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The Pretransplant Dialysis Modality is not Associated with Short-Term Surgical Complications after Kidney-Pancreas Transplantation

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Abstract

Background: Pancreas and kidney transplantation remains the best option for end-stage renal disease in type 1 diabetic patients. Although advances in surgical technique and immunosuppression have increased transplant outcomes, these patients are at high risk for surgical issues. The dialysis modality prior to transplant has been associated with surgical complications after grafting, but controversial results are found in the literature. Therefore, we aimed to evaluate whether the type of renal replacement therapy preceding the transplant was associated with early surgical complications.

Methods: We evaluated 194 recipients of all modalities of kidney and pancreas transplantation performed in our center. Clinical data, demographics, HLA mismatch, type of immunosuppressive therapy and dialysis vintage were recorded. Patients were classified according to the pre-transplant dialysis status (hemodialysis -HD-, peritoneal dialysis -PD- or pre-emptive transplantation) and analyzed as potential factors associated with surgical problems. Surgical complications registered across the first-year post-transplant were classified according to Clavien-Dindo classification.

Results: 92.3 % (n=179) were SPK and 7.7 % (n=16) were either PAK or KAP. The age of patients at the time of grafting was 38.6 ± 7.2 (mean ±SD) years and was similar between groups. A higher proportion of males were receiving Hemodialysis (HD) before transplantation. Dialysis vintage vas shorter for HD patients compared to PD. 43% of the patients did not show surgical issues. The most frequent surgical complications were bleeding (17%) and infections (16%). Grade III surgical complications were the most prevalent (i.e., need of surgical, endoscopic or radiological intervention, pharmacological treatment or blood transfusions). Patients on Peritoneal Dialysis (PD) showed a slightly higher percent of abdominal infections (21%) compared with HD (13%) or pre-emptive patients (17%), but statistically, no significant differences were found. The percentage of bleeding requiring reintervention was comparable between groups.

Conclusions: Although surgical complications after kidney and pancreas transplantation are prevalent, the type of pretransplant dialysis modality is not associated with a different rate or more severe surgical problems.

Introduction

Pancreas and kidney transplantation remain the best option of treatment for type 1 diabetic suffering end-stage Chronic Kidney Disease (CKD) [1,2]. Although patient and graft outcomes have significantly improved over the last years [3,4], surgical complications remain a significant risk factor for graft failure [4]. Many factors may be associated with early surgical complications after pancreas transplantation. Diabetes itself and its associated comorbidities in uremic patients, as well as the immunosuppressive therapy required for transplantation, may affect surgical outcomes in these patients [5]. However, diabetes duration disease before transplantation does not seem to have a definite influence in the development of early complications after transplantation [6,7]. Nonetheless, pancreas transplantation continue to be associated with a remarkable rate of surgical complications [8]. Diabetes has been associated with overall worse outcome in dialysis patients [9-13]. In this population, it remains controversial whether HD or PD are better techniques regarding patient survival [14,15]. However, it is clear that the time spent on the waiting list while receiving dialysis correlates with worse patient survival [16,17]. Concerning dialysis modality and pancreas transplant outcomes, some studies have shown that peritoneal dialysis may be associated with a higher risk of abdominal infections [18,19] and pancreatectomy [20] after pancreas transplantation. Nevertheless, other studies have failed to demonstrate such an association [21,22].

Therefore, we aimed to evaluate whether the modality of Renal Replacement Therapy (RRT) before pancreas and kidney transplantation had any influence on the rate of early surgical complications early grafting.

Patients and methods

We selected all patients that underwent pancreas and kidney transplantation in our center from January 2000 to December 2016. We gathered clinical data such as the type of RRT before transplantation and its duration (hemodialysis, HD; peritoneal dialysis, PD and preemptive transplantation). Complications were also recorded and contrasted in terms of different RRT and type of pancreas transplantation, either simultaneous (SPK) pancreas-kidney transplantation or sequential transplantation: Pancreas After Kidney (PAK) or Kidney after Pancreas (KAP). Complications were categorized according to whether they appeared early after grafting (0 to the second month) or late (2nd to 12th month). Complications were also classified according to Clavien-Dindo classification as described elsewhere [23].

In all cases, enteric duct drainage and systemic (cava) venous drainage was performed [24]. All patients received the same immunosuppressive regimen at the time of grafting, which included induction therapy (basiliximab in most cases) and corticosteroids, mycophenolic acid, and calcineurin inhibitors. Corticosteroids (Prednisone, 5 to 10 mg per day) were maintained as long-term therapy. Categorical variables were described using percentage and quantitative variables depending on if they followed a normal distribution (mean ± Standard Deviation [SD]) or not (median, interquartile range). Non-parametric data were analyzed by the Mann-Whitney U-test or Kruskal-Wallis test. For all tests, statistical significance was assumed at $P < 0.05$. Data were analyzed using SPSS Statistics software version 15.0 (SPSS, Inc., Chicago, Ill, United States) or the GraphPad Prism 6.0c (GraphPad Software, La Jolla, CA).

