Impact of pre-transplant dialysis modality on the outcome and health-related quality of life of patients after simultaneous pancreas-kidney transplantation

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Abstract

Background Simultaneous pancreas-kidney transplantation (SPKT) profoundly improves the Health-related quality of life (HRQoL) of the recipients. However, the influence of the pre-transplant dialysis modality on the success of the SPKT and post-transplant HRQoL is still unknown.

Methods We analyzed the surgical outcome, long-term survival, as well as HRQoL of 83 SPKTs that were performed between 2000 and 2016 in our Hospital. Prior to transplant, 63 patients received hemodialysis (HD) and 19 patients received peritoneal dialysis (PD). Physical and mental quality of life results from eight basic scales and the physical and mental component summaries (PCS and MCS) were measured using the Short Form 36 (SF-36) survey.

Results Peri- and postoperative complications, as well as patient and graft survival were similar in both groups. Both groups showed improvement of HRQoL in all SF-36 domains after transplantation. Compared to patients who received HD before transplantation, PD-patients showed significantly better results in five of the eight SF-36 domains: physical functioning ($P = 0.02$), bodily pain ($P = 0.001$), general health ($P = 0.038$), vitality ($P = 0.014$), role limitations emotional ($P = 0.048$) and PCS ($P = 0.002$) after SPKT. In the overall study population, graft loss was associated with significant worsening of the HRQoL in all physical components (each $P < 0.01$).

Conclusions The results of this analysis show that pre-transplant dialysis modality has no influence on outcome and survival rate after SPKT. Regarding HRQoL, patients receiving PD prior to SPKT seems to entail a slight advantage compared to patients with HD before transplantation.

Background

Simultaneous pancreas-kidney transplantation (SPKT) offers considerable survival benefits for patients with insulin dependent diabetes mellitus and end-stage renal disease (ESRD), because it restores long-term glycemic control and can reduce secondary diabetic complications [1–6].

Due to organ shortage, most of these patients must perform long-term renal replacement therapy (RRT) prior to SPKT. With hemodialysis (HD) and peritoneal dialysis (HD), two efficient RRTs are available pre-transplant. However, both dialysis modalities substantially influence patients' health and their abilities to work and participate in social activities. Conventional HD is usually performed intermittently, three times a week in a dialysis center. During HD, uremic toxins are removed from the blood extracorporeally through a filter, which is generally considered as a stressful procedure, with an increased risk for cardiovascular diseases [7, 8]. In contrast, PD uses the peritoneum as a filter through which substances are exchanged with the blood. In general, PD offers greater flexibility as it can be performed at different time points and independent from medical staff, but carry the risk of metabolic complications related to systemic glucose absorption from the dialysate (e.g. hyperlipidemia and decompensation of diabetes mellitus), and catheter associated complications. PD-catheter infection can lead to subsequent peritonitis, which remains the major cause of morbidity and mortality in PD patients [7, 9].

Apart from mere graft and patient survival rates after transplantation, measurement of the Health-Related Quality of Life (HRQoL) has become an issue of further interest, as it provides an overall view of the impact of the disease process on psychosocial status. Monitoring of the HRQoL helps define how disease symptoms affect the patient's life, their physical and mental functioning, and their ability to cope with the new life situation after transplantation.

Recent studies have shown that patients after SPKT generally experience better quality of life in comparison to dialysis patients [4, 10–13]. However, the influence of dialysis modality prior to SPKT on the surgical outcome and

HRQoL after transplantation is less clear. Thus, the current study has sought to analyze the outcome and HRQoL in diabetic patients with ESRD undergoing SPKT, in regard to pre-transplant dialysis modality.

Methods

Study Population

Medical data from patients with insulin dependent diabetes mellitus (type 1 or 2) and end-stage renal diseases (ESRD) who received simultaneous pancreas-kidney transplantation (SPKT) at the University Hospital of Leipzig between 2000 and 2016 were retrospectively analyzed. Our data source comprised a prospectively collected electronic database. Approval for this analysis was granted by the local ethics committee [AZ: Nr: 111–16–14032016]. Patients undergoing pre-emptive transplantation, re-transplants, living donor kidney transplantation, younger than 18 years, and those with missing data were excluded from the study.

Outcome measures

Special emphasis was placed on the outcome of dialysis modality before transplantation (hemodialysis (HD) versus peritoneal dialysis (PD)), recipient and donor characteristics, intra- and postoperative variables and complications, such as patient, graft as well as health-related quality of life outcomes before (during dialysis) and after transplantation.

Characteristics included age, gender, body mass index (BMI, weight in kg/height in m^2), duration of insulin dependent diabetes mellitus, duration of dialysis, time on the waiting list. Cardiovascular disease included information about peripheral arterial obstructive disease and coronary heart disease (coronary artery bypass graft or stent). Peri- and post-transplant data included information on cold ischemia time of kidney/pancreas, immunosuppressive therapy as well as patient and organ graft function.

