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Living- versus deceased-donor renal transplant recipients: A comparison on pulmonary complications

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Abstract:

BACKGROUND: In renal transplant recipients, evaluation of pulmonary complications and investigation of reduction interventions are important due to the potentially fatal results of pulmonary complications after transplant surgery. However, data are lacking about pulmonary complications in renal transplant recipients with living- or deceased-renal donors. Therefore, we aimed to assess the pulmonary complications in living- versus deceased-donor renal transplant recipients.

METHODS: We retrospectively searched the medical records of patients who underwent renal transplantation in our tertiary referral center between 2013 and 2018. Sociodemographic characteristics, pulmonary complications, and major comorbidities were compared according to the donor type (living or deceased).

RESULTS: Fifty-two of 100 transplantations from living donors and 48 of 100 transplantations from deceased donors were formed the patient groups. There were no statistically significant differences in terms of sociodemographic and clinical characteristics between the groups except with regard to pneumonia complication. The pneumonia rates were 11/48 (22.9%) and 3/52 (5.8%), $P=0.020$, for the deceased- and living-donor renal transplant recipients, respectively. Deceased-donor transplant recipients had a 4.8-fold risk of developing pneumonia (odds ratio, 4.8; 95% confidence interval, 1.2–18.6; $P=0.021$).

CONCLUSION: Deceased-donor renal transplant recipients are more vulnerable to pulmonary complications than are living-donor ones and should thus be monitored closely.

Keywords:

Deceased donor, living donor, pneumonia, pulmonary complication, renal transplantation

Introduction

Renal transplantation is the most commonly performed solid organ transplantation (SOT) worldwide.^[1]

Meanwhile, pulmonary complications are important in the prognosis of renal transplant recipients,^[2] and respiratory tract infections are the most frequently observed complications and an important cause of mortality and morbidity.^[1,2]

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Immunosuppression therapy is the most likely cause of pulmonary complications. However, investigation data regarding the differences of pulmonary complications according to the donor type (living or deceased) are lacking. To the best of our knowledge, no study has examined the pulmonary complications in renal transplant recipients according to donor type. Therefore, we aimed to assess the postoperative pulmonary complications in living- versus deceased-donor renal transplant recipients who underwent surgery at our center.

Materials and Methods

This retrospective study was conducted in the Department of Chest Diseases and approved by the Local Ethics Committee (Approval No. 26379996/82). We retrospectively reviewed the medical records of patients who underwent renal transplantation at our center between 2013 and 2018 in terms of postoperative pulmonary complications. The recipients' demographic characteristics, renal disease etiology, preoperative posteroanterior lung radiography findings, concomitant medications, tuberculin skin test (TST) results, smoking status, and baseline pulmonary function test results were recorded from their medical files. Pulmonary complications of the patients and the diagnostic methods were noted. The renal transplant recipients were grouped on the basis of whether transplantation was performed from living or deceased donors. The groups were then compared in terms of age, gender, and type of pulmonary and extrapulmonary complications.

Statistical analysis

IBM SPSS Statistics for Windows, version 20.0 (IBM, Armonk, NY, USA) was used for the statistical analyses. The normal distribution of the data was assessed with the Kolmogorov–Smirnov test, and descriptive statistics were defined as mean, standard deviation, number, and percentage values. Variables were compared according to the mean and standard deviation for continuous data. The Chi-square test was used to find differences between the categorical variables, and Student's *t*-test was used to determine differences between group means for the continuous variables. $P < 0.05$ indicated statistical significance.

Results

The medical files of 168 patients who had undergone renal transplantation were retrospectively reviewed. One hundred patients did not have missing data in their medical files and were thus included in the analyses. Of the recipients, 64% were men and 36% were women. The mean ages were 44.8 ± 11.3 , 44.2 ± 11.3 , and 45.9 ± 11.4 years for all patients,

for men, and for women, respectively. Fifty-two and 48 of the 100 transplantations were performed from living and deceased donors, respectively. The patients were administered different combinations of tacrolimus, mycophenolic acid (MPA), cyclosporine, antithymocyte globulin, and methylprednisolone as immunosuppressive therapy.