Results

Overall, one hundred and ninety-four transplants were performed along the study period. 92.3 % (n=179) were SPK and 7.7 % (n=16) were either PAK or KAP. Clinical characteristics of the patients included are described in (Table 1). Among all the patients included in the analysis, 63.4% (n=123) and 16.4% (n=32) received HD or PD respectively before transplantation. 20.1% (n=39) has received a preemptive transplantation.

Age of the patients at the time of grafting was similar between groups (p=0.24). There was a higher percentage of males received HD before grafting (Table 1). HLA mismatches and cold ischemia time for pancreas graft were comparable between groups. However, time on the waiting list was higher for those who received preemptive transplantation. The shorter time on the waiting list was for those receiving HD (p=0.02); (Table 1). However, time until transplantation was not associated with the risk of early surgical complications (p=0.83).

Variable	All	Preemptive	PD	HD	p
Gender (%, n)					
Male	74.7 (145)	16.6 (24)	15.2 (22)	68.3 (99)	
Female	25.3 (49)	30.6 (15)	20.4 (10)	49.0 (24)	0.04
Age	38.6 ± 7.2	39.8 ± 7.4	40.2 ± 7.5	37.9 ± 7.0	0.24
Type of graft					
SPK	92.3 (179)	19.6 (35)	16.8 (30)	63.7 (123)	0.78
PAK	3.1 (6)	0	0	100 (6)	0.16
KAP	5.2 (10)	40.0 (4)	20.0 (2)	40.0 (4)	0.21
HLA mismatch (0-6)	3.8 ± 2.0	3.9 ± 2.1	3.8 ± 2.0	3.8 ± 1.9	0.84
Cold ischemia time (hours)	11.7 ± 3.4	12.3 ± 2.2	12.2 ± 5.3	11.4 ± 3.0	0.34
Time on waiting list (months)	14.5 (7.9-24.2)	19 (11.9-45.0)	17.1 (10.3-29.0)	12.5 (7.2-22.9)	0.02

Table 1: Demographics and clinical features of patients included in the analysis.

(Figure 1) summarizes the most common type of complications observed after SPK. Nearly half of the patients did not display any surgical complication. Among those that showed any complication, bleeding and abdominal infection were the most common with a 17 and 16% respectively. 92.7% of the complications raised within the first sixty days following grafting, and again, they were comparable between groups (p=0.37).

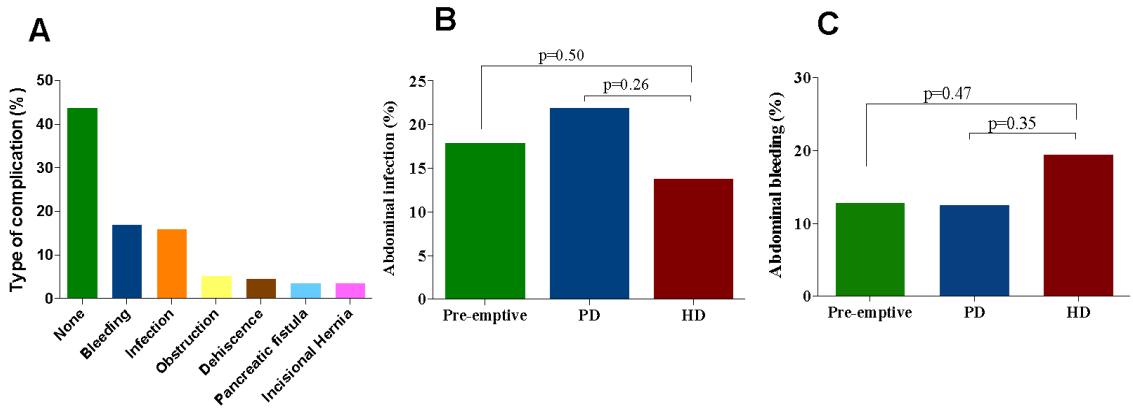

Figure 1: Surgical complications after transplantation. A) Overall rate and type of complications after pancreas-kidney transplantation. B) Abdominal infection according to RRT before transplantation. C) Bleeding (requiring a blood transfusion) according to RRT before transplantation.

The distribution of complications following Clavien-Dindo classification and according to RRT type is shown in (Table 2). In general, most patients showed a grade III complication (27.3%) followed by grade II complications (17.5%), meaning that most of the complications required surgical, endoscopic or radiological intervention, pharmacological treatment or blood transfusions. More severe (grade IV, V) complications were less frequent (overall 8.2%).