Furthermore, complications occurring during the first three months after transplantation were analyzed. Surgical complications were defined as the need for relaparotomy within the first 3 months after transplantation. Intraabdominal infections were defined as the development of infected fluid collection that required an intervention and/or antibiotic drug therapy. Gastrointestinal bleedings were defined as bleedings requiring relaparotomy or endoscopy, or patients suffering from sudden anemia combined with either melena or hematemesis. Other bleedings, consisting of intra-abdominal hemorrhages, were diagnosed by CT scan or relaparotomy performed due to acute anemia.

Health-related Quality of Life (HRQoL)

For measuring the HRQoL in this study, the mostly used and internationally validated Medical Outcomes Study 36-Item Short Form Health Survey (SF-36) questionnaire was used. Patients were asked to evaluate their HRQoL before transplantation (undergoing dialysis (HD versus PD)), such as one year after transplantation.

The SF-36 survey is suitable to compare the health status of chronically ill patients with the general population in terms of functional status and well-being.

In this study, HRQoL was evaluated in a second assessment through written HRQoL questionnaires (SF-36) sent to all patients with invitation to complete a quality of life survey retrospectively.

The SF-36 survey was sent by mail to patients' home addresses. Additionally, patients were interviewed via telephone or during clinical visit, as indicated. Return envelopes were included free of charge. A period of two weeks was envisaged for questionnaire return. All patients who had not returned the questionnaire after two weeks were contacted a second time via mail or telephone within another 14 days. Altogether, patients had four weeks for their responses. Prior to the study, informed consent of all patients and the consent of the local ethics committee [AZ: Nr: 111–16–14032016] were obtained. Because the HRQoL assessment was performed separately, it was not possible to correlate HRQoL scores with all clinical data. The average time span between SPKT and completion of the questionnaires was 8.6 ± 2.9 years.

The SF-36 has thirty-six questions (without specific for renal failure or diabetes) which assess ability to perform vigorous activities and activities for daily living and participate in social, family and occupational activities. Eight scales/dimensions describe domains of physical functions (PF, 10 items), role limitations due to physical problems (PR, 4 items), bodily pain (BP, 2 items), a general perception of health (GH, 5 items), energy and vitality (VIT, 4 items), social functions (SF, 2 items), role limitations due to emotional problems (RE, 3 items), and mental health (MH, 5 items). The subscales can be combined into two summation scales measuring the overall physical and mental HRQoL: a physical component summary (PCS = PF + PR + BP + GH) and a mental component summary (MCS = VIT + SF + RE + MH). Subscale scores were transformed to a 0–100 scale, with 0 representing the least well-being to 100 representing the greatest well-being.

Surgical Techniques

As described previously, pancreas and kidney grafts were procured following the international standards and guidelines provided by the Deutsche Stiftung für Organtransplantation (DSO) [14, 15]. In short, the pancreas was explanted in a no-touch technique en-bloc with the spleen and duodenum. Back table preparation included removal of the spleen and peripancreatic fat. Reconstruction of the superior mesenteric and the lineal artery was performed using the donor iliac Y-graft.

The pancreas was transplanted into the right iliac fossa using a standard technique with an intraperitoneal location in the right iliac fossa. The Y-graft was anastomosed to the recipient's common iliac artery using 6 − 0 Prolene running sutures. The portal vein was connected to the inferior vena cava of the recipient [16]. Exocrine drainage was carried out with a hand-sutured side-to-side duodenojejunostomy 40 cm beyond the flexure of Treitz [3, 17]. At the end of pancreas implantation, PD catheters were removed in all recipients, and catheter tip culture was routinely performed.

All Kidneys were transplanted into the contralateral iliacal fossa. Vascular anastomoses were performed to the external iliac artery and vein. The ureter was implanted into the bladder according to the Lich-Gregoir technique using a double J catheter as an intraureteral splint [16]. Splint removal was performed 3–4 weeks after successful transplantation. The peritoneal catheter was removed during surgery.

Immunosuppression

The immunosuppressive protocol consisted of an induction therapy followed by triple maintenance therapy.

For induction, antithymocyte globulin with a dose of 4 mg/kg body weight was applied as a single dose before transplantation and followed by a 1 mg/kg body weight infusion on postoperative days 1–3. As an alternative, the interleukin-2 receptor antagonist basiliximab (Simulect ®, 20 mg before transplantation and 20 mg on post-

operative day 4) was used in patients with contraindications for ATG therapy. Main contraindications comprised Leukocytopenia, Thrombocytopenia or prevalent urinary tract infections.

