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# Factors Associated with Mortality and Admission in Intensive Care for Kidney and Kidney-Pancreas Transplant Recipients with Respiratory Infection

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## ABSTRACT

**Background and Objective:** Kidney transplantation is a therapy of choice for chronic kidney disease at an advanced stage, however, such intervention has postoperative complications and adverse effects related to immunosuppressive therapy, namely infectious conditions. This study aims to investigate risk factors for mortality and admission to intensive care in kidney transplant recipients with respiratory tract infections.

**Methods:** Prospective observational study carried out between December 2017 and March 2020 in a single reference center for organ transplantation in the state of Minas Gerais, Brazil. We included 70 kidney or kidney-pancreas transplant (adults?) patients hospitalized with high suspicion or pulmonary infection. Patients were followed up to the outcome and received standard care. Variables whose comparison showed a p-value less than 0.20 entered the multiple logistic regression analysis. The multivariate models presented death and ICU admission as outcomes.

**Results:** XXIt was observed that the highest incidence of infectious events occurred in the female population, associated with the outcome of death or ICU (p = 0.029). There was a significant association between the use of calcineurin inhibitors and death or ICU (p=0.036). Patients who died or were transferred to ICU had a higher proportion (62.1%) of CMV. Those who did not (9.8%) (p<0.001), as well as the proportion of heart failure (27.3%, p=0.042).

**Conclusion:** Cytomegalovirus infection and heart failure associated with immunosuppression by calcineurin inhibitors or Methylprednisolone in females leads to a worse prognosis on the occurrence of respiratory tract infection in kidney transplant patients.

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**Keywords:** Kidney Transplantation, Respiratory Tract Infections, Mortality, Risk Factors

## Introduction

Kidney transplantation is the treatment of choice for patients with advanced chronic kidney disease. Compared to dialysis, it is an intervention that ensures a better quality of life [1]. However, solid organ transplant recipients are at risk for complications related to surgical procedures, immunosuppressive therapy, and infections. Infections are frequent complications after solid organ transplantation [2]. Its pathophysiology involves a complex interaction between exposure to pathogens and immunosuppression against rejection [3].

Among infections, previous studies have reported that those located in the lower respiratory tract are frequent in post-kidney

transplant patients, with incidence varying according to the region studied since various factors interfere with risk, as well as exposure to pathogens and socioeconomic profile [4]. These infections may vary according to the time of surgery and the immunosuppression profile [1]. But are more common in the first three months after transplantation due to therapeutic immunosuppression. Most common opportunistic respiratory infections in this population include *Pneumocystis jirovecii* pneumonia, Cytomegalovirus (CMV) infection, and systemic fungal infections such as Histoplasmosis, Cryptococcosis, and mycobacteriosis. These events lead to unfavorable outcomes, such as increased morbidity and mortality [5].

A study in Australia and New Zealand investigated the characteristics related to mortality due to infection in several sites after kidney transplantation, with older age, female sex, indigenous ethnicity, T-cell depletion therapy, and transplantation from deceased donors observed as risk factors [6]. Another study evaluated the incidence and risk factors of infectious episodes in kidney transplant recipients through 1,676 medical records in hospitals affiliated with the Federal University of São Paulo, Brazil. The authors identified that infections have a high prevalence in the first year of follow-up after transplantation and that the lung comprises 5.2% of infectious site4. However, its study was not specific to kidney transplantation and did not refer to the Brazilian scenario [7]. Therefore, few studies have specifically investigated individuals after kidney transplantation with lower respiratory tract infections, especially considering the Brazilian population.

Thus, the present study seeks to investigate risk factors associated with mortality and admission to intensive care in kidney transplant patients with lower respiratory tract infections.

## Methods

This was a prospective cohort study carried out between December 2017 and March 2020 at a state reference hospital for solid organ transplants in the State of Minas Gerais - Hospital Felício Rocho - located in Belo Horizonte. This study followed the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) checklist for observational studies [8].

