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Research Article

Preservation Fluid Cultures In Simultaneous Pancreas And Kidney Transplantation: 20 Years Of Experience.

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Short title: Preservation Fluid Cultures in SPK Transplantation

Abstract

Simultaneous pancreatic and kidney transplantation (SPK) improves survival and quality of life in patients with type 1 and 2 diabetes mellitus with renal failure. However, postoperative infections remain the main cause of morbidity and mortality, and the role of preservation fluid (PF) as a potential vector for microorganisms is not completely defined. There is limited evidence on the clinical relevance of positive cultures of PF in SPK.
Objective: Evaluate the incidence and clinical relevance of microbial contamination of PF in SPK with complications.
Materials and methods: A retrospective study of 163 patients submitted to SPK was conducted. Microbiological PF cultures were analyzed, classifying the isolates as pathogens or contaminants. The association between positive cultures and postoperative complications was evaluated by multivariate statistical analysis.
Results: 35% of the PFs were positive, with 24% pathogenic isolations. No evaluation was found between positive cultures and infectious complications (p=0.49), pancreatic (p=0.58) or renal (p=0.16). There was no impact on hospital stay (p=0.54) or on the rejection rate of Graff.
Conclusion: Despite the detection of microorganisms in the PF, there is no evidence of clinical impact on postoperative results. This is the first large-scale SPK study to our knowledge that questions the need to modify current antibiotic management protocols. Prospective studies are needed to define whether the identification of pathogens in PF justifies changes in therapy.

Keywords: organ preservation solutions; culture techniques; pancreas transplantation; kidney transplantation..

INTRODUCTION

Simultaneous Pancreas and Kidney Transplantation (SPK) has become the treatment of choice to improve overall well-being and life expectancy in selected patients with type 1 and type 2 diabetes with associated comorbidities, particularly chronic kidney disease[1].

Due to the need for immunosuppressive therapy to prevent graft rejection after transplantation, infections represent the leading cause of morbidity and mortality, particularly during the first postoperative month. Infections during this period typically originate from the donor, the recipient, or surgical complications[2,3].

Preservation fluids (PF) used during organ procurement lack antimicrobial agents and can thus support microbial proliferation, potentially acting as a direct pathway for infection to the recipient colonizing them at any stage of their handling or manipulation[4,5]. This fluid plays a crucial role in preserving the functional and anatomical integrity of pancreatic and renal cells until reperfusion during the implantation surgery[6]. Despite the advancements achieved in recent years, unexpected contamination may still occur and, according to previous reports on solid organ transplants, it could lead to clinical repercussions in recipients[7].

Previous research on the clinical implications of contamination or the presence of pathogenic microorganisms in preservation fluid is limited. Most studies either focus on solid organ transplantation as a whole or specifically on liver

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transplantation, as we have recently reported. However, data regarding SPK remain scarce, even nonexistent, to the best of our knowledge.

The aim of the present study is to analyze the preservation fluid cultures, identify the isolated microorganisms, and evaluate their relationship with postoperative complications in SPK transplantation, particularly infections.

MATERIAL Y MÉTHODS

A retrospective study based on prospective data was conducted, analyzing the preservation fluid cultures from pancreas-kidney transplants performed between November 2003 and December 2024, correlating the results with postoperative complications.

All patients who underwent pancreas-kidney transplantation with preservation fluid cultures performed during the specified time period were included, provided that proper documentation was available in their medical records. Cases of isolated pancreas transplantation were excluded from the analysis.

Preservation fluid samples were submitted for specialized microbiological analysis at the end of the back table procedure to culture for aerobic and anaerobic bacteria, as well as fungi. We considered the development of 10^5 CFU of microorganisms in the samples as positive, and negative when no microbial growth was observed after 5 days for bacteria and 42 days for fungi. The isolation of methicillin-sensitive Staphylococcus, coagulase-negative Staphylococcus, polymicrobial flora, Corynebacterium, and Streptococcus viridans was considered contamination. In contrast, the isolation of Staphylococcus aureus, methicillin-resistant Staphylococcus aureus (MRSA), Streptococcus pyogenes, enterobacteria, enterococci, aerobic bacilli, aerobic gram-negative bacteria (such as Pseudomonas aeruginosa), and any fungal growth was classified as pathogenic.