Hypertension (37%) and diabetes mellitus (15%) were the most common concomitant chronic diseases in our study population [Table 1]. Hypertension (27%), diabetes mellitus (15%), and polycystic kidney disease (12%) were the major causes of renal failure among the renal transplant recipients. The other etiological causes of renal failure are depicted in Table 2.

Table 1: Preoperative demographic characteristics of the patients with renal transplant recipients

Variables	The renal transplant recipients (n=100)
Gender, n (%)	
Female	36 (36)
Male	64 (64)
Age (years) (mean \pm SD*)	
Female	44.2 \pm 11.3
Male	45.9 \pm 11.4
Smoking status, n (%)	
Smoker	5 (5)
Nonsmoker	95 (95)
Type of donor, n (%)	
Living donor	52 (52)
Cadaveric	48 (48)
Comorbidities, n (%)	
Hypertension	37 (37)
Diabetes mellitus	15 (15)
Coronary artery disease	4 (4)
Asthma bronchiolae	3 (3)
Congestive heart failure	1 (1)
COPD	2 (2)
PPD (+), n (%)	69 (69)

Values are given as mean \pm SD and n (%). COPD: Chronic obstructive lung disease, PPD: Purified protein derivative, SD*: Standard deviation

Table 2: Etiology of the renal disease

Cause of renal failure	The renal transplant recipients (n=100), n (%)
Idiopathic	27 (27)
Hypertension	27 (27)
Diabetes mellitus	15 (15)
Polycystic kidney disease	12 (12)
Familial Mediterranean fever	8 (8)
Nephrolithiasis	3 (3)
Chronic pyelonephritis	3 (3)
Alport syndrome	2 (2)
Vesicoureteral reflux	1 (1)
Nephrotic syndrome	1 (1)
Good posture	1 (1)

Values are given as n (%)

A comparison of the renal transplant recipients according to donor type (deceased versus living) revealed that the average ages of the deceased- and living-donor renal transplant recipients were 46.7 ± 7.8 and 43.1 ± 13.7 years, respectively. The difference between average ages was not statistically significant. Similarly, there were no statistical differences in sociodemographic characteristics, including gender, concomitant chronic diseases, diabetes mellitus, cardiovascular diseases, and chronic lung diseases between the deceased- and living-donor renal transplant recipients [Table 3]. By contrast, the difference in pulmonary complications was statistically significant; the results were 13/48 (27.1%) and 4/52 (7.7), $P = 0.015$, in the deceased- and living-donor renal transplant recipients, respectively. Appearance times of postoperative pulmonary complications in the renal transplant recipients are shown in Figure 1. Pneumonia and pulmonary thromboembolism were categorized as pulmonary complications, whereas urinary tract infections, acute gastroenteritis, soft-tissue infections, malignant colon carcinoma, and acute respiratory distress syndrome were categorized as extrapulmonary complications. A statistically significant difference was found solely with regard to pneumonia; the pneumonia rates were 11/48 (22.9%) and 3/52 (5.8%), $P = 0.020$, in the deceased- and living-donor renal transplant recipients, respectively [Table 4].

Pulmonary complication and pneumonia were significantly associated with deceased-donor transplantation (odds ratio [OR], 4.4; 95% confidence interval [CI], 1.3–14.8; $P = 0.015$ for pulmonary complication, and OR, 4.8; 95% CI, 1.2–18.6; $P = 0.021$ for pneumonia).

Discussion

We conducted this study to assess the complications,

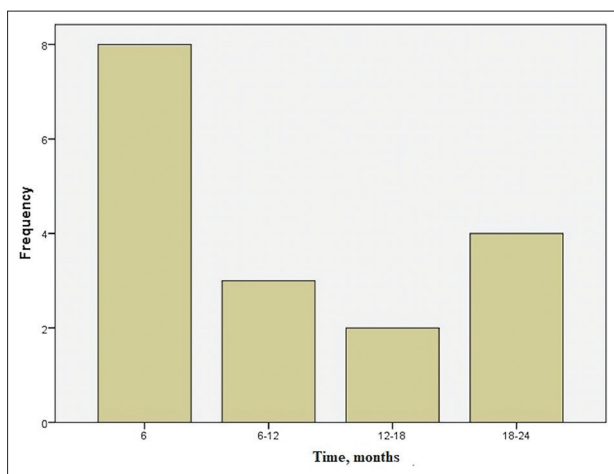


Figure 1: Time of postoperative pulmonary complications in renal transplant recipients

