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Simultaneous pancreas-kidney transplantation and the impact of postoperative complications on hospitalization cost.

Impacto das complicações pós-transplante simultâneo pâncreas-rim sobre o custo da internação hospitalar.

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A B S T R A C T

Objective: considering simultaneous pancreas-kidney transplantation cases, to evaluate the financial impact of postoperative complications on hospitalization cost. **Methods:** a retrospective study of hospitalization data from patients consecutively submitted to simultaneous pancreas-kidney transplantation (SPKT), from January 2008 to December 2014, at Kidney Hospital/Oswaldo Ramos Foundation (Sao Paulo, Brazil). The main studied variables were reoperation, graft pancreatectomy, death, postoperative complications (surgical, infectious, clinical, and immunological ones), and hospitalization financial data for transplantation. **Results:** the sample was composed of 179 transplanted patients. The characteristics of donors and recipients were similar in patients with and without complications. In data analysis, 58.7% of the patients presented some postoperative complication, 21.8% required reoperation, 12.3% demanded graft pancreatectomy, and 8.4% died. The need for reoperation or graft pancreatectomy increased hospitalization cost by 53.3% and 78.57%, respectively. The presence of postoperative complications significantly increased hospitalization cost. However, the presence of death, internal hernia, acute myocardial infarction, stroke, and pancreatic graft dysfunction did not present statistical significance in hospitalization cost (in average US$ 18,516.02). **Conclusion:** considering patients who underwent SPKT, postoperative complications, reoperation, and graft pancreatectomy, as well as surgical, infectious, clinical, and immunological complications, significantly increased the mean cost of hospitalization. However, death, internal hernia, acute myocardial infarction, stroke, and pancreatic graft dysfunction did not statistically interfere in hospitalization cost.

Keywords: Transplants. Pancreas Transplantation. Postoperative Complications. Economics, Medical. Costs and Cost Analysis. Hospitalization.

INTRODUCTION

Simultaneous pancreas-kidney transplantation (SPKT) is the main procedure performed for pancreas transplantation[1]. It is mainly indicated for diabetic patients with terminal chronic kidney disease (CKDT)[2]. SPKT assures normal levels of glycemia and glycosylated hemoglobin (HbA1c), allows dietary freedom and exogenous insulin independence, and prevents chronic complications related to diabetes[3]. However, SPKT has a significant incidence of complications. In more than 100 simultaneous transplantations, Campos Hernández *et al*.[4] have described 65.5% of cases with postoperative complications. Banga *et al*.[5] have reported 23% of surgical complications in almost 200 SPKT cases. Morbidity experienced in SPKT is one of the largest among abdominal visceral transplantations.

The emergence and incorporation of new technologies in patient care, associated to the management of limited and finite resources for health financing, have aroused the interest of analytical studies concerning surgical patients' care cost. Some studies have shown that the presence of postoperative complications have increased the care cost in oncological, hepatic, pancreatic, and bariatric surgeries, as well as in liver transplantation (LT)[6-11]. However, the relationship of postoperative complications in SPKT with hospitalization cost has only been studied in literature by two groups and in a limited way[12-14]. Therefore, the financial viability of

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SPKT with complications is questionable and literature is unclear on what types of complications actually impact SPKT patients' hospitalization cost.

The objective of this study is to compare hospitalization costs for SPKT with and without complications, as well as the different types of complications. We also detail hospitalization costs according to the presence of complication, type of complication, reoperation, and graft pancreatectomy.

METHODS

This study was approved by the Ethics and Research Committee of Federal University of Sao Paulo and by the Education and Research Center of Kidney Hospital/Oswaldo Ramos Foundation, Sao Paulo, Brazil (Protocol # 756.950/14). We studied hospitalization clinical and financial data from patients consecutively submitted to SPKT, from January 1st, 2008 to December 31st, 2014, at Kidney Hospital/Oswaldo Ramos Foundation. Inclusion criteria were primary SPKT, with systemic endocrine drainage and exocrine drainage, performed from January 2008 to December 2014. Exclusion criteria were the performance of another modality of pancreas transplantation, incomplete or unavailable clinical and/or financial data, retransplantation, and SPKT with portal-endocrine drainage and/or urinary exocrine drainage.

Initial immunosuppression for SPKT included tacrolimus, prednisone, and mycophenolate sodium in all cases. Intraoperative induction was performed with methylprednisolone and basiliximab. Thymoglobulin was used as an induction therapy in patients with a panel-reactive antibody (PRA) test greater than 30%. Preferably, the pancreas was implanted first (PBK) and into the right iliac fossa. Endocrine pancreatic drainage was performed for the iliac vessels or inferior vena cava (IVC), and exocrine pancreatic drainage was performed for the terminal ileum.

