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ORIGINAL PAPER

Bacterial and Fungal Infections in Postoperative Liver Transplantation and Their Relationship with the Donor

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ABSTRACT

Introduction: Nosocomial infections remain a significant cause of adverse outcomes following liver transplantation. Donor-derived infections (DDIs) are rare but potentially life-threatening in this context. Bacterial and fungal infections are among the most common forms of DDI. Given the shortage of organs and the high number of patients on the waiting list, it is crucial to determine whether the use of organs from donors with positive cultures is harmful or feasible. **Objectives:** To evaluate the incidence and impact of general infections, of the use of positive-culture donors, and of DDIs on liver transplant outcomes. **Methods:** This retrospective observational study was conducted at the Hospital Geral, Universidade de Campinas. Digital records of all transplant recipients from April 2021 to January 2024 were reviewed to identify positive cultures, records of infection at the time of positive culture, and donor cultures. DDI was considered present when patients developed infection by the same agent isolated from the donor, provided they had not been colonized before. Kaplan-Meier curves were used to define survival, with Breslow's test for comparison between groups with or without infection and with or without positive donor cultures. **Results:** Ninety liver transplants were performed in 86 patients. Among the 90 donors, nine (10%) had positive cultures, and four (4.4%) met the criteria for bloodstream infection. Among the recipients, 26 (30.2%) developed infections with positive cultures during the 60 days following liver transplantation. No infections in recipients were linked to donors. There was no difference in mortality between those who received livers from positive-culture donors and negative-culture donors. Additionally, no difference in mortality was observed between those who developed infections and those who did not. Intensive care unit length of stay was higher in recipients who developed infections. **Conclusion:** Infections remain an important cause of postoperative morbidity among liver transplant recipients, justifying concern about DDIs. However, positive-culture donors might be suitable for transplantation when no evident sepsis is present at the time of organ harvest. The design of this study is limited, and therefore, it is imperative to confirm these findings with further prospective studies.

Descriptors: Liver Transplantation; Infections; Organ Donor.

Infecções Bacterianas e Fúngicas em Pós-Operatório de Transplante Hepático e Sua Relação com Doador

RESUMO

Introdução: Infecções nosocomiais continuam sendo uma causa significativa de desfechos adversos após o transplante de fígado. Infecções relacionadas ao doador são raras, mas potencialmente fatais nesse contexto. Infecções bacterianas e fúngicas estão entre as formas mais comuns de infecções relacionadas ao doador. Dada a escassez de órgãos e o elevado número de pacientes na lista de espera, é crucial determinar se o uso de órgãos de doadores com culturas positivas é prejudicial ou viável. **Objetivos:** Avaliar a incidência e o impacto das infecções em geral, do uso de doadores com culturas positivas e das infecções relacionadas ao doador nos desfechos do transplante hepático. **Métodos:** Este estudo observacional retrospectivo foi realizado no Hospital Geral da Universidade de Campinas. Foram revisados os prontuários digitais de todos os receptores de transplante hepático entre abril de 2021 e janeiro de 2024 para identificar culturas positivas, registros de infecção no momento da cultura positiva e culturas dos doadores. Considerou-se infecção relacionada ao doador presente quando os pacientes desenvolveram infecção pelo mesmo agente isolado do doador, desde que não estivessem previamente colonizados. Curvas de Kaplan-Meier foram utilizadas para definir a sobrevida, com o teste de Breslow para comparação entre os grupos com ou sem infecção e com ou sem culturas positivas

dos doadores. **Resultados:** Foram realizados 90 transplantes de fígado em 86 pacientes. Entre os 90 doadores, nove (10%) apresentaram culturas positivas, e quatro (4,4%) atenderam aos critérios para infecção da corrente sanguínea. Entre os receptores, 26 (30,2%) desenvolveram infecções com culturas positivas nos 60 dias após o transplante hepático. Nenhuma infecção nos receptores foi relacionada aos doadores. Não houve diferença na mortalidade entre aqueles que receberam fígados de doadores com culturas positivas e aqueles com culturas negativas. Além disso, não foi observada diferença na mortalidade entre os que desenvolveram infecções e os que não desenvolveram. O tempo de permanência na unidade de terapia intensiva foi maior nos receptores que desenvolveram infecções. **Conclusão:** As infecções continuam sendo uma causa importante de morbidade pós-operatória entre receptores de transplante hepático, justificando a preocupação com as infecções relacionadas ao doador. No entanto, doadores com culturas positivas podem ser adequados para transplante quando não há sepse evidente no momento da captação do órgão. O desenho deste estudo é limitado, sendo necessário confirmar esses achados com estudos prospectivos adicionais.

