Factors associated with hospital mortality in renal transplant patients admitted to the intensive care unit with acute respiratory failure

Fatores associados à mortalidade hospitalar em pacientes com transplante renal admitidos na unidade de terapia intensiva com insuficiência respiratória aguda

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Abstract

Introduction: The lungs are often involved in a variety of complications after kidney transplantation. Acute respiratory failure (ARF) is one of the most serious manifestations of pulmonary involvement. **Objective:** To describe the main causes of ARF in kidney transplant patients who require intensive care and identify the factors associated with mortality. **Methods:** This retrospective study evaluated adult patients with ARF admitted to the intensive care unit of a center with high volume of transplants from August 2013 to August 2015. Demographic, clinical, and transplant characteristics were analyzed. Multivariate logistic regression analysis was performed to identify factors associated with hospital mortality. **Results:** 183 patients were included with age of 55.32 ± 13.56 years. 126 (68.8%) were deceased-donor transplant, and 37 (20.2%) patients had previous history of rejection. The ICU admission SAPS3 and SOFA score were 54.39 ± 10.32 and 4.81 ± 2.32, respectively. The main cause of hospitalization was community-acquired pneumonia (18.6%), followed by acute pulmonary edema (15.3%). Opportunistic infections were common: PCP (9.3%), tuberculosis (2.7%), and cytomegalovirus (2.2%). Factors associated with mortality were requirement for vasopressor (OD 8.13, CI 2.83 to 23.35, $p < 0.001$), invasive mechanical ventilation (OD 3.87, CI: 1.29 to 11.66, $p = 0.016$), and SAPS3 (OD 1.04, CI 1.0 to 1.08, $p = 0.045$). **Conclusion:** Bacterial pneumonia is the leading cause of ARF requiring intensive care, followed by acute pulmonary edema. Requirement for vasopressor, invasive mechanical ventilation and SAP3 were associated with hospital mortality.

Keywords: intensive care units; kidney transplantation; respiratory insufficiency.

Resumo

Introdução: Os pulmões são frequentemente envolvidos em uma variedade de complicações após o transplante renal. A insuficiência respiratória aguda (IRA) é uma das manifestações mais graves do envolvimento pulmonar. **Objetivo:** Descrever as principais causas de IRA em pacientes transplantados de rim que necessitaram de cuidados intensivos e identificar os fatores associados à mortalidade. **Métodos:** Estudo retrospectivo que avaliou pacientes adultos com diagnóstico de insuficiência respiratória aguda internados na unidade de terapia intensiva (UTI) de um centro com alto volume de transplantes, no período de agosto de 2013 a agosto de 2015. Dados demográficos, clínicos e características do transplante foram analisados. Análise de regressão logística multivariada foi realizada para identificar os fatores associados a mortalidade hospitalar. **Resultados:** Foram incluídos 183 pacientes com idade de 55,32 ± 13,56 anos. 126 (68,8%) receberam rim de doador falecido e 37 (20,2%) tiveram histórico prévio de rejeição. O SAPS3 de admissão na UTI foi de 54,39 ± 10,32 e o SOFA de 4,81 ± 2,32. A principal causa de internação foi pneumonia comunitária (18,6%), seguida de edema agudo de pulmão (15,3%). Infecções oportunistas foram comuns, como pneumocistose (9,3%), tuberculose (2,7%) e citomegalovírus (2,2%). Os fatores associados a mortalidade foram necessidade de vasopressor (OD 8,13, IC 2,83-23,35, $p < 0,001$), ventilação mecânica invasiva (OD 3,87, IC: 1,29-11,66, $p = 0,016$) e SAPS3 (OD 1,04, IC 1,0-1,08, $p = 0,045$). **Conclusão:** Pneumonia bacteriana foi a principal causa de insuficiência respiratória aguda com necessidade de cuidados intensivos, seguida por edema agudo de pulmão. Necessidade de vasopressor, ventilação mecânica invasiva e SAP3 foram associados a mortalidade.