Maintenance therapy included calcineurin inhibitors (Cyclosporin (Sandimmun Neoral ® or Tacrolimus (Prograf ®), and/or antimetabolites (Sirolimus (Rapamune ®), Mycofenolate Mofetil (MMF); (Cell Cept ®, Myfortic ®) and tapered steroids (Prednisolone ®). Whole blood levels of Tacrolimus were adjusted to 10–12 ng/ml for the first 3 months and 8–10 ng/ml for month 4 to 12. One year after transplantation levels were reduced to 6 to 8 ng/ml. In parallel, MMF was given at an oral dose of 1 g (Cell Cept ®) or 720 mg (Myfortic ®) twice daily.

A rapid steroid-tapering regimen was applied in all our patients, starting with 500 mg methylprednisolone intraoperatively to reach a dose of 25 mg prednisolone at the end of the first week after transplantation. Further reduction intended a daily maintenance dose of 5 mg. Whenever possible, steroids were rapidly withdrawn and discontinued at the end of the first year.

Statistical analysis

Baseline data are presented as mean values with standard deviation (SD), minimum or maximum range such as proportion percentage (%). Baseline data were compared with appropriate statistical significance test including Student´s t–test, $\chi 2$, analysis of variance (ANOVA), Kruskal-Wallis and Wilcoxon–Mann–Whitney test. Comparing HRQoL measurements between PD, HD and the entire SPKT group ANOVA and post-hoc NIR test were used. Survival rates were calculated using the Kaplan-Meier analysis and the log-rank test was applied to test statistical significance. Multivariate Cox proportional hazards analysis was applied to assess independent predictors of patient death and pancreas graft failure, including clinically relevant variables and/or those presenting $P \leq 0.15$ in univariate analysis: recipient gender, BMI and age, dialysis modality (HD versus PD), time on dialysis, years of diabetes mellitus, concomitant cardiovascular disease and surgical complications. All data were analysed by using SPSS software (SPSS Inc., Chicago, Illinois, USA, version 21.0). A P value < 0.05 was considered statistically significant.

Results

Baseline characteristics

Overall study population included 83 patients receiving simultaneous pancreas-kidney transplantation (SPKT) between 2000 and 2016 in our Department. At the time of transplantation, 64 patients obtained hemodialysis (HD) and nineteen patients used peritoneal dialysis (PD). Continuous ambulatory peritoneal dialysis was used by 14 patients (74%) and automatic peritoneal dialysis was used by 5 patients (26%) of the PD group. Recipient, donor and graft characteristics according to the different dialysis types prior to transplantation are summarized in Table 1. Both groups were similar for the majority of their pre-transplant characteristics. Number of female recipients was higher in the PD-group ($P = 0.017$). And history of depression was more frequent in the HD-group ($P = 0.049$). HLA mismatches, post-transplant immunosuppressive regimes and lengths of hospital stay did not show significant difference between both groups (data not shown).

Table 1

Variables	HD (n = 64)	PD (n = 19)	P-value
Recipient			
Age, years	43.8 ± 9.1	43.2 ± 9.7	0.845
Gender			
Male	40 (62.5%)	6 (31.6%)	0.017
Female	24 (37.5%)	13 (68.4%)	
BMI (kg/m²)	25.8 ± 4.4	24 ± 3.6	0.105
Duration Diabetes mellitus, years	27.1 ± 8.4	26.1 ± 8.6	0.685
Time on dialysis, months	30.5 ± 21.3	27.0 ± 22.1	0.536
HbA1c pre-transplantation, %	7.7 ± 1.8	7.7 ± 1.2	0.940
Time on waiting list, months	10.9 ± 13.6	7.2 ± 6.9	0.242
Comorbidities			
Diabetic Retinopathy	56 (87.5%)	13 (68.4%)	0.050
Diabetic Neuropathy	39 (60.9%)	11 (57.9%)	0.812
Arterial obstructive disease			
Yes	12 (18.8%)	2 (10.5%)	0.401
No	52 (81.2%)	17 (89.5%)	
Coronary heart disease			
Yes	21 (32.8%)	2 (10.5%)	0.050
No	43 (67.2%)	17 (89.5%)	
Depression	21 (32.8%)	2 (10.5%)	0.049
Taking aspirin pre-SPKT	23 (35.9%)	9 (47.4%)	0.367
Donor			
Age, years	24.1 ± 11.8	19.2 ± 7.8	0.109
Gender			
Male	37 (57.8%)	14 (73.3%)	0.212
Female	27 (42.2%)	5 (26.3%)	
BMI (kg/m²)	22.4 ± 3.1	22.1 ± 2.8	0.987

Variables	HD (n = 64)	PD (n = 19)	P-value
Graft			
Kidney cold ischemia (hrs)	11.0 ± 3.3	11.1 ± 2.6	0.978
Pancreas cold ischemia (hrs)	10.1 ± 1.9	10.9 ± 3.9	0.294
CMV status			
CMV D+	31 (48.4%)	11 (64.7%)	0.211
CMV R+	36 (56.3%)	13 (68.4%)	0.343
Induction Therapy			
ALG/ATG	54 (84.4%)	15 (78.9%)	0.864
IL2-RA	7 (10.9%)	3 (15.8%)	0.568
None	3 (4.7%)	1 (5.3%)	0.916

Outcome

Complications

There were no significant differences in the frequency of peri- and postoperative complications between HD- and PD SPKT recipients (Table 2). The global relaparotomy rate was similar in both groups (HD: 35% versus PD: 36%; P = 0.77).