Descritores: Transplante de Fígado; Infecções; Doador de Órgãos.

INTRODUCTION

Whereas rejection, surgical technique, and organ preservation have significantly improved over the past decades, nosocomial infections remain a significant cause of adverse outcomes following liver transplantation.[1,2] During the first 60 days following the procedure, bacterial and fungal infections are most commonly attributable to nosocomial pathogens and may result from recipient colonization or donor infection.[1] Donor-derived infections (DDI) are rare but represent potentially life-threatening complications in this context, occurring usually in the first 45 days following surgery.[3,4] Bacterial and fungal infections are among the most frequently encountered forms of DDI, adversely affecting transplant outcomes.[5-7]

Although viral infections also contribute to posttransplant morbidity, most viral diseases can be excluded through serologic screening. Common viral infections, such as cytomegalovirus, are considered expected and managed with well-established strategies.[3,7]

The transmission dynamics of bacterial and fungal infections from donor to recipient remain unclear. A 2020 study[5] reported a high transmission rate, with high impact when using organs from infected donors. Another 2020 study found transmission from bacteremic donors to be rare and with low impact on outcome.[8] Furthermore, there are not numerous studies addressing these specific dynamics.

In Brazil, about 53% of all donor-derived infections are caused by bacteria, followed by viruses (17%) and fungi (10%).[9] Infections other than hepatitis B or C, Chagas' disease, and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection are usually the most important causes for organ disposal.[10] Although justified by concern with the recipient's safety, this disposal worsens the situation for those waiting for a transplant.

Given the organ shortage and the high number of patients on the waiting list, it is crucial to determine whether the use of organs from donors with positive cultures is harmful or feasible.

Objectives

We aimed to evaluate the incidence and impact of DDI on outcomes, as well as the incidence and outcomes of general positive culture infections in liver transplant recipients.

METHODS

We reviewed all liver transplants performed at the Hospital Geral, Universidade de Campinas, from April 2021 to January 2024. A comprehensive record review was conducted to identify infectious complications and positive cultures occurring in the first 60 days following surgery, with data retrieved from donor blood, urine, and tracheal secretion cultures provided by the organ procurement organization. These samples were processed in the original hospital. No samples were submitted for processing in our laboratory, except for those related to our organ procurement organization. Organs were procured by either our surgical team or remote surgical teams, depending on the location. For positive blood cultures (in both donor and recipient), we considered two positive samples for coagulase-negative *Staphylococci* or a single positive culture for other pathogens. For other cultures, any isolate was considered positive. Recipient infection was defined by the association of a positive culture with documented infection in the patient's medical record. Pathogen resistance phenotype definitions were defined according to the Centers for Disease Control and Prevention's[11] definitions. DDI was considered when the recipient developed an infection caused by the same pathogen isolated from the donor, provided they had not been colonized before by the same pathogen before. DDI was excluded when the donor had no positive cultures or the recipient was previously

colonized by the same agent. Recipients were classified as intervened upon without documented transmission (IWDT) when they received empirical treatment with coverage for the donor-isolated pathogen, interfering with culture results. These definitions were simplified from Garzoni and Ison's definitions.[12] We also retrieved intensive care unit (ICU) length of stay (LOS) and recipients' survival rate. All recipients were given standard immunosuppression, consisting of corticoids, calcineurin inhibitors, and purine and pyrimidine synthesis inhibitors. Usual antibiotic prophylaxis consisted of ampicillin and sulbactam for 48 h after surgery. At the discretion of the assisting team, antimicrobial prophylaxis may have been converted into treatment with broad-spectrum antimicrobial drugs. For survival comparison, we used a Kaplan-Meier curve with Breslow's test. Deaths occurring within 48 h of the procedure were excluded from survival analysis, as they were most likely attributable to causes other than infection. For comparison between ICU LOS, we used Mann-Whitney's *U* test. For comparison between proportions, we used Fisher's test.