### Inclusion and Exclusion Criteria

The selected people were patients: with kidney or kidney-pancreas transplants, aged 18 years or older, hospitalized with a suspected diagnosis of parenchymal pulmonary infection. Add characterized by the presence of one or more respiratory symptoms such as fever (defined as Tax > 38,0oc) or hypothermia (Tax < 36.0oC), acute cough, purulent sputum, chest discomfort or dyspnea associated with new radiological opacity of a supposedly infectious nature, documented in high-resolution chest tomography, with identification of an infectious agent by serological methods, direct identification of the agent in a lung specimen or lung biopsy (transbronchial or surgical lung biopsy) or through indirect methods, such as research for surface or cell wall antigens and molecular biology tests.XX

Exclusion criteria were withdrawal from participation in the study, presence of medical records with incomplete data, and acute pulmonary infiltrate of a non-infectious nature.

### Collected Data

The data collected was: age, sex, profession, type of transplant (kidney or kidney-pancreas), address, region of residence, type of donor (living or deceased), date of transplant, body mass index, duration of pre—transplant dialysis, post-transplant antimicrobial prophylaxis, previous pulmonary, pre-transplant tuberculin test, diagnosis of diabetes mellitus, diagnosis of (noninfectious?) pulmonary diseases before transplantation; etiology of kidney disease, cardiovascular diseases; active or past neoplastic diseases; recurrent urinary tract infection; immunosuppression regimen, and status of cytomegalovirus infection.

Blood was collected for the following laboratory tests: complete blood count, C-reactive protein (CRP), serum dosage of immunosuppressants (tacrolimus and sirolimus), urea, creatinine, CMV antigens or polymerase chain reaction (PCR), liver function (aminotransferases, gamma GT, alkaline phosphatase, total bilirubin, and protein, and fractions), sodium, potassium, magnesium, calcium, phosphorus and two samples for blood cultures.

Chest computed tomography was performed to verify the presence of recent radiological opacity, opacity with ground-glass attenuation, consolidation, nodule, and cavitation.

The bronchoalveolar lavage samples were submitted to Gram bacterioscopy, cytology and total and differential cytometry, bacterial culture and antibiogram, and direct research for germs: *Pneumocystis jirovecii*, AFB, fungi, and parasites research. Culture for mycobacteria, fungi, and investigation of galactomannan in bronchoalveolar lavage were also performed in all included patients.

### Statistical Analysis

For data analysis, exploratory statistical techniques were used, which allowed better visualization of the general characteristics of the data. Data had presented in frequency tables with absolute frequencies and their respective percentages, as well as descriptive measures (mean, median, standard deviation, 25th, and 75th percentiles) for quantitative data. Continuous variables were tested for normality using the Kolmogorov-Smirnov test. For comparative tests involving continuous variables, we used the Mann-Whitney test and the Student's t-test for nonnormal and normal distribution, respectively.

Categorical variables were performed using the chi-square test and Fisher's test or Monte Carlo simulation, when necessary. To investigate the characteristics associated with the composite outcome of death or ICU admission, variables whose comparison showed a p-value less than 0.20 in the bivariate analysis entered the multiple logistic regression model. The method used was stepwise, with the reference category being the first and model adequacy evaluated.

In all tests, the significance level adopted was 5%. The software used for the analysis was SPSS version 20.0.

### Ethical Aspects

All participants agreed and signed the Informed Consent Form (TCLE). This research project was approved by the Felício Rocho Health Sciences Center / Research Ethics Committee of the Felício Rocho Hospital (CAAE: 88306218.5.0000.5125, Opinion: 2.704.792) and by the Research Ethics Committee (COEP) of the Federal University of Minas Gerais (UFMG). All patients received the standard treatment for their case. It considers the infectious etiology and follows the current protocols, and they were followed up until the end of each outcome.

## Results

### Patients

Table 1 shows the main characteristics of the 70 patients included in the study. The Gender variable was significantly associated with the outcome of death or ICU (p = 0.029), and a higher proportion of women died or were transferred to the ICU (55.2%).