particularly pulmonary complications, in renal transplant patients. We compared existing pulmonary complications in living- and deceased-donor renal transplant recipients as well. Only pneumonia (pulmonary and extrapulmonary complications) was seen to be in a greater rate among the deceased-donor renal transplant recipients (11%) than among the living-donor renal transplant recipients (3%).

Due to the increasing frequency of renal transplantation procedures all over the world and the postoperative use of immunosuppressive therapies, patients and health-care professionals encounter several complications of infectious. Respiratory tract infections, pulmonary thromboembolism, and pulmonary complications that may develop secondary to medications are among the most commonly reported clinical conditions. Pulmonary complications are the most important cause of mortality and morbidity.^[2]

Table 3: The comparison of the sociodemographic characteristics of living- versus cadaveric-donor renal transplant recipients

Variables	Cadaveric donor (n=48)	Living donor (n=52)	P
Age, (years)	46.7±7.8	43.1±13.7	0.106
Gender, n (%)			
Female	16 (33.3)	20 (38.5)	0.678
Male	32 (66.7)	32 (61.5)	
Diabetes mellitus, n (%)	5 (10.4)	10 (19.2)	0.269
Cardiovascular diseases, n (%)	22 (45.8)	19 (36.5)	0.417
Chronic lung diseases, n (%)	2 (4.2)	3 (5.8)	1.000
Pulmonary complications, n (%)	13 (27.1)	4 (7.7)	0.015*

* $P < 0.015$ is considered statistically significant. Values are given as mean±SD and n (%). SD: Standard deviation

Table 4: The comparison of the postoperative pulmonary and extrapulmonary complications in living- versus cadaveric-donor renal transplant recipients

Variables	Cadaveric donor (n=48), n (%)	Living donor (n=52), n (%)	P
Pulmonary complications	13 (27.1)	4 (7.7)	0.015*
Pneumonia	11 (22.9)	3 (5.8)	0.020
Pulmonary thromboembolism	2 (4.2)	1 (1.9)	0.606
Extrapulmonary complications	24 (50)	21 (40.4)	0.422
Urinary tract infections	14 (29.2)	11 (21.2)	0.368
Acute gastroenteritis	10 (20.8)	8 (15.4)	0.604
Soft-tissue infections	2 (3.8)	0	0.496
Malignancy colon carcinoma	1 (1.9)	0	1.000
ARDS	1 (2.1)	1 (1.9)	1.000
Death	1 (2.1)	1 (1.9)	1.000

* $P < 0.015$ is considered statistically significant. Values are given as median (minimum–maximum) and n (%). ARDS: Acute respiratory distress syndrome

Immunosuppressive treatment protocols for SOT increase the susceptibility of recipients to several infections. Among these, lower respiratory tract infections are the most common.^[1] In this patient group, the incidence of pneumonia ranges between 8% and 18%.^[3] Sarnak and Jaber demonstrated that pulmonary infections increased the mortality rate twofold in their studied renal transplant recipients compared with that for their overall population.^[4] Prolonged hospitalization, tracheal damage resulting from endotracheal tubes, and impaired clearance of respiratory secretions contribute to the occurrence of pneumonia. Although infections commonly exhibit onset within the 1st year after transplantation, life-threatening viral and fungal infections mostly occur within the first 2 months after the procedure. The incidence of infections is higher during the first 3–6 months than after 6 months,^[5] and immunosuppressive therapies administered during the postoperative period substantially contribute to the development of respiratory tract infections and drug-related pulmonary complications. Meanwhile, tacrolimus and cyclosporine are the two most commonly used calcineurin inhibitors. Their major side effects are endothelial damage and interstitial fibrosis-related nephrotoxicity.^[6] Other side effects include infection, malignancy, hypertension, hyperglycemia, neurotoxicity, and hyperlipidemia.^[6,7] Furthermore, MPA may cause abdominal pain, diarrhea, nausea, bone marrow suppression, and (particularly at high doses) *Cytomegalovirus* infection. The side effects of the antibodies include allergic reactions, serum sickness, seizures, thrombocytopenia, arthralgia, and an increased risk of infection.^[6] In the present study, the incidence of pneumonia was 14% in accordance with the literature in all patients. Deceased-donor transplantation presented a 4.8-fold risk of developing pneumonia (OR, 4.8; 95% CI, 1.2–18.6; $P = 0.021$). Extrapulmonary complications were more common (45%), but fatal infections resulted only from acute respiratory distress syndrome (ARDS) secondary to pneumonia.