RESULTS

Eighty-six patients underwent liver transplantations during the study period. Four of them underwent retransplantation, totaling 90 donors. Both donor-positive and donor-negative culture recipients had similar ICU LOS, age, Model for End-Stage Liver Disease (MELD)-Na scores, and sex proportions (Table 1).

Table 1. Variable distribution between recipients of donors with or without positive cultures.

Variable	Median (IQR)		*p*-value
	Positive donor culture	Negative donor culture	
ICU LOS (days)	5 (2-12)	5 (3-10)	0.949*
Age (years)	59 (52-61)	59 (52-65)	1.000*
MELD-Na (points)	12 (9-22)	20 (12-27)	0.101*
Sex (F/M)	22.2% (F)/77.8% (M)	27.3% (F)/ 2.7% (M)	1.000†

Source: Elaborated by the authors. F = female; M = male. *Mann-Whitney *U* test. †Fisher's test.

Among the donors, nine (10%) had some kind of positive culture. Four donors (4.4%) met the criteria for bloodstream infections (BSI), five (5.6%) had positive urine cultures, and one (1.1%) had a positive culture for lower respiratory tract material.

No donor BSI was caused by multidrug-resistant organisms (MDRO). For urine samples, one (1.1%) had an MDRO. For lower respiratory tract cultures, one (1.1%) donor had a positive culture for a non-MDRO.

Among the recipients, 26 (30.2%) developed some sort of infection with a positive culture. Pneumonia was the most frequent, with 14 cases (16.3%), followed by BSI (17 episodes in 13 patients [15.1%]), urinary tract infections (UTI) with 11 cases (12.8%), and ascitic fluid infection with seven cases (7.8%). Twelve recipients (13.3%) with infection had an MDRO isolated from culture. MDRO isolates were more frequent in blood and urine samples (Table 2).

Table 2. Distribution of resistance patterns of isolated pathogens by site of infection in liver transplant recipients.

Infection site	MDRO (n [%])	Non-MDRO (n [%])
BSI	6 (46.2)	7 (53.8)
Pneumonia	5 (35.7)	9 (64.3)
UTI	5 (45.5)	6 (54.5)
Ascitic fluid infection	0 (0.0)	5 (100.0)

Source: Elaborated by the authors.

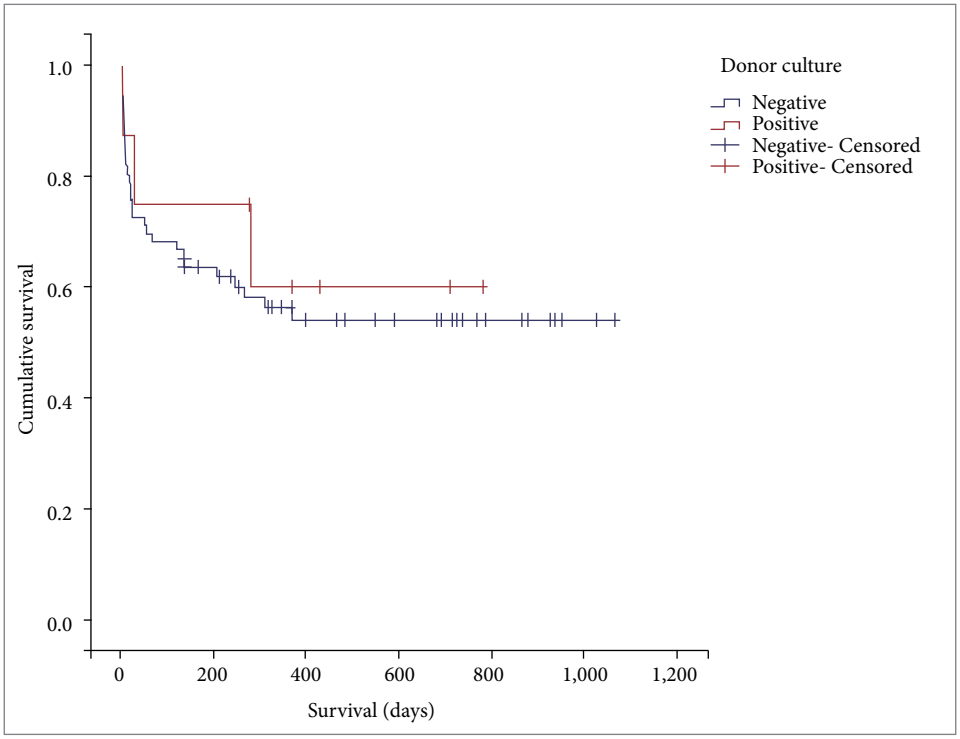
Fungi were isolated from 22.4% of all samples, with the highest isolation rate observed in tracheal secretions (Table 3).