Palavras-chave: insuficiência respiratória; transplante de rim; unidades de terapia intensiva.

Introduction

The number of patients immunosuppressed because of solid organ transplants has been increasing steadily.[1] The absolute number of solid organ transplants in Brazil in 2015 was 7,936; and renal transplantation represented 70.3% of this total.[2] It is considered the treatment of choice for patients with end-stage chronic kidney disease, providing benefits in terms of quality of life and survival when compared to dialysis.[3-5] However, long-term immunosuppressive therapy increases the risk of cardiovascular disease, infection, toxicity and cancer.[6]

The lungs are often involved in a variety of complications after renal transplantation, and can affect up to 36% of these patients.[7] Acute respiratory failure (ARF) is one of the most severe manifestations of pulmonary involvement, accounting for about half of hospitalizations in intensive care units (ICUs).[8-10] Bacterial and opportunistic infections are common causes of ARF, and are also factors associated with in-hospital mortality.[8]

The epidemiological characteristics of ARF may be influenced by regional aspects.[11,12] Endemic diseases, mainly infectious, are relevant for solid organ transplants.[13] However, contemporary data from emerging countries regarding this complication in renal transplant patients are scarce. Thus, this study carried out in Brazil aimed to identify the main causes of ARF that led to the need for intensive care and the factors associated with hospital mortality.

Methods

The study was carried out in a 16-bed ICU of a center with a large volume of kidney transplants in Brazil.[14] The data was collected retrospectively for the period from August 2013 to August 2015. The Institutional Research Ethics Committee approved the study and dispensed the informed consent (Research Ethics Committee - Federal University of São Paulo, reference number: 269628).

All renal transplant recipients over 18 years of age using immunosuppressants, who had been admitted to the ICU were included sequentially. ARF was defined as the presence of arterial oxygen saturation < 90% by pulse oximetry, or tachypnea > 30 incursions per minute, or resting respiratory discomfort. ARF re-hospitalizations patients and those who had previously been admitted for palliative care were excluded.

Demographic, clinical and transplantation data were obtained through the electronic medical records or administrative database of the ICU, which are fed prospectively. For the definition of sepsis, the 2001 Consensus Conference criteria were used.[15]

The period between the onset of symptoms that led to the demand for medical care, as long as it was directly related to the pulmonary disease, up to the date of ICU admission was defined as symptom time. If the patient was admitted for non-pulmonary diseases, it was decided to count the start date of the respiratory symptoms initiating after admission to the hospital until the date of ICU admission.

Statistical analysis

This was a descriptive study in which the categorical variables were expressed as percentage values, and the numerical variables were expressed as mean (± standard deviation) or median (interquartile 25-75%), according to the Shapiro-Wilk test. The Pearson's chi-square test or Fisher's test for categorical variables was used for comparison between survivors and non-survivors. For continuous variables, the Mann-Whitney test or Student's T-test, according to the variable distribution. A logistic regression analysis was also carried out to identify factors associated with mortality. For this model, the variables that presented $p < 0.05$ in the univariate analysis were included. The results were considered significant if the value of $p < 0.05$.

The statistical analysis was carried out using the Statistical Package for Social Sciences (SPSS) program for Windows, version 19.0.

Results

During the study period, 197 patients were eligible for participation, of which 14 were excluded: 7 for readmissions and 7 for lack of data on transplantation. The final sample consisted of 183 patients. Clinical characteristics and variables related to the renal transplantation are depicted in table 1. The patients had a long transplant time and baseline creatinine of 2.34 ± 1.49 mg/dl. Most of them were admitted to the ICU coming from the Emergency Care Unit.