Tuberculosis (TB) is the tenth leading cause of death worldwide^[8] and the most significant opportunistic infection in transplant recipients. While the rate of TB varies between 1.2% and 6.4% in developing countries, it may reach 15% in transplant recipients from endemic regions. In such areas, the TB incidence is 8.5-fold higher among SOT recipients than among the overall population.^[9] In Turkey, the incidence of TB is 18/10,000.^[10] Immunosuppressive therapy increases the risk of TB development by 100 times.^[11] In the present study, none of the patients had a history of TB. A review of the medical files showed that 69% of the patients with TST results ≥ 5 mm were administered prophylactic

INH therapy. Such therapy is recommended for renal transplant recipients with TST ≥ 5 mm (with a booster effect or in the first test).^[11–14] In countries with a high prevalence of TB, prophylactic INH therapy is recommended for recipients whose donors have positive TST results.^[15] Hence, at our clinic, renal transplant recipients with TST results exceeding 5 mm also undergo prophylactic INH therapy. None of our patients developed TB. In a large patient series, TB developed 1 year after transplantation.^[16] Sayiner *et al.* demonstrated that TB in Turkey was diagnosed at a mean of 6 months after transplantation (range: 3–111 months).^[17]

Venous thromboembolism (VTE) is another important health problem that may be encountered by renal transplant recipients. Its incidence varies between 0.6% and 25%. VTE can be associated with the surgical procedure, impaired hemostatic balance, impaired fibrinolysis, and/or ongoing hypercoagulation.^[18,19] In the current study, the incidence of VTE was 3%, and all cases were noted within the first 6 months after transplantation. One of these cases involved massive pulmonary thromboembolism, which led to a life-threatening right ventricular dysfunction. The risk of recurrent thrombosis was also higher in this patient group. Poli *et al.* showed that the risk of recurrent VTE was tenfold higher after the first episode in renal transplant recipients.^[19] In this patient group, pulmonary embolism is a significant, life-threatening health concern after pulmonary infections.

We found an association between deceased-donor transplantation and pulmonary complications. It is known that living donors offer longer graft survival^[20,21] and have better outcomes than do deceased donors.^[22,23] Guimarães *et al.* found that living donors have shorter hospitalization times and lower postoperative infection rates.^[23] The fact that rates of pulmonary complications in deceased-donor transplantation are higher than those in living-donor transplantation may be due to donor waiting period, prolonged exposure to chronic renal failure effects, and extended periods of dialysis.

In this study, we found that extrapulmonary complications were more common than pulmonary complications in the renal transplant recipients, but the patients responded well to the medical therapy. Meanwhile, despite being less frequent, pulmonary complications could increase mortality and threaten life.

The present study had certain limitations because of the lack of adequate data on the induction therapy and doses of the patients before surgery. Induction therapy regimens before the transplantation surgery may contribute to postoperative complications.

Conclusion

The findings of this work showed that the deceased-donor renal transplant patients had a greater risk of developing pneumonia than did the living-donor renal transplant patients. Potential pulmonary complications in the renal transplant recipients may cause significant health problems that affect survival, quality of life, and therapeutic success. Most of the pulmonary complications developed within the first 6 months after transplantation under intense immunosuppressive regimens. Renal transplant recipients should, therefore, be investigated carefully through such means as systematic assessments and pulmonary examinations. Patients receiving transplants from deceased donors are more susceptible to pulmonary complications and should thus be closely monitored.

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Conflicts of interest

There are no conflicts of interest.

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