Broad-spectrum prophylaxis with 3 g of intravenous ampicillin-sulbactam was routinely administered to all patients 30 minutes before the skin incision and continued four times daily for 48 hours post-surgery. In cases of positive preservation fluid cultures or other donor cultures (such as blood cultures or any other tissue or fluid considered potentially infected), antibiotic therapy was initiated in all cases according to the corresponding antibiogram, except for preservation fluid cultures classified as contamination. In cases without evidence of infection, prophylaxis was routinely and protocolary discontinued.

Routine cultures were not performed on recipients during their hospital stay and were reserved only for those presenting with clinical signs of infection, such as fever (axillary temperature ≥ 38°C) or hypothermia (axillary temperature ≤ 36°C), combined with any other signs or symptoms of infection, including tachypnea (> 20 breaths per minute), pCO_2 > 32 mmHg, tachycardia (> 90 bpm), leukocytosis (> 12,000 WBC/ml), leukopenia (< 4,000 cells/ml), or more than 10% of immature neutrophils.

The percentage of positive PF cultures was determined, and each case was categorized by frequency of occurrence. We defined 'direct correlation' as the identification of the same microorganism, with an identical antimicrobial susceptibility and resistance profile according to the antibiogram, in both the PF and any recipient culture.

The demographic variables analyzed included age, sex, body mass index (BMI), type of diabetes, years since diabetes diagnosis, glycated hemoglobin at the time of transplantation, and type of dialysis (no dialysis, hemodialysis, or peritoneal dialysis). Preservation fluid (PF) cultures were classified as negative, positive, or contaminated. The isolated microorganisms were grouped in order of frequency.

Postoperative complications were classified into infectious, pancreatic, and renal categories, with each group organized by frequency of occurrence. Only complications deemed major (>Grade 3a) based on the Clavien-Dindo classification were included in the analysis.

The data were collected using a Microsoft Excel spreadsheet specifically designed for this purpose. For descriptive statistics, absolute and relative frequencies were calculated for qualitative variables, while means and standard deviations were estimated for quantitative variables. To examine the relationship between qualitative variables, Pearson's Chi-Square test was used when applicable, and Fisher's Exact Test was employed for small sample sizes. For the analysis of quantitative variables, Student's t-test or the Mann-Whitney U test was used as appropriate, and ANOVA was applied for the analysis of three groups (contamination, pathogens, or negative). In all cases, multivariate analysis was performed using binary logistic regression. Statistical analysis was conducted using SPSS version 25, with a significance level of 0.05 applied in all cases.

RESULTS

During the study period, 172 transplants were performed, of which 163 patients met the inclusion criteria, while 9 cases involving isolated pancreas transplants were excluded.

No evidence of a 'direct correlation' was found between the preservation fluid culture and any recipient culture.

The median age was 35.5 years, with an interquartile range (IQR) of 31 to 44 years. Of the participants, 67 (41%) were female and 96 (59%) were male. In terms of body mass index (BMI), the weight distribution was as follows: 6% (n=10) of participants were classified as underweight, 63% (n=103) as normal weight, 26% (n=42) as overweight, and 5% (n=8) as obese, with obesity defined as a BMI greater than 30.

Table 1 provides a comprehensive summary of the demographic data, including variables such as diabetes type, duration of the disease, dialysis modality, and other relevant factors.

Table 1. Demographic variables.