Table 1 Clinical and transplant-related characteristics

Variable	Total Sample 183	Survivors 129 (70,5%)	Non-survivors 54 (29,5%)	*p*-Value
Age	55.32 ± 13.56	54.84 ± 14.10	56.46 ± 12.23	0.465[1]
Males	114 (62.3%)	78 (60.5%)	36 (66.7%)	0.430[2]
Comorbidities				
SAH	132 (72.3%)	91 (71.3%)	40 (74.1%)	0.705[2]
DM	76 (41.5%)	56 (43.4%)	20 (37.0%)	0.425[2]
CAD/OCI	32 (17.5%)	19 (14.7%)	13 (24.1%)	0.129[2]
HF	12 (6.6%)	9 (7.0%)	3 (5.6%)	1.000[3]
COPD	16 (8.7%)	10 (7.8%)	6 (11.1%)	0.567[3]
Renal failure causes				0.052[3]
DM	19 (10.4%)	13 (10.1%)	6 (11.1%)	
Glomerulonephritis	37 (20.2%)	32 (24.8%)	5 (9.3%)	
SAH	40 (21.9%)	27 (20.9%)	13 (24.1%)	
Undetermined	56 (30.6%)	34 (26.4%)	22 (40.7%)	
Other	31 (16.9%)	23 (17.8%)	8 (14.8%)	
Transplant type				0.321[3]
Renal	179 (97.8%)	125 (96.9%)	54 (100.0%)	
Pancreas-kidney	4 (2.2%)	4 (3.1%)	0 (0.0%)	
Kidney retransplant	8 (4.4%)	6 (4.7%)	2 (3.7%)	1.000[3]
Transplant time (years)	4.53 (1.67 - 8.60)	4.58 (1.23 - 8.48)	4.37 (2.01 - 9.47)	0.483[4]
Immunosuppression				
Prednisone	177 (96.2%)	127 (98.5%)	50 (92.6%)	0.063[3]
Tacrolimus	133 (72.7%)	98 (76.0%)	35 (64.8%)	0.123[2]
Azathioprine	34 (18.6%)	20 (15.5%)	14 (25.9%)	0.098[2]
Myfortic	83 (45.4%)	65 (50.4%)	18 (33.3%)	0.035[2]
Other	58 (31.7%)	38 (29.5%)	20 (37.0%)	0.315[2]
Donor type				0.524[2]
Live	57 (31.2%)	42 (32.6%)	15 (27.8%)	
Deceased	126 (68.8%)	87 (67.4%)	39 (72.2%)	
Pre-transplant dialysis type				0.830[3]
Preemptive	1 (0.6%)	1 (0.8%)	0 (0.0%)	
HD	178 (97.3%)	125 (96.9%)	53 (98.2%)	
Peritoneal	2 (1.1%)	2 (1.6%)	0 (0.0%)	
Both	2 (1.1%)	1 (0.8%)	1 (1.9%)	
Rejection	37 (20.2%)	25 (19.4%)	12 (22.2%)	0.662[2]
Rejection time (years)	0.97 (0.36 - 3.08)	1.36 (0.36 - 3.24)	0.67 (0.27 - 2.51)	0.746[4]
Baseline creatinine (mg/dl)	2.34 ± 1.49	2.37 ± 1.61	2.25 ± 1.19	0.548[1]
Origin				0.657[3]
ER	108 (59.0%)	78 (60.5%)	30 (55.6%)	
Infirmary	74 (40.4%)	50 (38.8%)	24 (44.4%)	
Others	1 (0.6%)	1 (0.8%)	0 (0.0%)	
Hospitalization time before the ICU (days)	0 (0 - 5)	0 (0 - 4)	5.0 (0 - 8.0)	0.477[4]

SAH: systemic arterial hypertension, DM: *diabetes mellitus*, CAD: coronary artery disease, HF: heart failure, COPD: chronic obstructive pulmonary disease, ICU: intensive care unit. [1] Descriptive level of probability of Student's t test. [2] Descriptive level of probability of the chi-square test. [3] Descriptive level of probability of the Fisher exact test. [4] Descriptive level of probability of the non-parametric Mann-Whitney test.