Table 3. Proportion of pathogens isolated from all samples according to sample type in liver transplant recipients.

	Pathogen type						Total	
	N-MDR bacteria		MDR bacteria		Fungi			
	n	%	n	%	n	%	n	%
Blood (first episode)	6	46.2	4	30.8	3	23.1	13	100.0
Ascitic fluid	6	85.7	0	0.0	1	14.3	7	100.0
Tracheal secretion	3	21.4	5	35.7	6	42.9	14	100.0
Blood (second episode)*	2	50.0	2	50.0	0	0.0	4	100.0
Urine	5	45.5	5	45.5	1	9.1	11	100.0
Total	22	44.9	16	32.7	11	22.4	49	100.0

Source: Elaborated by the authors. N-MDR = non-multidrug resistant. *Collected from the second episode of BSI in the same patient.

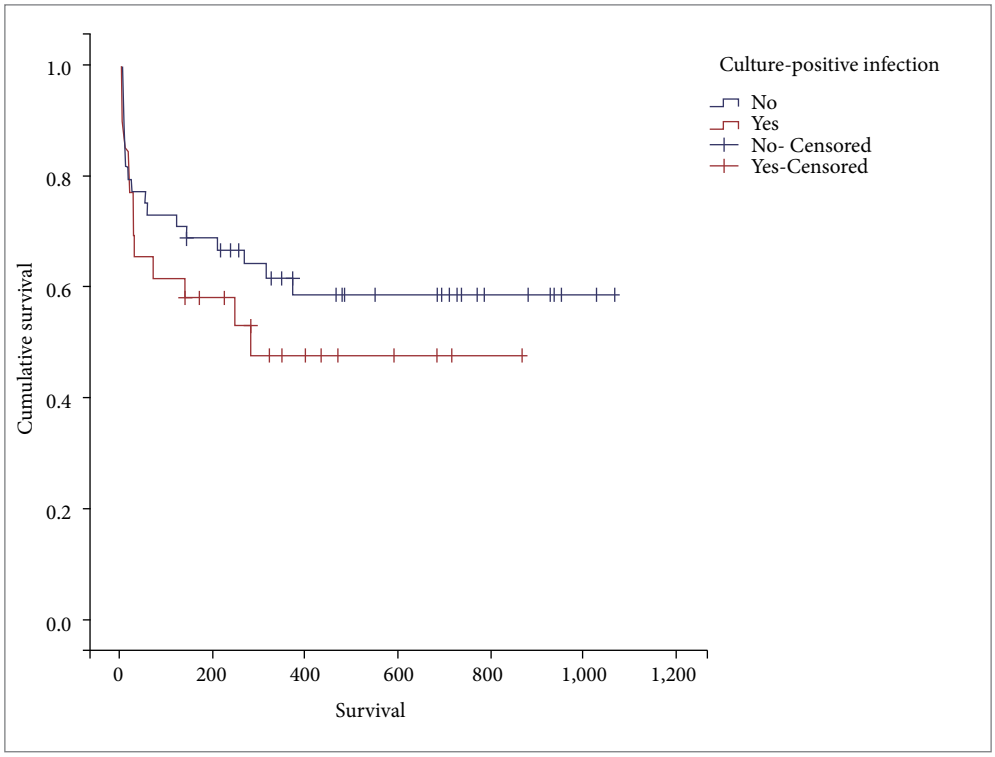
None of the recipient infections could be classified as DDI. Four cases (4.4%) were classified as IWDT. However, all patients who received organs from positive blood culture donors also received antimicrobial drugs with an appropriate spectrum. Survival rates were similar between recipients from donors with or without positive culture samples, with a *p*-value of 0.632 (Breslow) (Fig. 1).