Table 2

Variables	HD (n = 64)	PD (n = 19)	P-value
Acute combined graft rejection	12 (19%)	3 (16%)	0.769
Delayed graft function kidney	10 (16%)	2 (11%)	0.8
Anastomotic leak	2 (3%)	1 (5%)	0.66
Graft thrombosis	7 (11%)	4 (21%)	0.254
GI-Bleeding	7 (11%)	1 (5%)	0.426
Other major bleeding	9 (14%)	2 (11%)	0.69
Intraabdominal Infection	13 (20%)	5 (26%)	0.577
Graft Pancreatitis	11 (17%)	3 (16%)	0.88
CMV infection	21 (33.3%)	5 (26.3%)	0.564
Wound infections	9 (14%)	3 (16%)	0.851
Re-operation/ relaparotomy	23 (35%)	7 (36%)	0.77
Causes relaparotomy			
Infection	8 (13%)	2 (11%)	0.76
Bleeding	6 (9%)	1 (5%)	0.51
Thrombosis	7 (11%)	3 (16%)	0.54
Others	2 (3%)	1 (5%)	0.66

After transplantation, 18 patients developed intra-abdominal infections (HD: 20% versus PD: 26%; P = 0.577). There were eight bacterial infections, two fungal infections and eight cultured positive for both bacteria and fungi. Intraabdominal infections were complicated with graft pancreatitis in nine cases (HD: 10% versus PD: 11%; P = 0.89) and relaparotomy was necessary in ten cases (HD: 13% versus PD: 11%; P = 0.76). Four out of 19 PD patients had a history of peritonitis during their time on dialysis, including two patients with two or more episodes of peritonitis. History of peritonitis was not associated with increased risk of complications after transplantation, only one of these patients had an intraabdominal infection and one patient developed pancreatitis post-transplant.

Patient and graft survival

The 1-, 3- and 5-year patient survival rates for patients after SPKT showed no significant difference between the HD and PD group (90.6%, 89.0%, and 87.1% in HD versus 89.2%. 89.2% and 82.8% in PD, respectively; P = 0.782). Similarly, the 1-, 3- and 5- year pancreas graft survival rates (85.8%, 81.8% and 77.7% in HD versus 78.9%, 73% and 73% in PD, respectively; P = 0.836) and kidney graft survival rates (90.4%, 88.7% and 84.9% in HD versus 88.9%,

83.0% and 83.0% in PD, respectively; P = 0.78) did not show any significant differences between both groups (Fig. 1).

As shown in Table 3 no significant differences were found between type of pre-transplant dialysis modality and causes for patient death and graft failure. However, we noted a tendency to higher graft losses due to thrombosis in PD patients (HD: 4.7% versus PD: 15.8%; P = 0.1).

Table 3

Variables	HD (n = 64)	PD (n = 19)	P-value
Patient death			
Total	12 (19%)	3 (16%)	0.78
Cardiovascular	6 (9.4%)	2 (10.5%)	0.88
Infection	4 (6.3%)	1 (5.3%)	0.87
Other	2 (3.1%)	0 (0%)	0.43
Pancreas graft failure			
Total	15 (23%)	5 (26%)	0.79
Rejection	3 (4.7%)	0 (0%)	0.33
Thrombosis	3 (4.7%)	3 (15.8%)	0.1
Bleeding	2 (3.1%)	0 (0%)	0.43
Infection	5 (7.8%)	2 (10.5%)	0.70
Other	2 (3.1%)	0 (0%)	0.43
Kidney graft failure			
Total	13 (20%)	3 (16%)	0.19
Rejection	6 (9%)	1 (5%)	0.32
Thrombosis	2 (3%)	1 (5%)	0.66
Infection	3 (5%)	1 (5%)	0.91
Other	2 (3%)	0 (0%)	0.45

Multivariate Cox regression analysis of the total study population revealed that the presence of cardiovascular disease is an independent predictor of patient death. Moreover, preoperative presence of cardiovascular disease, recipient age, BMI, duration of pre-transplant dialysis and surgical complications could be identified as independent predictors of pancreas and kidney graft loss (Table 4).