Aspects of disease severity are shown in Table 2. The need for invasive ventilatory support, renal replacement therapy, and vasopressor drugs was high in this population. Forty-five (24.5%) patients were submitted to transbronchial biopsy. Nine patients (4.9%) required tracheostomy.

The main causes of ARF were bacterial pneumonia (18.6%), cardiogenic pulmonary edema (15.3%), extrapulmonary sepsis (13.7%) and pneumocystis (9.3%). In addition to pneumocystis, there were also a variety of other opportunistic agents, accounting for 19.1% of the cases (supplementary material). The number of ARF without definitive diagnosis was high (16.4%). Among bacterial pneumonia, 6 cases (3.3%) were of hospital pneumonia. Of the cases of extrapulmonary sepsis, four were related to candidemia. The 106 cases of infection presented criteria of organic dysfunction that allowed the characterization of severe sepsis or septic shock in the first 24 hours of admission to the ICU.

ICU mortality was 23.5%, and hospital mortality was 29.5%. The mortality data stratified by each disease is in the supplemental material. In the multivariate analysis, to identify factors associated with mortality, we included all variables that were significantly different between survivors and non-survivors (Table 1 and 2). Those associated with mortality in the final model were: the need for vasopressor drugs, the need for invasive mechanical ventilation and SAPS3 (Table 3). The accuracy of the model was 86.4% and the adequacy was accepted ($p = 0.095$).

Discussion

Bacterial pneumonia was the main cause of ARF, followed by cardiogenic pulmonary edema. There were also a considerable number of cases involving opportunistic agents. Need of vasopressor, invasive mechanical ventilation and SAPS3 were associated with mortality.

The findings of this study agree with the majority of those who evaluated respiratory complications in renal transplant patients.[8,16-19] Regarding the causes of ARF, the largest case series on the subject, a retrospective study involving 9 French centers specifically evaluating patients with ARF, showed bacterial pneumonia as the main cause (35.5%), followed by cardiogenic pulmonary edema (24, 5%).[8] In another smaller series from Turkey, also involving renal transplant patients with ARF, but at an earlier time after renal transplantation, the results were similar: bacterial pneumonia (56%) and cardiogenic pulmonary edema (44%).[16]

In our study, the two main individual causes of ARF were repeated. However, there is a peculiarity in our results, which is the greater proportion of different opportunistic agents causing ARF. We believe that this locally endemic diseases and socioeconomic aspects, as suggested in a national retrospective study of renal and hepatic transplant recipients at four transplant centers, demonstrated that a significant proportion of the patients (4.7%) had an opportunistic disease, mainly tuberculosis.[13]

Another aspect that may be discussed is that the history of prophylaxis for opportunistic agents has not been evaluated, and may have an impact on the causes of ARF. In our study, for instance, pneumocystis was frequent. In this case, prophylaxis can be considered for a longer time,[20] since there is a description that the disease may occur later in those who are no longer using prophylactic medication.[21]

It is important to note that although urinary infection is the most common in the renal transplant,[22] pulmonary infection is the main cause of sepsis and hospitalization in the ICU.[8,10,23,24] Traditionally, a greater number of infections are expected in the first 6 months of transplantation, a period in which immunosuppression is more intense.[25,26] However, it is interesting to note that patients included in this study had on average more than 5 years of transplantation.

Even when the time for transplantation is analyzed for each infectious disease individually, all occurring later, except for cytomegalovirus. This finding is no different from other studies in this population, which report severe pulmonary complications more frequently after 6 months of transplantation,[8,9,16,18,23,24,27] although there are cases with different results.[17,28]

Cardiogenic pulmonary edema is another condition often implicated in the genesis of ARF. Renal transplants present risk factors for the development of cardiovascular diseases,[29] which are frequent comorbidities and are the main cause of morbidity and mortality in this population.[30] Although it is reported more frequently in the initial phase after transplantation,[8] in our study this characteristic was not observed.