**Table 1: General Characteristics of the Patients According to Occurrence of Death or ICU Admission During the Hospital Stay**

| Variables | | DEATH OR ICU ADMISSION | | Total | P Value |
|---|---|---|---|---|---|
| | | No (n= 41) | Yes (n=29) | | |
| Age (years) | Median (IQR) | 59 (45-63) | 53 (41 - 60) | | 0,238* |
| Pre-transplant dialysis time (months) | | 72 (22- 84) | 30 (18 - 72) | | 0,206* |
| Time since TX (months) | | 71 (23- 160) | 68 (26 - 143) | | 0,612* |
| Serum creatinine at the time of infection | | 1,86 (1,26 - 2,58) | 2,51(1,85 - 3,08) | | 0,042* |
| Tacrolimus (serum dosage) | | 5,90 (4,00 - 9,80) | 4,60 (2,90 - 7,40) | | 0,349* |
| Sirolimus (serum dosage) | | 7,25 (2,00 - 10,20) | 9,55 ( 5,60 - 10,85) | | 0,379* |
| RCP - Admission | | 100,6 (58,30 - 163) | 86,0 (39,10 - 170,0) | | 0,779* |
| **Gender** | | | | | |
| Female | n | 12 | 16 | 28 | 0,029** |
| | % | 29,3% | 55,2% | 40,0% | |
| Male | n | 29 | 13 | 42 | |
| | % | 70,7% | 44,8% | 60,0% | |
| **BMI** | | | | | |
| Underweight | n | 5 | 5 | 10 | 0,528** |
| | % | 12,2% | 17,2% | 14,3% | |
| Normal | n | 22 | 18 | 40 | |
| | % | 53,7% | 62,1% | 57,1% | |
| Overweight | n | 9 | 5 | 14 | |
| | % | 22,0% | 17,2% | 20,0% | |
| Obese | n | 5 | 1 | 6 | |
| | % | 12,2% | 3,4% | 8,6% | |
| **Donor** | | | | | |
| Corpse | n | 33 | 23 | 56 | 0,903** |
| | % | 80,5% | 79,3% | 80,0% | |
| Living | n | 8 | 6 | 14 | |
| | % | 19,5% | 20,7% | 20,0% | |

* Mann-Whitney test; ** Chi-square test; IQR: Interquartile Range: P25 - P75

### Immunosuppressants

There was a significant association between the use of calcineurin inhibitors and death or ICU admission (p=0.036). Also, a higher proportion of these inhibitors had been used in patients who died or were transferred to the ICU (89.7%). Those who did not use this factor were lower (68.3%). Moreover, the proportion of deaths or ICU transfers for those who used methylprednisolone (31%) was higher than for those who did not use it (4.9%) (p=0.006). Table 2 depicts the the data regarding…

**Table 2: Class of Immunosuppressants and Pulse Therapy According to the Outcome of Death or ICU Admission**

| Variables | | DEATH OR ICU ADMISSION | | Total | P Value* |
|---|---|---|---|---|---|
| **Class of immunosuppressants** | | | | | |
| **Calcineurin inhibitors** | | | | | |
| No | n | 13 | 3 | 16 | 0,036* |
| | % | 31,7% | 10,3% | 22,9% | |
| Yes | n | 28 | 26 | 54 | |
| | % | 68,3% | 89,7% | 77,1% | |
| **Antiproliferative agents** | | | | | |
| No | n | 4 | 6 | 10 | 0,299* |
| | % | 9,8% | 20,7% | 14,3% | |
| Yes | n | 37 | 23 | 60 | |
| | % | 90,2% | 79,3% | 85,7% | |
| **Corticosteroids** | | | | | |
| No | n | 2 | 1 | 3 | 1,000** |
| | % | 4,9% | 3,4% | 4,3% | |
| Yes | n | 39 | 28 | 67 | |
| | % | 95,1% | 96,6% | 95,7% | |
| **m-TOR inhibitors** | | | | | |
| No | n | 27 | 25 | 52 | 0,055* |
| | % | 65,9% | 86,2% | 74,3% | |
| Yes | n | 14 | 4 | 18 | |
| | % | 34,1% | 13,8% | 25,7% | |
| **Pulse therapy with: Methylprednisolone** | | | | | |
| No | n | 39 | 20 | 59 | 0,006** |
| | % | 95,1% | 69,0% | 84,3% | |
| Yes | n | 2 | 9 | 11 | |
| | % | 4,9% | 31,0% | 15,7% | |
| **Use of anti-lymphocyte Ab:** | | | | | |
| No | n | 39 | 24 | 63 | 0,118* |
| | % | 95,1% | 82,8% | 90,0% | |
| Yes | n | 2 | 5 | 7 | |
| | % | 4,9% | 17,2% | 10,0% | |
| Total | n | 41 | 29 | 70 | |
| | % | 100,0% | 100,0% | 100,0% | |