Patients' clinical data were obtained through the documentary and electronic database of Kidney Hospital/Oswaldo Ramos Foundation, as well as through the written records of patients' hospitalization and the donation forms of the transplant center.

Postoperative complications in the recipient were divided into four groups: surgical, infectious, clinical, and immunological. The analysis was limited to complications diagnosed during hospitalization for SPKT.

The raw financial data were provided by the management and information technology team of Kidney Hospital/Oswaldo Ramos Foundation and obtained through Philips Tasy Electronic Medical Record (USA). These individual pieces of information from each patient presented the supply, service, or environment utilized by the patients, their unit cost, and the number of times or the period of use. All data were grouped, summed up, and subdivided into five categories of expenditures: supplies, medical fees, surgical center, intensive care unit (ICU), and ward. After summing up the five categories, a percentage of administrative expenses was added, comprising all indirect costs related to the patient who underwent SPKT. The value was also adjusted according to the National Broad Consumer Price Index (IPCA, in Portuguese) of the Brazilian Institute of Geography and Statistics (IBGE) and corrected monthly. Subsequently, the resulting product was converted into dollars. The sum, subdivision into categories, corrections for administrative expenditures and inflation, and conversion into dollars were performed by a specialist in the field of Health Economics and Management.

We employed Mann-Whitney U test, for the inferential analysis performed in the association between quantitative and qualitative variables. Pearson's chi-square test was performed in the association between

categorical variables. Kruskal-Wallis test was used for multiple comparisons between cost and different types of complications. An alpha significance level of 5% (p=0.05) was used in all the conclusions obtained through the inferential analysis. Statistical analyzes were performed with the statistical software R 3.3.2 (R Core Team, United States, 2016).

RESULTS

The sample consisted of 179 SPKT patients. Demographic characteristics of recipients and donors, as well as the implant characteristics, are described in tables 1 and 2. Comparing patients with and without postoperative complications, the samples are similar, except on recipients' hospitalization, ICU, and ward days, and sodium levels of donors.

Table 1. *Recipients' characteristics.*

Recipients	Complications		p
	Yes	No	
Gender			0.704
Male	58 (57.4%)	43 (60.3%)	
Female	47 (42.6%)	31 (39.7%)	
Age (years)	36.3±7.4	34.8±6.1	0.169
Hospitalization days	22.2±17.5	8.9±2.6	0.0001
ICU days	15±12.4	6±2.9	0.0001
Ward days	22.3±17.4	8.9±2.6	0.0001
First organ transplanted			
Pancreas	54 (51.4%)	43 (58.1%)	0.377
Kidney	51 (48.6%)	31 (41.9%)	

Table 2. *Donors' characteristics.*

Donors	Complications		p
	Yes	No	
Gender			0.722
Male	68 (59.6%)	46 (40.4%)	
Female	37 (56.9%)	28 (43.1%)	
Age (years)	28.7±8.3	28.5±8.8	0.942
BMI*(kg/m^2)	24.2±2.5	24.3±2.6	0.809
PCR**			0.808
Yes	17 (56.7%)	13 (43.3%)	
No	88 (59.1%)	61 (40.9%)	
Use of vasoactive drug			0.258
Yes	94 (60.3%)	62 (39.7%)	
No	11 (47.8%)	12 (52.2%)	
Amylase (U/L)	126±185	138±147	0.112
Glycemia (mg/dL)	152±65	153±66	0.999
Sodium (mmol/L)	159±12	155±14	0.04
Pancreas cold ischemia time (minutes)	855.1±151.8	853±153.2	0.811

**BMI: body mass index; **CA: cardiac arrest.*

In this study, 105 patients (58.7%) had some postoperative complications, 39 patients (21.8%) required reoperation, 22 patients (12.3%) needed graft pancreatectomy, and 15 patients (8.4%) evolved to death during hospitalization. The most common postoperative complication was the immunological one (32.4%).

The average hospitalization cost of a SPKT patient was US$ 18,516.02 ± 11,448.37. Regarding the cost components, the expense associated with supplies presented the largest portion of the total value (US$ 6,523.89 ± 4,507.91) and the expense associated with the surgical center presented the lowest portion of the total value (US$ 1,413.25 ± 796.14). Table 3 shows the relationship of reoperation cost, graft pancreatectomy, and recipient's death. Table 4 presents the relationship of cost with the most frequent surgical, infectious, clinical, and immunological complications.