Regarding factors associated with mortality, our study also repeats results from studies of renal transplant patients requiring intensive care, showing that

Table 2 Clinical characteristics

Variable	Total sample (n = 183)	Survivors (n = 129)	Non-survivors (n = 54)	*p*-Value
Symptoms duration (days)	3.0 (1.0 - 8.0)	3.0 (1.0 - 7.0)	5.0 (0 - 10.25)	0.478[4]
PaO_2/FiO_2 ratio*	238.69 + 95.57	239.26 + 96.88	237.31 + 93.23	0.900[1]
SAPS3	54.39 + 10.32	52.62 + 9.70	58.61 + 10.61	< 0.001[1]
Respiratory SOFA*	2.0 (1.0 - 2.0)	2.0 (1.5 - 2.0)	2.0 (1.0 - 2.0)	0.583[4]
Total SOFA*	4.81 + 2.32	4.50 + 2.03	5.56 + 2.78	0.014[1]
Lactate (mg/dl)*	10.65 (7.2 - 15.17)	10.85 (6.87 - 14.42)	10.35 (7.82 - 18.57)	0.418[4]
Circulatory shock *	13 (7.1%)	6 (4.7%)	7 (13.0%)	0.060[3]
Severe sepsis	106 (57.9%)	67 (63.2%)	39 (83.0%)	0.015[2]
Use of vasopressor	65 (35.5%)	21 (16.3%)	44 (81.5%)	< 0.001[2]
IMV	78 (42.6%)	33 (25.6%)	45 (83.3%)	< 0.001[2]
NIMV	163 (89.1%)	110 (85.3%)	53 (98.2%)	0.011[2]
Dialysis	81 (44.3%)	40 (31.0%)	41 (75.9%)	< 0.001[2]
Time in ICU (days)	7.0 (4.0 - 11.0)	6.0 (3.0 - 9.0)	11.0 (5.75 - 17.25)	< 0.001[4]
Hospitalization time (days)	19.0 (11.0 - 33.0)	21.0 (11.0 - 33.0)	19.0 (11.0 - 33.5)	0.763[4]

PaO_2/FiO_2: arterial oxygen partial pressure/inspired oxygen fraction, SAPS3: Simplified Acute Physiology Score 3, SOFA: Sequential Organ Failure Assessment (Sequential Organ Failure Assessment), IMV: invasive mechanical ventilation, NIMV: non-invasive mechanical ventilation, ICU: Intensive Care Unit. * At the time of admission to the Intensive Therapy Unit [1] Descriptive level of probability of the Student t test. [2] Descriptive level of probability of the chi-square test. [3] Descriptive level of probability of the Fisher exact test. [4] Descriptive level of probability of the non-parametric Mann-Whitney test.

Table 3 Associated factors to hospital mortality

Variable	OD	CI 95	*p*-Value
Vasopressor use	8.13	(2.83; 23.35)	< 0.001
VMI	3.87	(1.29; 11.66)	0.016
SAPS3	1.04	(1.00; 1.08)	0.045

OD: odds ratio, CI: confidence interval, IMV: invasive mechanical ventilation, SAPS 3: *Simplified Acute Physiology Score 3*.

none of the transplant-related characteristics was associated with mortality, but rather factors related to disease severity.[10] Among 5% to 10% of renal transplant recipients who at some time present complications requiring intensive care,[10] about half are admitted for ARF.[8]

The mortality reported in these cases ranges from 22.5% to 66.6%.[8,18] In our study it was 29.5%. The comparison with other centers is not doable, since the causes of ARF are different and severity scores are not always reported. It should also be emphasized again that socioeconomic aspects can have an impact on the outcome of the patients. In a multicenter, prospective cohort study involving 773 patients in 45 national ICUs submitted to ventilatory support, mortality was high when compared to global epidemiological data, especially in patients with moderate to severe acute respiratory distress syndrome, reaching 60%. Unequal access to health care was one of the factors to explain the results.[12,31]

This study stands out for including a specific population of patients that has become more numerous. The data was collected consecutively and in a short time interval, minimizing fluctuations in diagnosis and treatment that may occur when there are very long periods of time. However, there are many limitations. As a unicentral study, the findings may not be reproducible, even in other regions of the country.