Table 4

Variables	HR (95CI)	P-value
Patient death		
Cardiovascular disease	6.12 (1.7-21.19	0.005
Dialysis modality (PD vs HD)	1.72 (0.37–7.71)	0.70
Recipient age	0.96 (0.90–1.04)	0.33
Recipient gender (male vs female)	1.36 (0.41–4.44)	0.60
Months on dialysis	1.01 (0.9-1.0)	0.25
Years of diabetes	1.01 (0.9–1.2)	0.65
Recipient BMI	1.02 (0.88–1.18)	0.75
Pancreas graft failure		
Cardiovascular disease	3.36 (1.14–9.89)	0.02
Dialysis modality (PD vs HD)	1.35 (0.43–4.27)	0.60
Recipient age	1.2 (0.99–1.12)	0.01
Recipient gender (male vs female)	2.01 (0.81–4.92)	0.129
Months on dialysis	0.98 (0.96–1.10)	0.001
Years of diabetes	1.02 (0.94–1.06)	0.95
Surgical complications	6.48 (2.66–15.74)	0.001
Recipient BMI	1.2 (1.08–1.35)	0.01
Kidney graft failure		
Cardiovascular disease	2.53 (0.82–7.46)	0.019
Dialysis modality (PD vs HD)	1.01 (0.28–3.59)	0.986
Recipient age	1.2 (0.99–1.12)	0.01
Recipient gender (male vs female)	2.1 (0.75–6.1)	0.15
Months on dialysis	0.96 (0.93–1.2)	0.001
Years of diabetes	1.1 (0.95–1.08)	0.74
Surgical complications	3.4 (1.5–6.9)	0.03
Recipient BMI	1.19 (1.06–1.33)	0.003

Health-related Quality of Life (HRQoL)

Impact of pre-transplant dialysis modality

Tables 5 compares the HRQoL scores of SPKT recipients according to their dialysis modality before and after transplantation. Both groups showed improvement of HRQoL in all SF-36 domains after transplantation. There were statistically significant improvements in six of the eight SF-36 domains in the HD-group, and in seven of the eight SF-36 domains in the PD-group.

Table 5

SF-36 dimensions	**HD-group (n = 64)**			**PD-group (n = 19)**		
	Before SPKT	After SPKT	P-value	Before SPKT	After SPKT	P-value
Physcial functioning (PF)	48.3 ± 13.3	68.9 ± 8.9	< 0.01	63.8 ± 17.7	81.3 ± 15.9	0.03
Role limitations- physical (PR)	38.3 ± 31.3	60.7 ± 25.4	0.04	56.2 ± 43.8	72.9 ± 19.8	< 0.01
Bodily Pain (BP)	44.2 ± 21.2	71.1 ± 8.5	< 0.01	64.1 ± 17.6	85.3 ± 9.8	< 0.01
General health (GH)	36.5 ± 16.1	61.6 ± 7.5	< 0.01	48.8 ± 7.0	67.9 ± 6.8	< 0.01
Social function (SF)	55.8 ± 17.6	65.2 ± 12.2	0.110	68.8 ± 11.6	73.9 ± 11.2	0.329
Vitality (VIT)	42.7 ± 11.2	61.1 ± 7.4	< 0.01	48.8 ± 18.5	67.9 ± 5.4	< 0.01
Role limitations- emotional (ER)	44.4 ± 29.9	61.9 ± 28.8	0.122	66.7 ± 30.9	83.3 ± 22.5	0.178
Mental Health (MH)	51.4 ± 16.4	63.4 ± 5.8	0.01	49.5 ± 2.8	62.3 ± 8.2	< 0.01
Physical Component Summary (PCS)	34.9 ± 5.8	45.6 ± 4.6	< 0.01	43.1 ± 8.6	50.8 ± 2.5	< 0.01
Mental Component Summary (MCS)	40.2 ± 6.6	44.7 ± 4.5	0.042	41.6 ± 5.4	46.8 ± 3.8	0.021

Before transplantation, benefits were seen for the PD-patients, with statistically significant differences in terms of physical functioning (P = 0.028), bodily pain (P = 0.034), and in the physical component summary (PCS) (P = 0.013) compared to patients receiving HD prior to transplantation (Table 6). After SPKT, PD-patients showed significantly better results in 5 of the 8 SF-36 domains: physical functioning (P = 0.02), bodily pain (P = 0.001), general health (P = 0.038), vitality (P = 0.014), role limitations emotional (P = 0.048) and PCS (P = 0.002) compared to HD-patients.