Variables.	**n=163**
Age – median (IQR)	35,5 (31-44)
Gender	n (%)
Female	67 (41)
Male	96 (59)
Weight Status	n (%)
Underweight	10 (6)
Normal weight	103 (63)
Overweight	42 (26)
Obesity	8 (5)
Type of Diabetes	n (%)
Type 1	140 (86)
Type 2	23 (14)
Duration of Diabetes – median (IQR)	21 (17-26)
Glycated Hemoglobin – median (IQR)	8,3 (7,2-9,2)
Type of Dialysis	n (%)
CAPD	13 (8)
HD	135 (83)
None	15 (9)

**IQR: Interquartile range; CAPD: Continuous ambulatory peritoneal dialysis; HD: Hemodialysis.*

Microorganisms were isolated in 35% (n=57) of the preservation fluid cultures. Of these, 68,4% (n=39) were positive, 31,6% (n=18) were contaminated, and 65% (n=106) were negative. The pathogenic microorganisms identified are listed in order of frequency in **Table 2**.

Table 2. Pathogen Isolates in Positive CSF Cultures.

INSOLUTION.	**n (%)**
Polymicrobial Flora.	10 (18)
Methicillin-Resistant Staphylococcus Aureus (MRSA).	9 (16)
Methicillin-Sensitive Staphylococcus.	7(12)
Staphylococcus Aureus.	7 (12)
Streptococcus Pyogenes.	7 (12)
Enterococcus.	6 (10.5)
Aerobic Gram-Negative Bacteria.	6 (10.5)
Aerobic Bacilli.	4 (7)
Staphylococcus Epidermidis.	1 (2)

**MRSA: Methicillin-Resistant Staphylococcus Aureus.*

No statistically significant associations were identified between positive or negative preservation fluid cultures and recipient outcomes regarding postoperative infectious complications, including urinary tract infections (p=0.613), pneumonia (p=0.532), and surgical site infections (p=0.49). Similarly, pancreatic complications such as pancreatitis (p=0.584), thrombosis (p=0.074), and pancreatic leak (p=0.728) did not show statistical significance. Renal complications also lacked statistical significance (p=0.16). A detailed breakdown of these findings can be found in **Tables 3 and 4**. Furthermore, no significant association was observed between positive cultures and rejection, with a p-value of 0.874. Of the total postoperative complications, 32% (N=37) were classified as major according to the Clavien-Dindo classification. When comparing complications across the groups with negative, positive, and contaminated cultures, no statistically significant differences were found (p=0.48).

Table 3. Complications Based on Preservation Fluid Culture Results Pancreatic Complications.

Type of Complication	Negative (n=106)		Positive (n=39)		Contaminated (n=18)		p-value
	n	Percentage	n	Percentage	n	Percentage	
Pancreatitis.	14	14,3%	6	18,8%	1	7,1%	0,584
Pancreatic Thrombosis.	16	16,3%	11	34,4%	2	14,3%	0,074
Duodenal Fistula.	4	4,1%	1	3,1%	0	0,0%	0,728
SSI.	51	52,0%	17	53,1%	5	35,7%	0,496
UTI.	26	26,5%	8	25,0%	2	14,3%	0,613
Pneumonia.	6	6,1%	1	3,1%	0	0,0%	0,532
Line Infection.	6	6,1%	1	3,1%	0	0,0%	0,532
Rejection	4	3,8%	5	13%	4	22,27%	0,874

**SSI: (Surgical Site Infection); UTI: (Urinary Tract Infection).*

Tabla 4. Renal complications.

Type of Complication	Negative (n=106)		Positive (n=39)		Contaminated (n=18)		p-value
	n	Percentage	n	Percentage	n	Percentage	
Urinary Fistula.	1	0,6%	1	0,6%	0	0%	0,496
Recurrent UTI.	0	0%	0	0%	1	0,6%	0,613
Need for Hemodialysis During ICU Stay.	0	0%	1	0,6%	0	0,0%	0,532
Renal Collection.	0	0%	0	0%	1	0,6%	0,496
Hemorrhagic Acute Abdomen Due to Renal Artery Jet Lesion.	1	0,6%	0	0%	0	0%	0,613
Acute Occlusion of the Right Femoral Artery	1	0,6%	0	0%	0	0,0%	0,532
Thrombosis and Necrosis of the Renal Implant.	0	0%	1	0,6%	0	0,0%	0,532
Partial renal graft thrombosis due to ptosis.	1	0,6%	0	0,6%	0	0%	0,496
Venous Thrombosis of the Renal Graft.	0	0%	0	0%	1	0,6%	0,613
Rejection.	8	7,50%	10	25,6%	3	16,7%	0,87