Despite being one of the studies with the largest number of cases on the subject, a larger sample would give power to the statistical findings. The information for the study was drawn from a database for administrative purposes, which although they were fed prospectively did not have the rigor of a prospective study. In addition, there may have been some losses of patients who had ARF and were not admitted to the ICU. The previous history of hospitalizations for respiratory complications was not raised. Finally, the lack of a better characterization of the impact of ARF on renal graft function, an aspect that is relevant in this population, was not analyzed.

Conclusion

The main cause of ARF in our study was bacterial pneumonia. There were also a considerable number of infectious cases involving opportunistic agents. None of the characteristics related to transplantation were associated with mortality, but rather factors related to the severity of the disease.

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References

1. Salvadori M, Bertoni E. What's new in clinical solid organ transplantation by 2013. World J Transplant 2014;4:243-66. DOI: http://dx.doi.org/10.5500/wjt.v4.i4.243
2. Associação Brasileira de Transplantes de Órgãos. Registro Brasileiro de Transplantes. 2016. [acesso 2017 Out 27]. Disponível em: http://www.abto.org.br/abtov03/default.aspx?c=1099
3. Wolfe RA, Ashby VB, Milford EL, Ojo AO, Ettenger RE, Agodoa LY, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. N Engl J Med 1999;341:1725-30. PMID: 10580071 DOI: http://dx.doi.org/10.1056/NEJM199912023412303
4. de Groot IB, Veen JI, van der Boog PJ, van Dijk S, Stiggelbout AM, Marang-van de Mheen PJ; PARTNER-study group. Difference in quality of life, fatigue and societal participation between living and deceased donor kidney transplant recipients. Clin Transplant 2013;27:E415-23. DOI: http://dx.doi.org/10.1111/ctr.12165
5. Gremigni P, Cappelli G. Psychosocial well-being after kidney transplantation: A matched-pair case-control study. J Health Psychol 2016;21:599-606. DOI: http://dx.doi.org/10.1177/1359105314532506
6. Silkensen JR. Long-term complications in renal transplantation. J Am Soc Nephrol 2000;11:582-8.
7. Pencheva V, Petrova D, Genov D, Georgiev O. Pulmonary Complications as a Cause of Death after Renal Transplantation. Open J Int Med 2014;4:41-6. DOI: http://dx.doi.org/10.4236/ojim.2014.42007
8. Canet E, Osman D, Lambert J, Guitton C, Heng AE, Argaud L, et al. Acute respiratory failure in kidney transplant recipients: a multicenter study. Crit Care 2011;15:R91. DOI: http://dx.doi.org/10.1186/cc10091
9. Klouche K, Amigues L, Massanet P, Garrigue V, Delmas S, Szwarc I, et al. Outcome of renal transplant recipients admitted to an intensive care unit: a 10-year cohort study. Transplantation 2009;87:889-95. DOI: http://dx.doi.org/10.1097/TP.0b013e31819a688a
10. Canet E, Zafrani L, Azoulay É. The Critically Ill Kidney Transplant Recipient: A Narrative Review. Chest 2016;149:1546-55. PMID: 26836919 DOI: http://dx.doi.org/10.1016/j.chest.2016.01.002
11. Franca SA, Toufen C Jr, Hovnanian AL, Albuquerque AL, Borges ER, Pizzo VR, et al. The epidemiology of acute respiratory failure in hospitalized patients: a Brazilian prospective cohort study. J Crit Care 2011;26:330.e1-8. DOI: http://dx.doi.org/10.1016/j.jcrc.2010.10.010