Table 6

SF-36 dimensions	Before SPKT			After SPKT		
	HD-group (n = 64)	PD-group (n = 19)	P-value	HD-group (n = 64)	PD-group (n = 19)	P-value
Physcial functioning (PF)	48.3 ± 13.3	63.8 ± 17.7	0.028	68.9 ± 8.9	81.3 ± 15.9	0.020
Role limitations- physical (PR)	38.3 ± 31.3	56.2 ± 43.8	0.267	60.7 ± 25.4	72.9 ± 19.8	0.190
Bodily Pain (BP)	44.2 ± 21.2	64.1 ± 17.6	0.034	71.1 ± 8.5	85.3 ± 9.8	0.001
General health (GH)	36.5 ± 16.1	48.8 ± 7.0	0.053	61.6 ± 7.5	67.9 ± 6.8	0.038
Social function (SF)	55.8 ± 17.6	68.8 ± 11.6	0.077	65.2 ± 12.2	73.9 ± 11.2	0.070
Vitality (VIT)	42.7 ± 11.2	48.8 ± 18.5	0.333	61.1 ± 7.4	67.9 ± 5.4	0.014
Role limitations-emotional (ER)	44.4 ± 29.9	66.7 ± 30.9	0.109	61.9 ± 28.8	83.3 ± 22.5	0.048
Mental Health (MH)	51.4 ± 16.4	49.5 ± 2.8	0.681	63.4 ± 5.8	62.3 ± 8.2	0.697
Physical Component Summary (PCS)	34.9 ± 5.8	43.1 ± 8.6	0.013	45.6 ± 4.6	50.8 ± 2.5	0.002
Mental Component Summary (MCS)	40.2 ± 6.6	41.6 ± 5.4	0.624	44.7 ± 4.5	46.8 ± 3.8	0.232

Impact of demographical and clinical variables

We separately analyzed the possible impact of three factors age, gender and graft loss on the HRQoL of the overall study population after SPKT (Table 7). Regarding patients age, there was a significant difference in physical functioning (P = 0.04) and role limitations (P = 0.03). In the univariate analysis patient's gender showed no influence on HRQoL after SPKT. Graft loss (kidney or pancreas) led to a significant decrease in all physical components (each P < 0.01) and mental health status (P = 0.01) of the SF-36.

Table 7

SF-36 dimensions	Age			Gender			Graft loss		
	< 45 years	> 45 years	P-value	Male	Female	P-value	Yes	No	P-value
Physcial functioning (PF)	80.1 ± 11.2	69.8 ± 14.3	0.04	77.8 ± 13.4	74.2 ± 14.3	0.499	86.8 ± 6.8	65.6 ± 10.3	< 0.01
Role limitations-physical (PR)	73.5 ± 20.6	61.1 ± 13.1	0.09	69.3 ± 17.6	67.6 ± 20.1	0.308	76.3 ± 15.1	45.8 ± 10.2	< 0.01
Bodily Pain (BP)	80.1 ± 11.7	72.2. ± 9.6	0.1	79.8 ± 12.3	76.1 ± 11.1	0.416	81.8 ± 8.9	67.9 ± 7.7	< 0.01
General health (GH)	67.9 ± 5.8	59.8 ± 7.6	< 0.01	63.1 ± 9.1	66.4 ± 5.2	0.276	82.8 ± 8.5	46.7 ± 5.8	< 0.01
Social function (SF)	72.1 ± 10.4	63.9 ± 14.6	0.11	68.2 ± 15.6	70.0 ± 10.4	0.719	73.9 ± 11.2	65.0 ± 12.1	0.08
Vitality (VIT)	66.2 ± 5.7	61.8 ± 9.2	0.15	67.3 ± 7.2	61.3 ± 6.7	0.047	66.4 ± 5.9	55.2 ± 5.1	0.06
Role limitations-emotional (ER)	82.1 ± 22.4	61.5 ± 23.7	0.03	68.9 ± 29.4	75.8 ± 21.6	0.545	80.1 ± 5.1	61.1 ± 20.3	0.09
Mental Health (MH)	63.3 ± 7.9	62.4 ± 5.6	0.66	63.7 ± 7.5	61.8 ± 6.3	0.498	65.1 ± 5.6	57.1 ± 1.3	0.01

Discussion

Post-transplant Outcome and Survival

Infectious complications remain a significant cause of morbidity and mortality after simultaneous pancreas-kidney transplantation (SPKT) [3, 4, 6, 18]. A much-debated question is whether pre-transplant peritoneal dialysis (PD) increases the risk for intraabdominal infections after transplantation due to risk of catheter associated peritonitis. Binaut et al. showed a higher rate of parietal sepsis in PD-patients after kidney transplantation alone (KTA), compared to patients who received HD prior to transplantation [19]. Martins et al. reported a significantly higher rate of pancreas loss due to infection among PD patients after SPKT (HD: 3.4% versus PD: 12.8%; P = 0.042), whereas 10 out of 39 (25.6%) PD patients had peritonitis in their past [20]. In contrast to that, other studies reported no difference in surgical outcome between HD and PD patients after SPKT [21–24]. Our analysis couldn't reveal significant differences in intraabdominal infection rates after SPKT between both groups. And there was no correlation between incidence of pre-transplant peritonitis and post-transplant intraabdominal infection. Besides

dialysis modality, incidence of intraabdominal infection after SPKT may be related to other factors, namely surgical technique (especially pancreas-anastomosis), the length of hospital stays and intensity of immunosuppression.

