diabetics undergoing simultaneous pancreas and kidney transplantation. *Transplantation* 2003; **76**: 1691.
25. Vaziri ND, Shah GM, Winer RL, *et al.* Coagulation cascade, fibrinolytic system, antithrombin III, protein C and protein S in patients maintained on continuous ambulatory peritoneal dialysis. *Thromb Res* 1989; **53**: 173.
26. Metha BR, Mogridge C, Bell JD. Changes in red cell mass, plasma volume and hematocrit in patients on CAPD. *Trans Am Soc Artif Intern Organs* 1983; **29**: 50.
27. Juhan-Vague I, Alessi MC, Mavri A, Morange PE. Plasminogen activator inhibitor-1, inflammation, obesity, insulin resistance and vascular risk. *J Thromb Haemost* 2003; **1**: 1575.
28. Douzdjian V, Abecassis M. Deep wound infections in simultaneous pancreas-kidney transplant recipients on peritoneal dialysis. *Nephrol Dial Transplant* 1995; **10**: 533.
29. Moon SJ, Han SH, Kim DK, *et al.* Risk factors for adverse outcomes after peritonitis-related technique failure. *Perit Dial Int* 2008; **28**: 352.
30. Nakamoto H, Hamada C, Shimaoka T, *et al.* Accumulation of advanced glycation end products and beta 2-microglobulin in fibrotic thickening of the peritoneum in long-term peritoneal dialysis patients. *J Artif Organs* 2014; **17**: 60.
31. Troppmann C, Gruessner AC, Dunn DL, Sutherland DE, Gruessner RW. Surgical complications requiring early relaparotomy after pancreas transplantation: a multivariate risk factor and economic impact analysis of the cyclosporine era. *Ann Surg* 1998; **227**: 255.
32. Gruessner AC. 2011 update on pancreas transplantation: comprehensive trend analysis of 25,000 cases followed up over the course of twenty-four years at the International Pancreas Transplant Registry (IPTR). *Rev Diabet Stud* 2011; **8**: 6.