Table 3. *Summary measures of SPKT patients' hospitalization costs, according to reoperation, graft pancreatectomy, and death.*

Variables	SPKT patients' hospitalization cost (US$)		p
	Average	Standard deviation	
Reoperation			
Yes	25.432	13.106	<0.001
No	16.589	10.184	
Graft pancreatectomy			
Yes	30.152	15.049	<0.001
No	16.885	9.863	
Death			
Yes	25.323	14.440	0.061
No	17.893	10.980	

Table 4. *Summary measures of SPKT patients' hospitalization costs, according to the most frequent postoperative complications.*

Variables	SPKT patients' hospitalization cost (US$)		p
	Average	Standard deviation	
Postoperative complication			
Yes	21.831	13.839	<0.001
No	13.811	2.907	
Surgical complication			
No	16.513	10.439	<0.001
Peripancreatic bleeding	21.247	7.168	
Graft vascular thrombosis	26.558	16.644	
Infectious complication			
No	15.900	6.363	<0.001
Urinary tract infection	29.582	28.857	
Abdominal abscess	30.017	13.866	
Clinical complication			
No	17.656	8.205	0.019
AMI*	18.847	6.935	
DVT**	32.078	4.080	
Immunological complication			
No	17.145	8.636	<0.001
DGF***	18.964	6.772	
Acute kidney rejection	24.102	11.067	

** AMI: acute myocardial infarction; ** DVT: deep vein thrombosis; *** DGF: delayed renal graft function.*

In the multivariate analysis of postoperative complications and hospitalization cost, the presence of internal hernia, acute myocardial infarction, stroke, and pancreatic graft dysfunction did not statistically interfere in SPKT patient's hospitalization cost (Table 5). In Brazil's public health system, the average hospitalization cost of a SPKT patient was US$ 20,594.16, regardless of the presence or absence of complications.

Table 5. *Results of multiple comparisons among different types of postoperative complications.*

	Cost analysis of SPKT	p
Surgical complication	without complication < peripancreatic bleeding	<0.001
	without complication < graft pancreatitis	0.001
	without complication < graft vascular thrombosis	0.013
	without complication < urinary fistula	0.035
	without complication < enteric fistula	0.005
	without complication = internal hernia	0.386
Infectious complication	without complication < surgical wound infection	0.007
	without complication < pneumonia	0.001
	without complication < abdominal abscess	<0.001
	without complication < fungal infection	0.001
	without complication < urinary tract infection	<0.001
	without complication < viral infection	0.004
Clinical complication	without complication = AMI*	0.610
	without complication < DVT**	0.009
	without complication = stroke	0,075
	without complication = AMI	0.610
Immunological complication	without complication < DGF#	0.001
	without complication = pancreatic graft dysfunction	0.443
	without complication < acute pancreas rejection	0.025
	without complication < acute kidney rejection	0.006

** AMI: acute myocardial infarction; ** DVT: deep vein thrombosis; # DGF: delayed renal graft function.*

DISCUSSION

The sample of this study was represented by 179 patients submitted to SPKT. In the same study period, 825 patients underwent SPKT in Brazil. Our sample corresponded to 21.69% of the national cases. The presence or absence of postoperative complication did not show statistical difference regarding the demographic characteristics of donors and recipients, forming two similar and comparable groups for possible outcomes.

In this study, 105 patients (58.7%) had some type of postoperative complication. In the whole sample, the most common surgical complications were peripancreatic bleeding (7.3%) and graft vascular thrombosis (6.7%). During hospitalization after SPKT, 39 patients (21.8%) required reoperation, 22 patients (12.3%) needed graft pancreatectomy, and 15 patients (8.4%) evolved to death. In samples with more than 100 simultaneous transplantations, Campos Hernández *et al*.[4] and Jiménez-Romero *et al*.[15] have described more than 60% of cases with postoperative complications.

Considering postoperative complications, the results of our sample were similar to literature concerning larger groups of transplanted patients[4,15-18].

The results of this research sample showed that the presence of reoperation, graft pancreatectomy, and postoperative complications increased the hospitalization cost of SPKT (p<0.001). However, there was no statistical difference in relation to death during hospitalization (p=0.061). Up to now, there are only three papers in world literature that associate postoperative complications with hospitalization cost after SPKT[12-14]. Gruessner *et al*.[12] and Troppmann *et al*.[13] have published a same series of patients and demonstrated an increase of 66.17% in the cost of transplanted patients who have undergone reoperation after SPKT. Cohn *et al*.[14] have reported that, in SPKT patients with some postoperative surgical complication, hospitalization cost has increased by 27%.

The results of our sample showed that, in the presence of reoperation, graft pancreatectomy, and postoperative complication, the total hospitalization cost of SPKT increased by 53.3%, 78.57%, and 58%, respectively. Death was one of the few variables that were not related to the increase of hospitalization value of SPKT. Results showed that recipients who evolved to death had an average hospitalization of 18.27 days and ICU stay of 5.4 days (21.89% and 179%, respectively, lower than recipients with any other type of complication). Therefore, we conclude that death does not increase the total hospitalization cost of SPKT patients, because it reduces the length of hospital stay and ICU days and the consumption of supplies. However, death is also related to indirect costs, that is, productivity loss of patients in the labor market and, therefore, this fact implies an inestimable financial loss for society. This study ratified results previously presented in literature, and, above all, it added value because of its suitable methodology from the sampling and financial point of view.