Grade	All	Preemptive	PD	HD
I (%, n)	3.1 (6)	2.6 (1)	0 (0)	4.1 (5)
II (%, n)	17.5 (34)	20.5 (8)	28.1 (9)	12.8 (17)
III (%, n)	27.3 (53)	33.3 (13)	21.9 (7)	26.8 (33)
IV (%, n)	6.7 (13)	2.6 (1)	12.5 (4)	6.5 (8)
V (%, n)	1.5 (3)	1.6 (2)	3.1 (1)	0 (0)

Table 2: Distribution of complications according to Clavien-Dindo classification and RRT type.

Irrespective of the kind of RRT before pancreas-kidney transplantation, the rate of complications was comparable among groups (p=0.92). Indeed, although those receiving preemptive transplantation showed the higher percent of grade III complications compared to other groups, these results did not reach statistical difference. PD patients displayed a higher proportion of grade II complications although proportions among groups were also comparable (p=n.s.).

Regarding the most common type of complications, both abdominal infections (p=0.50), as well as bleeding, were comparable between groups (p=0.47).

Finally, among those requiring reintervention, 39 of 65 (60%) of patients from HD group underwent a reintervention, whereas 12 of 21 (57.1%) and 10 of 23 (43.5%) did so on both PD and preemptive groups respectively (p=0.38).

Discussion

The present study aimed to evaluate whether the type of RRT before transplantation was associated with a higher rate of early surgical complications. We show that the rate of complications was comparable between patients coming from HD or PD or received preemptive transplantation. Furthermore, although bleeding and infection were the most common type of complications after grafting, the percent of subjects in each group presenting these issues was similar among groups.

Outcomes of pancreas transplantation have improved over the last years [4,25,26]. However, early surgical complications following pancreatic transplantation remain on great concern because of the higher risk of pancreatic graft failure [4]. Thus, the identification of any risk factor that may contribute to graft survival is needful. Although many risk factors have been demonstrated to affect long-term pancreas graft survival, little is known about the influence of the dialysis modality before transplantation on grafts outcome; furthermore, the available previous studies in this topic showed controversial results [4,19].

Our study demonstrates that early surgical complications after pancreas transplantation are not associated with the modality of RRT before transplantation. Indeed, the rate of complications between the different groups (HD, DP or preemptive transplantation) was similar. Other studies comparing the outcomes of patients after SPK [27] or isolated kidney transplantation concerning RRT before transplantation are in line with our results [28,29].

The abdominal infection has been shown to be one of the most common problems after this surgical procedure [4,18,19]. The rate of abdominal infections in our study rounded 16%, and half of them required reintervention. The infection complication could be justified by the immunological impairment of the DM [12], the effect of the uremia on T cells [10,30] and the high burden of immunosuppressive therapy used in the peri-operatory period. In our center, all patients receive induction therapy with either an anti-CD25 or thymoglobulin, all of which may worsen immunological responses from patients. The leak of intestine sutures may be another factor associated with infection and mostly ever requires reintervention [26]. All of these factors are presented in our study population. However, we have not found differences in the infectious complications rate associated with the type of RRT before transplantation.

Another important complication in our study was bleeding, and in this case, all patients underwent a reintervention. Many factors may contribute to this issue. Although uremia is associated with platelet dysfunction [31], bleeding related to the surgery itself is probably the leading cause of bleeding. Again, we did not find any difference in the rate of bleeding complications among RRT groups before transplantation.

Time of follow-up before transplantation was different between groups, being shorter in patients receiving HD. Time on dialysis is associated with worse outcomes after kidney transplantation [16,17]. In our hospital, dialysis patients in waiting list have priority over those with end-stage renal disease not yet on dialysis. That could justify the lower waiting time of patients on HD in our study. However, it is preferable to perform the kidney-pancreas transplantation before starting dialysis as this modality gives the best outcomes. In our study, patients from the HD group seemed to have lower time on waiting list, but their outcomes were not different when compared to patients on PD or preemptive transplantation.

The rate of complications requiring reintervention rounded 30%. It is similar to the data reported in other studies [25]. Moreover, after classifying those complications according to Clavien-Dindo classification, there were no differences between dialysis categories.

Our study has some limitations. First, as enteric-drained or bladder-drained have changed over time and it has been demonstrated that bladder-drained showed a higher rate of long-term complications, we did not access this issue. However, after the year 2000, all pancreas transplants performed at our center

were made with enteric duct drainage technique. Thus, it may not have influenced the results. Second, bloodstream infections were not included as complications as they may have multiple origins either from donor or recipient himself. Finally, the rate of rejections was neither evaluated. Intensification of immunosuppressive medications is mandatory to treat rejection episodes; therefore, a higher risk for infections is expected. However, most of the abdominal infections observed in the short-term in our patients were related to the surgery.

In conclusion, although bleeding and abdominal infections remain significant complications after pancreatic and kidney transplantation, the modality of renal replacement therapy before transplantation is not associated with the risk of developing higher early surgical complications.

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