Source: Elaborated by the authors.

Figure 1. Survival rates for recipients from donors with and without positive cultures. Deaths occurring within 48 hours were excluded.

There was no difference in ICU LOS between recipients of organs from donors with positive or negative cultures. Survival rates (excluding deaths within 48 h of the procedure) for patients with or without positive culture infections (Fig. 2) were similar as well ($p = 0.425$, Breslow).



Source: Elaborated by the authors.

Figure 2. Kaplan-Meier curve for recipients with and without culture-positive infection.

Culture-positive infection was associated with higher ICU LOS, with 15 days (interquartile range [IQR]: 7-25) vs. 4 days (IQR: 2-6) for those without infection (Table 4).

Table 4. ICU LOS for patients with or without culture-positive infection.

Culture-positive infection	ICU LOS (days)	
	Mean	Median (IQR)
No	4	4 (2-6)
Yes	19	15 (7-25)

Source: Elaborated by the authors. $p = 0.000$ (Mann-Whitney *U* test).

DISCUSSION

In this sample, we had relatively few positive donor cultures, with no documented infection and no difference in survival rates for both recipients from donors with and without positive cultures, as previously reported by other authors.8 This result may be affected by early recognition of donors' culture results with subsequent early preemptive antimicrobial therapy. The absence of MDRO isolated from donors may also play an important role, considering that usual antimicrobial prophylaxis could prevent the progression to recipient infection. Also, it is important to say that despite having positive cultures reported to the center after transplantation, at the time of organ procurement, no donor showed evident signs of uncontrolled sepsis.

Regarding general infections in postoperative liver transplant recipients, our incidence of culture-positive cases was similar to that reported in the literature.[13,14] These infections had a surprisingly low impact on survival, although the lack of statistical significance may be due to limited sample size. One limitation of our study is that we did not analyze all antimicrobial agents administered during the period. However, a low threshold for clinical suspicion may have contributed significantly to the observed outcomes. Additionally, the high prevalence of non-MDR bacteria may help explain the limited impact of these infections on patient survival. As expected, ICU LOS was longer in patients who developed infections.[15] We also observed a high rate of fungal isolates from tracheal secretions in patients diagnosed with pneumonia. However, these were likely

contaminants rather than true pathogens. Even cases with *Aspergillus* sp. did not meet criteria for invasive aspergillosis,[16] suggesting colonization rather than infection.

CONCLUSION

Infections remain a significant cause of postoperative morbidity in liver transplant recipients, particularly by increasing ICU LOS. This morbidity underscores the importance of monitoring for DDIs. However, in our study, no cases of donor-to-recipient transmission were identified, suggesting that donors with positive cultures may still be suitable for transplantation when there is no clinical evidence of sepsis at the time of organ procurement. Given the limitations of our study design, these findings should be confirmed in future prospective studies.

CONFLICT OF INTEREST

Nothing to declare.

AUTHOR'S CONTRIBUTION

Substantive scientific and intellectual contributions to the study: Chueiri Neto F, Ataíde EC, Boin IFSF. **Conception and design:** Chueiri Neto F. **Data analysis and interpretation:** Chueiri Neto F, Alves RT, Jucá RH, Perales SR. **Article writing:** Chueiri Neto F, Alves RT. **Critical revision:** Chueiri Neto F, Ataíde EC. **Final approval:** Chueiri Neto F.

DATA AVAILABILITY STATEMENT

Data will be made available upon request.

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