*Chi-square test; ** Fisher's test

## Comorbidities

CMV infection and heart failure were associated with death or ICU. Thus, patients who died or were transferred to ICU had a higher proportion (62.1%) of CMV infection. Those who did not (9.8%) ($p<0.001$), as well as the proportion of heart failure (27.3% versus 7.001. $p=0.042$). (Table 3).

**Table 3: Comorbidities Presented According to the Outcome of Death or ICU**

| Comorbidities | | DEATH OR ICU ADMISSION | | Total | P Value* |
|---|---|---|---|---|---|
| | | No (n= 41) | Yes (n=29) | | |
| **COPD** | | | | | |
| No | n | 39 | 29 | 68 | 0,508** |
| | % | 95,1% | 100,0% | 97,1% | |
| Yes | n | 2 | 0 | 2 | |
| | % | 4,9% | 0,0% | 2,9% | |
| **Bronchiectasis** | | | | | |
| No | n | 34 | 27 | 61 | 0,289** |
| | % | 82,9% | 93,1% | 87,1% | |
| Yes | n | 7 | 2 | 9 | |
| | % | 17,1% | 6,9% | 12,9% | |
| **Pulmonary arterial hypertension** | | | | | |
| No | n | 41 | 27 | 68 | 0,168** |
| | % | 100,0% | 93,1% | 97,1% | |
| Yes | n | 0 | 2 | 2 | |
| | % | 0,0% | 6,9% | 2,9% | |
| **Asthma** | | | | | |
| No | n | 39 | 28 | 67 | 1,000** |
| | % | 95,1% | 96,6% | 95,7% | |
| Yes | n | 2 | 1 | 3 | |
| | % | 4,9% | 3,4% | 4,3% | |
| **Diabetes Mellitus** | | | | | |
| No | n | 25 | 20 | 45 | 0,492* |
| | % | 61,0% | 69,0% | 64,3% | |
| Yes | n | 16 | 9 | 25 | |
| | % | 39,0% | 31,0% | 35,7% | |
| **Systemic Arterial Hypertension** | | | | | |
| No | n | 10 | 5 | 15 | 0,473* |
| | % | 24,4% | 17,2% | 21,4% | |
| Yes | n | 31 | 24 | 55 | |
| | % | 75,6% | 82,8% | 78,6% | |
| **Coronary artery disease** | | | | | |
| No | n | 37 | 26 | 63 | 1,000* |
| | % | 90,2% | 89,7% | 90,0% | |
| Yes | n | 4 | 3 | 7 | |
| | % | 9,8% | 10,3% | 10,0% | |
| **Cardiac Insufficiency** | | | | | |
| No | n | 38 | 21 | 59 | 0,042* |
| | % | 92,7% | 72,4% | 84,3% | |
| Yes | n | 3 | 8 | 11 | |
| | % | 7,3% | 27,6% | 15,7% | |
| **Dyslipidemia** | | | | | |
| No | n | 30 | 20 | 50 | 0,701 |
| | % | 73,2% | 69,0% | 71,4% | |
| Yes | n | 11 | 9 | 20 | |
| | % | 26,8% | 31,0% | 28,6% | |
| **Neoplasm (Tumor)** | | | | | |