In this study, when we estimated the mean income of a SPKT and the mean expenditure of patients with and without complications, SPKT represented a profit of US$ 6,782.66 in patients without postoperative complication. However, in patients who had some postoperative complication, SPKT represented a deficit of US$ 1,237.44. Therefore, an uncomplicated transplant was needed to pay for five complicating transplants.

We also studied the relationship among different types of postoperative complications and SPKT patient's hospitalization cost. The presence of surgical (p<0.001), infectious (p<0.001), clinical (p=0.019), and immunological (p<0.001) postoperative complications increased hospitalization cost of SPKT patients. However, in the multiple comparisons of each type of complication, the presence of internal hernia, acute myocardial infarction, stroke, and pancreatic graft dysfunction did not interfere in the total hospitalization cost of SPKT. There are no other papers in literature that associate the type of postoperative complication with SPKT patient's hospitalization cost. This research is an unpublished study that demonstrates what types of postoperative complications actually increase SPKT patient's hospitalization value. Interpreting results, we believe that the correction of an internal hernia without ischemia or intestinal necrosis does not significantly increase the length of hospital stay, nor does the need for insulin at the time of hospital discharge interfere in SPKT patients' hospitalization cost. However, cardiovascular complications, such as acute myocardial infarction and stroke, are related to death during hospitalization and, consequently, to a shorter hospital stay.

This research presents different relationships between postoperative complications and hospitalization cost considering SPKT patients. Its relevance is related to its sample size, manual and meticulous collection of financial data, and economic corrections caused by administrative expenditures and monthly inflation. Its weakness is associated with the period of data collection, which is restricted to the hospital stay period caused by SPKT. We think that the ideal would be a period of three months to a year, because the pancreas-kidney transplant patient, after hospital discharge, presents several episodes of new hospitalizations due to complications, and these new hospitalizations also have an impact on the financial value of this SPKT patient. However, post-hospitalization data collection is not feasible in our system and the financial data from these services are not available.

Therefore, we conclude that postoperative complications (surgical, infectious, clinical, and immunological ones), reoperation, and graft pancreatectomy significantly increase the mean cost of SPKT patient's hospitalization. However, the presence of death, internal hernia, acute myocardial infarction, stroke, and pancreatic graft dysfunction during hospitalization do not statistically interfere in this cost. Cost-benefit, cost-utility, and cost-effectiveness studies are essential for fund management and to answer questions about how society's resources can be best allocated among different health programs.

R E S U M O

Objetivo: *avaliar o impacto financeiro das complicações pós-operatórias no transplante simultâneo pâncreas-rim durante a internação hospitalar.* **Métodos:** *estudo retrospectivo dos dados da internação hospitalar dos pacientes submetidos consecutivamente ao transplante simultâneo pâncreas-rim no período de janeiro de 2008 a dezembro de 2014 no Hospital do Rim/Fundação Oswaldo Ramos. As principais variáveis estudadas foram a reoperação, pancreatectomia do enxerto, óbito, complicações pós-operatórias (cirúrgicas, infecciosas, clínicas e imunológicas) e os dados financeiros da internação para o transplante.* **Resultados:** *a amostra foi composta de 179 pacientes transplantados. As características dos doadores e receptores foram semelhantes nos pacientes com e sem complicações. Na análise dos dados, 58,7% dos pacientes apresentaram alguma complicação pós-operatória, 21,8% necessitaram de reoperação, 12,3%, de pancreatectomia do enxerto e 8,4% evoluíram para o óbito. A necessidade de reoperação ou pancreatectomia do enxerto aumentou o custo da internação em 53,3% e 78,57%, respectivamente. A presença de complicação pós-operatória aumentou significativamente o custo. Entretanto, a presença de óbito, hérnia interna, infarto agudo do miocárdio, acidente vascular cerebral e disfunção do enxerto pancreático não apresentaram significância estatística no custo, cuja média foi de US$ 18,516.02.* **Conclusão:** *complicações pós-operatórias, reoperação e pancreatectomia do enxerto aumentaram significativamente o custo médio da internação hospitalar do SPK, assim como as complicações cirúrgicas, infecciosas, clínicas e imunológicas. No entanto, o óbito durante a internação, a hérnia interna, o infarto agudo do miocárdio, o acidente vascular cerebral e a disfunção do enxerto pancreático não interferiram estatisticamente neste custo.*

Descritores: *Transplantes. Transplante de Pâncreas. Complicações Pós-Operatórias. Economia Médica. Custos e Análise de Custo. Hospitalização.*

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