**UTI: (Urinary Tract Infection); ICU: (intensive care unit)*

The mean hospitalization duration was 15.85 days (range 1–72), with an average stay in the intensive care unit of 5 days. No statistically significant differences were observed in hospital stay between the groups with positive and negative cultures (p=0.54)

DISCUSSION

The outcomes of patients undergoing SPK transplantation have progressively improved over time, driven by advancements in immunosuppressive therapies, surgical techniques, and the expanded use of antimicrobial prophylaxis[4]. Despite these improvements, infections remain the leading cause of morbidity and mortality[4,8,9]. Although preservation fluid is necessary to maintain organ viability, it can also serve as a vector for infection[10]. Donor-derived infections are a possible source of these infections in recipients[11]. These pathogens can be transmitted via the donor with an active or latent infection[12].

Research on risk factors and medium- to long-term outcomes of post-transplant infections has been a topic of debate in recent decades; however, the clinical implications of the presence of infection in organ preservation fluids remain unclear[2]. To our knowledge, there are no reports addressing this issue in patients who have undergone combined organ transplantation, a population that may be particularly vulnerable[2].

This study explores the clinical implications of PF cultures in SPK transplants, with a particular focus on the relationship between isolated microorganisms and postoperative complications. To date, this is the first comprehensive series reported in

SPK transplantation, underscoring the potential significance of our findings.

Previous studies have reported considerable variability in the incidence of microorganism growth in preservation fluids, likely due to differences in diagnostic criteria among researchers[13-16]. While some exclude cases they consider mere contamination, others include any microorganism growth regardless of its clinical significance, with a few focusing specifically on the impact of microorganisms classified as pathogens[7, 17]. Our analysis carefully examined each case, differentiating between microorganisms classified as contamination and those identified as pathogens, as outlined in Table 2.

Our findings revealed that 24% of preservation fluid cultures were positive, a result consistent with the meta-analysis conducted by Oriol et al[1] which reported a similar incidence, with an average of 37% positive cultures in PF. However, the same study reported a 4% rate of direct correlation, which was not observed in our analysis. In all these cases, as in the previously mentioned research, targeted antibiotic therapy was administered based on the antibiogram results. This approach may have reduced the likelihood of infection in recipients, potentially introducing a bias inherent to our analysis. Audet et al. expanded the boundaries by opting not to administer tailored antibiotic therapy, showing no significant impact on the rate of infectious complications.

In general, in cases of positive preservation fluid cultures, a genotypic analysis of the isolated microorganism could be performed to confirm whether the same germ is present in both the preservation fluid and the recipient, suggesting a 'direct correlation.' However, due to the limited accessibility and high costs associated with such analysis, we propose that matching antibiograms from both samples could serve as a practical proof of such correlation. Although other studies have reported collecting samples at different stages of procurement and cold ischemia for subsequent analysis, as previously mentioned, our team has chosen to standardize the sampling process by obtaining it at the conclusion of the back table procedure. This approach ensures that all stages where contamination might arise due to handling are thoroughly considered. Our series did not reveal any correlation between microorganisms isolated in cultures and some of the most common postoperative complications in pancreatic and renal grafts, as shown in Tables 3 and 4, respectively. Additionally, no statistical significance was observed in hospital stay duration, surgical site infection rates, or the incidence of acute rejection.

In conclusion, the presence of microorganisms in PF does not appear to have a direct impact on infectious or postoperative complications in SPK transplant recipients. However, the use of targeted antibiotic therapy in positive cases may have introduced a potential bias. In cases of contamination, standard antibiotic prophylaxis administered prior to implantation seems sufficient to prevent complications.

Randomized studies with a larger sample size are needed to draw more definitive conclusions regarding the clinical correlation of PF cultures, particularly in this highly vulnerable group of patients undergoing combined organ transplantation.

Conflict of interest

None to declare.

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Ethics committee statement

our work, retrospective and observational, does not require approval by the ethics committee.

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