| | | | | | |
|---|---|---|---|---|---|
| No | n | 37 | 28 | 65 | 0,395* |
| | % | 90,2% | 96,6% | 92,9% | |
| Yes | n | 4 | 1 | 5 | |
| | % | 9,8% | 3,4% | 7,1% | |
| **Recurrent Urinary Tract Infection** | | | | | |
| No | n | 34 | 25 | 59 | 0,753** |
| | % | 82,9% | 86,2% | 84,3% | |
| Yes | n | 7 | 4 | 11 | |
| | % | 17,1% | 13,8% | 15,7% | |
| **CMV Infection** | | | | | |
| No | n | 37 | 11 | 48 | <0,001* |
| | % | 90,2% | 37,9% | 68,6% | |
| Yes | n | 4 | 18 | 22 | |
| | % | 9,8% | 62,1% | 31,4% | |
| **Pneumonia In The Last 12 months** | | | | | |
| | | 32 | 20 | 52 | 0,392* |
| No | n | 78,0% | 69,0% | 74,3% | |
| | % | 9 | 9 | 18 | |
| Yes | n | 22,0% | 31,0% | 25,7% | |
| Total | n | 41 | 29 | 70 | |
| | % | 100,0% | 100,0% | 100,0% | |

* Chi-square test; ** Fisher test

The following variables: sex, calcineurin, mTOR inhibitors, methylprednisolone, antilymphocyte Ab, pulmonary arterial hypertension, heart failure, and CMV infection entered the multiple regression model. Table 4 shows the final model.

**Table 4: Final Multiple Logistic Regression Model for the Outcome Death or ICU**

| Variables | B | S.E. | Wald | df | P Value | OR | IC 95% for OR | |
|---|---|---|---|---|---|---|---|---|
| CMV Infection | 1,979 | ,834 | 5,630 | 1 | ,018 | 7,233 | 1,411 | 37,079 |
| Cardiac Insufficiency | 2,906 | ,689 | 17,801 | 1 | ,000 | 18,279 | 4,739 | 70,497 |

Percentage of correct classification = 80%, Pseudo R2 = 0,451, Hosmer-Lemeshow Test = 0,917

## Discussion

This study analyzed aspects that favor hospitalization in intensive care and mortality in patients who underwent kidney transplants and evolved with lower respiratory tract infection. Several factors are involved and can modify the results as the epidemiological characteristics of the observed population, the comorbidities, the immunosuppression profile, and the most prevalent infectious agents in each region. Thus, the data analyzed in this population, women are at greater risk. The adopted immunosuppression scheme also interfered with the unfavorable evolution. Furthermore, heart failure and cytomegalovirus infection were significant for the outcome of patients.

Infectious episodes had a higher incidence in the female population, which is in line with data found by Sousa in a study on post-transplant infections carried out with the São Paulo state population [4]. This difference could happen because the present study specifically analyzed pulmonary contamination and was in the Minas Gerais state.

The present study showed that the chance of an individual with heart failure dying or going to the ICU is 18.3 times greater than that of an individual without heart failure (Table 4). Although, several studies have compared the clinical outcomes of patients who underwent kidney transplantation [9-13]. No evidence addresses the impact of heart failure on the death and ICU stay in pulmonary infection post-transplant. Thus, no studies were found with a similar methodology for results direct comparison. One hypothesis that could explain this finding is that congestive heart failure is the most common cause of hospital admissions after kidney transplantation, followed by infections [14]. Therefore, the seriousness of these conditions is notorious.

However, some studies addressed the variables, but not all aggregated. Cardoso studied the component heart failure plus pulmonary infection in relation to the outcome of death [15]. However, the patients were not selected for kidney transplantation. Of the 260 selected patients, death was 26.9% for patients with associated conditions and 17.6% with heart failure only, without associated infection. In this sense, association of heart failure and pulmonary infection could increase mortality.