12. Azevedo LC, Park M, Salluh JI, Rea-Neto A, Souza-Dantas VC, Varaschin P, et al.; ERICC (Epidemiology of Respiratory Insufficiency in Critical Care) investigators. Clinical outcomes of patients requiring ventilatory support in Brazilian intensive care units: a multicenter, prospective, cohort study. Crit Care 2013;17:R63. DOI: http://dx.doi.org/10.1186/cc12594
13. Batista MV, Pierrotti LC, Abdala E, Clemente WT, Girão ES, Rosa DR, et al. Endemic and opportunistic infections in Brazilian solid organ transplant recipients. Trop Med Int Health 2011;16:1134-42. DOI: http://dx.doi.org/10.1111/j.1365-3156.2011.02816.x
14. Medina-Pestana JO. More than 1,000 kidney transplants in a single year by the "Hospital do Rim" Group in Sao Paulo - Brazil. Clin Transpl 2010:107-26.
15. Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, et al.; International Sepsis Definitions Conference. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. Intensive Care Med 2003;29:530-8. DOI: http://dx.doi.org/10.1007/s00134-003-1662-x
16. Ulas A, Kaplan S, Zeyneloglu P, Torgay A, Pirat A, Haberal M. Acute Respiratory Failure in Renal Transplant Recipients: A Single Intensive Care Unit Experience. Exp Clin Transplant 2015;13:44-7.
17. Kupeli E, Ulubay G, Colak T, Ozdemirel TS, Ozyurek BA, Akcay S, et al. Pulmonary complications in renal recipients after transplantation. Transplant Proc 2011;43:551-3. DOI: http://dx.doi.org/10.1016/j.transproceed.2011.01.063
18. Candan S, Pirat A, Varol G, Torgay A, Zeyneloglu P, Arslan G. Respiratory problems in renal transplant recipients admitted to intensive care during long-term follow-up. Transplant Proc 2006;38:1354-6. PMID: 16797301 DOI: http://dx.doi.org/10.1016/j.transproceed.2006.02.083
19. Tomotani DY, Bafi AT, Pacheco ES, de Sandes-Freitas TV, Viana LA, de Oliveira Pontes EP, et al. The diagnostic yield and complications of open lung biopsies in kidney transplant patients with pulmonary disease. J Thorac Dis 2017;9:166-75. DOI: http://dx.doi.org/10.21037/jtd.2017.01.09
20. Martin SI, Fishman JA; AST Infectious Diseases Community of Practice. Pneumocystis pneumonia in solid organ transplantation. Am J Transplant 2013;13:272-9. DOI: http://dx.doi.org/10.1111/ajt.12119
21. McKinnell JA, Cannella AP, Kunz DF, Hook EW 3rd, Moser SA, Miller LG, et al. Pneumocystis pneumonia in hospitalized patients: a detailed examination of symptoms, management, and outcomes in human immunodeficiency virus (HIV)-infected and HIV-uninfected persons. Transpl Infect Dis 2012;14:510-8. DOI: http://dx.doi.org/10.1111/j.1399-3062.2012.00739.x
22. Alangaden GJ, Thyagarajan R, Gruber SA, Morawski K, Garnick J, El-Amm JM, et al. Infectious complications after kidney transplantation: current epidemiology and associated risk factors. Clin Transplant 2006;20:401-9. DOI: http://dx.doi.org/10.1111/j.1399-0012.2006.00519.x
23. de Carvalho MA, Freitas FG, Silva Junior HT, Bafi AT, Machado FR, Pestana JO. Mortality predictors in renal transplant recipients with severe sepsis and septic shock. PLoS One 2014;9:e111610. DOI: http://dx.doi.org/10.1371/journal.pone.0111610
24. Bige N, Zafrani L, Lambert J, Peraldi MN, Snanoudj R, Reuter D, et al. Severe infections requiring intensive care unit admission in kidney transplant recipients: impact on graft outcome. Transpl Infect Dis 2014;16:588-96. DOI: http://dx.doi.org/10.1111/tid.12249
25. Green M. Introduction: Infections in solid organ transplantation. Am J Transplant 2013;13:3-8. DOI: http://dx.doi.org/10.1111/ajt.12093