In the literature, there are reports about an increased graft loss in PD patients in comparison to HD patients post-transplant. After KTA an increased graft loss in PD patients is reported, mainly due to renal vascular thrombosis [25, 26]. In a study investigating outcomes after SPKT, Martins et al. reported a significantly higher rate of thrombosis-driven relaparotomy in PD patients compared to HD patients. Moreover, they recognized a near significant higher rate of renal graft loss due to thrombosis in PD patients compared to HD patients [20]. In our study, no correlations were found between pre-transplant dialysis modality and patient or graft survival. Only, rate of pancreas graft failure due to thrombosis was non-significantly higher in the PD group (HD: 4.7% versus PD: 15.8%, P = 0.1). But these data must be interpreted with caution, because other variables, like patient comorbidities (cardiovascular diseases, BMI), along with recipient age and time on dialysis might be additional factors with impact on the outcome and survival.

Health-Related Quality of Life (HRQoL)

Pre-transplant HRQoL

Most of the published studies evaluating dialysis patients waiting for KTA showing inconclusive results related to pre-transplant HRQoL and dialysis modality [27]. Previous publications used a broad range of measures to assess HRQoL and analyzed among patients with different demographic characteristics and medical history. Our findings indicate that PD is associated with a significant higher physical functioning and physical component summary before SPKT, in comparison to patients receiving HD as pre-transplant dialysis modality. And besides mental health, all other components of the SF-36 score were (although not significantly) higher in PD patients. A reason for better reported quality of life among PD patients may stem from the positive effect of medical self-management through PD. PD can be performed independently or with the help of a caregiver and develops a sense of personal control which correlates positively with features of HRQoL. In contrast, conventional HD is a stressful process and time spend on dialysis ward can contribute to a lower quality of life, as the number of hours in HD hinders professional and social functioning.

Post-transplant HRQoL

HRQoL of patients improved in both study groups after transplantation, which underlines therapeutic success of SPKT, besides medical outcome and objective clinical parameters. This is in line with most published studies show a significant improvement in patient reported general HRQoL after SPKT and better diabetes specific quality of life [4, 10–13].

Psychiatric disorders could influence poor evaluation of the quality of life among HD patients [28]. HD carries the risk of vascular dehydration and hypotension following cerebellar hypoperfusion and may lead to cognitive impairment and cardiovascular diseases [29–31]. Sapilak could reveal a strong negative correlation of HRQoL of HD patients with depression symptoms and anxiety [32]. In a study by Smith et al., evaluating 37 patients pre-transplant and four months after SPKT, approximately half of the patients showed an improvement of HRQoL, but one-third even experienced decreased HRQoL. They could show that preexisting psychiatric disorders at the time of transplant was the only significant predictor of decreased quality of life following pancreas transplantation [33]. In line with these reports, in our study rate of depression in patient history was significantly higher in the HD-group (P = 0.049). However, with a small sample size and missing details about psychosocial status and longitudinal periodic assessment of depression disease caution must be applied, as the findings might not be representative.

In the literature, the relative importance of patients' gender on HRQoL after transplantation is debated. In a study by Rajkumar et al., twelve months after transplantation (KTA or SPKT) most HRQoL scores (7 out of 8) were better for women than for men. Moreover, HRQoL scores of female recipients were not statistically different from the control group in the general population [12]. They postulated that differences in expectation and appreciation of improvements in health after transplantation, differences of the social network and emotional support may be an explanation for these findings. Other reports favored men and have shown that female gender is a negative predictive factor of HRQoL after SPKT [10, 33]. In a study by Martin et al., evaluating HRQoL in 60 male and 66 female SPKT patients, no lower scores for female patients were observed [11]. Different results in the literature may be explained by different follow-up periods, study populations and study designs/ questionnaires. In our analysis, number of female recipients was significant higher in the PD-group (P = 0.017), but we did not observe gender-based differences in the overall study population.

In the present study, we have shown that graft loss has a significant impact on HRQoL after SPKT, due to loss of independence from insulin therapy and freedom from dialysis. This is in line with previous publications, in which graft loss was associated with significant worsening of the HRQoL [4, 34, 35], and maintenance of two functioning grafts seems to be an independent predictor for higher post-transplant quality of life scores [11]. Furthermore, results from Sutherland et al. indicate that achieving insulin independence improves QOL more than becoming dialysis-free [4].