The present study also found that the chance of an individual with CMV infection dying or ICU is 7.2 times greater than that of an individual who does not have this infection (Table 4). Cytomegalovirus infection is one of the main complications after

kidney transplantation and can be classified as a primary infection when transmission occurs through the graft [16]. The prevalence of CMV infection had been reported to reach up to 80% in kidney transplant patients [17]. The effects can be direct, which is the development of the disease, or indirect, such as an increase in the risk of acute rejection and chronic graft dysfunction, which could justify this study data [16].

Immunosuppression after kidney transplantation is essential to avoid the organ rejection process. However, it can favor the occurrence of side effects relevant, such as opportunistic infections [18]. A higher proportion of use of calcineurin inhibitors (Tacrolimus) had observed in patients who died of ICU compared with those who did not die of ICU. Corroborating these findings, Pencheva et al. investigated the use of these inhibitors with pulmonary infections and observed an increased risk of 1.83 times (OR = 1.83; P = 0.041) [5]. Such medication is often used in combination therapy in the maintenance phase and acts by blocking the production of interleukin 2, thus inhibiting the proliferation of T cells [19]. So, adaptive immunity decreases in patients with a greater propensity to infections.

Glucocorticoids inhibit the transcription of numerous inflammatory cytokines and are well-known additive drugs for kidney transplant patients) [1]. The present study showed that the proportion of deaths or ICU transfer for Methylprednisolone users was higher than for those who did not use it. Sousa related the use of methylprednisolone with a higher risk of developing infectious episodes (OR 1.29, CI 1 – 1.68). Also, they theorized that the use of additional doses of immunosuppression for these treatment rejections. Add increases the chances of infectious episodes [4]. It may be due to the association between this variable and the risk of developing infection cases. However, the study addressed infections at different sites, not restricting itself to lung infections. Pencheva also associated glucocorticoids use with an increased risk of pulmonary infection. This comparison was not performed because more than 90% of patients in both groups (with and without complications) used this medication [5].

No studies were found that specifically investigated lung infections in kidney transplant patients. This work has important scientific implications since Brazil occupies the third position in the world in kidney transplantation [20]. Therefore, the need to understand the worst prognosis is evident in these patients. Furthermore, when analyzing the definition of predictors of death or ICU in the selected population, it is possible to attribute individualized prognoses. Therefore, one can act directly in the associated comorbidities control and offer appropriate workup and assistance.

This study has some limitations, such as being a single-center study with a relatively small sample that affects the generalizability of the findings. Furthermore, this is a longitudinal observational study, subject to biases inherent to the prospective measurement of predictor variables. Despite this, the final multivariate logistic regression model was used for the outcome of ICU admission or death, with the clear advantage of determining the relative influence of one or more predictor variables.

## Conclusion

This study concluded that the following variables: CMV infection, heart failure, female sex, and the immunosuppression regimen using calcineurin inhibitors or glucocorticoids are related to a substantially higher hospitalization rate in intensive care and evolution to death in kidney transplant patients with opportunistic pulmonary infections.

## Interest Conflicts

All authors have nothing to declare.

## Indication of Authors Contribution

LMDF, VN and RAC elaborated the research planning, participated in the data collection and statistical analyses, in the writing of the article and carried out the final review of the article. MLDF, EARO and KAR participated in research planning, data analysis and final writing of the article.