26. Bafi AT, Tomotani DY, de Freitas FG. Sepsis in Solid-Organ Transplant Patients. Shock 2017;47:12-6. DOI: http://dx.doi.org/10.1097/SHK.0000000000000700
27. Dizdar OS, Ersoy A, Akalin H. Pneumonia after kidney transplant: incidence, risk factors, and mortality. Exp Clin Transplant 2014;12:205-11.
28. Wang X, Wang Y, Zhu Q, Guo G, Yuan H. Pulmonary infection in the renal transplant recipients: Analysis of the radiologic manifestations. Radiol Infec Dis 2014;1:3-6. DOI: http://dx.doi.org/10.1016/j.jrid.2014.10.001
29. Kasiske BL. Risk factors for accelerated atherosclerosis in renal transplant recipients. Am J Med 1988;84:985-92. PMID: 3287917 DOI: http://dx.doi.org/10.1016/0002-9343(88)90302-6
30. Shirali AC, Bia MJ. Management of cardiovascular disease in renal transplant recipients. Clin J Am Soc Nephrol 2008;3:491-504. DOI: http://dx.doi.org/10.2215/CJN.05081107
31. Bellani G, Laffey JG, Pham T, Fan E, Brochard L, Esteban A, et al.; LUNG SAFE Investigators; ESICM Trials Group. Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries. JAMA 2016;315:788-800. DOI: http://dx.doi.org/10.1001/jama.2016.0291

Supplementary Material

Diagnosis	number of patients	time for transplantation (days)	Hospital Mortality
Infection			
Bacterial pneumonia	34 (18.9)	1485 (672 - 3553)	11 (32.3)
Extrapulmonary sepsis	26 (14.4)	2208 (1170 - 4587)	11 (42.3)
Opportunistic infections			
Pulmonary aspergillosis	1 (0.6)	916	0 (0.0)
Cytomegalovirus	6 (3.3)	165 (59 - 1177)	4 (66.7)
Influenza	4 (2.2)	2060 (360 - 4539)	1 (25)
Pneumocystis	17 (9.4)	1111 (327 - 2112)	8 (47.0)
Tuberculosis	6 (3.3)	1924 (1258 - 3105)	2 (33.3)
Chagas disease - acute phase	1 (0.6)	43	0 (0.0)
Cardiogenic pulmonary edema	28 (15.6)	1729 (313 - 4107)	3 (10.7)
Mixed	11 (6.1)	2966 (1530 - 4492)	2 (18.2)
Other			
Organizing cryptogenic pneumonia	1 (0.6)	1733	0 (0.0)
Diffuse alveolar damage	1 (0.6)	610	0 (0.0)
Pleural effusion	2 (1.1)	2958	0 (0.0)
Chronic pulmonary obstructive disease	5 (2.8)	1463 (977 - 2560)	1 (20.0)
Shedding interstitial pneumonia	1 (0.6)	4722	0 (0.0)
Eosinophilic pneumonitis	1 (0.6)	1309	0 (0.0)
Drug reaction	2 (1.1)	399	0 (0.0)
Pulmonary embolism	1 (0.6)	56	0 (0.0)
Tumor	4 (2.2)	2943 (769 - 4818)	3 (75.0)
Broncho aspiration	1 (0.6)	1645	1 (100.0)
Without diagnostic definition	30 (16.7)	1995 (414 - 3097)	7 (23.3)