Limitations

There are some notable limitations of this study that should be mentioned, related to data source and study design. Main limitations of the study are its retrospective nature, the heterogenous group size and the fact that all data collection was done at one time make it difficult to evaluate the causality of the findings and associations. As such, there may be some amount of variation year to year with changes in the outcome and level of HRQoL. Secondly, not only disease or dialysis modality determine one's view of life quality, but many non-disease factors (work, education, other sociodemographic factors) play important additive role in the perception of HRQoL. Option for PD or HD normally depends on patient condition (comorbid situations, vascular and peritoneal conditions), patients' autonomy and convenience, as well as the health care system (dialysis-center factors).

Conclusions

Both dialysis modalities are generally associated with good outcomes and an improvement of HRQoL after SPKT. PD prior to SPKT seems to entail a slight advantage compared to HD before transplantation. Further prospective, controlled and randomized studies are needed in order to be able to evaluate sociodemographic factors with impact on the outcome and HRQoL.

Abbreviations

BMI	Body mass index
ESRD	End stage renal disease
HD	Hemodialysis

HRQoL	Health-related quality of life
KTA	Kidney Transplantation Alone
MMF	Mycophenolate mofetil
PD	Peritoneal dialysis
RRT	Renal replacement therapy
SD	Standard deviation
SF-36	Short Form 36
SPKT	Simultaneous pancreas-kidney transplantation

Declarations

Ethics approval and consent to participate

The study was approved by the local ethical commission board from the University of Leipzig (AZ EK: 111-16-14032016). Prior to the study, the patients were informed of the purpose of the research. Participants were assured of their right of refusal to participate or to withdraw from the study at any stage. The participants' names were removed from the data.

Consent for publication

Not applicable.

Availability of data and materials

Our database contains highly sensible data which may provide insight in clinical and personnel information about our patients and lead to identification of these patients. Therefore, according to organizational restrictions and regulations these data cannot be made publically available. However, the datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Author contributions

HMH and RS were responsible for the study conception and design; HMH, NJ, SR, ES and RS were responsible for data acquisition; HMH, SR; NJ, RS, US and DS analyzed and interpreted the data; US, HMH, SR and RS drafted the manuscript; and HMH, NJ, ES, DS, US and RS critically revised the manuscript. All authors read and approved the final manuscript.

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Figures

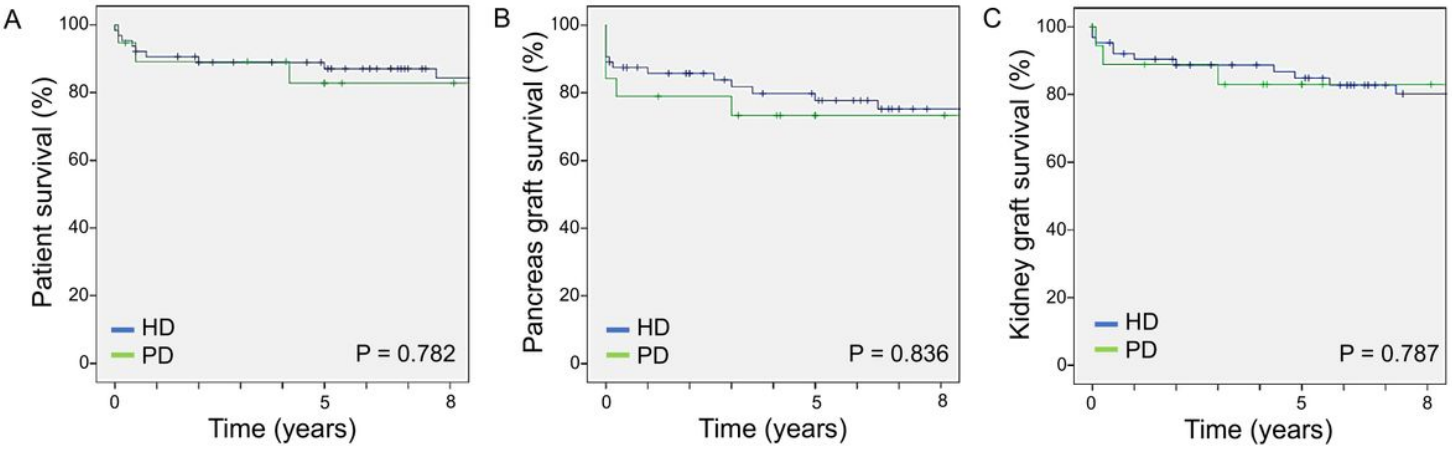

Figure 1

(A) Patient, (B) pancreas graft and (C) kidney graft survival after SPKT according to dialysis modality. HD, hemodialysis; PD, peritoneal dialysis.