## References

1. Foster JG, Foster KJ (2020) Care of the Renal Transplant Patient. Prim Care 47: 703-712.
2. Winterbottom F, Jenkins M (2017) Infections in the Intensive Care Unit: Posttransplant Infections. Crit Care Nurs Clin North Am 29: 97-110.
3. Dandamudi R, Smith J, Dharnidharka VR (2019) Renal transplantation and predisposition to opportunistic infections. Curr Opin Pediatr 31: 226-231.
4. Sousa S, Galante N, Barbosa D, Pestana J (2022) Incidência e fatores de risco para complicações infecciosas no primeiro ano após o transplante renal. [online] Pesquisa.bvsalud.org. Available at: <https://pesquisa.bvsalud.org/portal/resource/pt/lil-548398> [Accessed 29 June 2022].
5. Pencheva VP, Petrova DS, Genov DK, Georgiev OB (2015) Risk factors for lung diseases after renal transplantation. J Res Med Sci 20: 1127-1132.
6. Chan S, Pascoe EM, Clayton PA, McDonald SP, Lim WH, et al. (2019) Infection-Related Mortality in Recipients of a Kidney Transplant in Australia and New Zealand. Clin J Am Soc Nephrol 14: 1484-1492.
7. De Gasperi A, Feltracco P, Ceravola E, Mazza E (2014) Pulmonary complications in patients receiving a solid-organ transplant. Curr Opin Crit Care 20: 411-419.
8. Vandenbroucke JP, von Elm E, Altman DG, Gøtzsche PC, Mulrow CD, et al. (2014) Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. Int J Surg 12: 1500-1524.
9. Linares L, Cofán F, Cervera C, Ricart MJ, Oppenheimer F, et al. (2007) Infection-related mortality in a large cohort of renal transplant recipients. Transplant Proc 39: 2225-2227.
10. Wyld MLR, De La Mata NL, Masson P, O'Lone E, Kelly PJ, et al. (2021) Cardiac Mortality in Kidney Transplant Patients: A Population-based Cohort Study 1988-2013 in Australia and New Zealand. Transplantation 105: 413-422.
11. Freitas FGR, Lombardi F, Pacheco ES, Sandes Freitas TV, Viana LA, et al. (2018) Clinical Features of Kidney Transplant Recipients Admitted to the Intensive Care Unit. Prog Transplant 28: 56-62.
12. Silva RMD, Freitas FGR, Bafi AT, Silva Junior HT, Roza BA (2017) Factors associated with hospital mortality in renal transplant patients admitted to the intensive care unit with acute respiratory failure. J Bras Nefrol 39: 433-440.
13. Okidi OO, Van Dellen D, Sobajo C, Summers A, Greer JR, et al. (2017) Kidney Transplant Recipients Requiring Critical Care Admission Within One Year of Transplant. Exp Clin Transplant 15: 40-46.
14. Shirali AC, Bia MJ (2008) Management of cardiovascular disease in renal transplant recipients. Clin J Am Soc Nephrol 3: 491-504.
15. Cardoso JN, Del Carlo CH, Oliveira Junior MT, Ochiai ME, Kalil Filho R et al. (2018) Infection in Patients with Decompensated Heart Failure: In-Hospital Mortality and Outcome. Arq Bras Cardiol 110: 364-370.
16. Requião Moura LR, deMatos AC, Pacheco Silva A (2015) Cytomegalovirus infection in renal transplantation: clinical

aspects, management and the perspectives. Einstein (Sao Paulo) 13: 142-148.

17. Abou Jaoudé M, El Hage S, Akiki D, Fadlallah M, Ghaith AK, et al. (2021) Cytomegalovirus infection in kidney transplant patients: Prevalence, risk factors, and impact on outcome - A local multicentre experience. Transpl Immunol 69: 101473.
18. Manfro R, Gonçalves L (2022) Individualização da imunossupressão em pacientes transplantados renais. [online] Bases.bireme.br Available at: <http://bases.bireme.br/cgi-bin/wxislind.exe/iah/online/?IsisScript=iah/iah.xis&src=google&base=LILACS&lang=p&nextAction=lnk&exprSearch=691666&indexSearch=ID> [Accessed 29 June 2022].
19. Gruessner A (2022) Transplantation | Schwartz's Principles of Surgery, 11e | AccessSurgery | McGraw Hill Medical. [online] Accesssurgery.mhmedical.com. https://accesssurgery.mhmedical.com/content.aspx?bookId=2576&sectionId=216205012
20. (2022) Dimensionamento dos Transplantes no Brasil e em cada estado. https://site.abto.org.br/wp-content/uploads/2022/03/leitura_compressed-1.pdf