SERBIAN ARCHIVES OF MEDICINE Est.1872

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Paper Accepted* **ISSN Online 2406-0895**

Original Article / Оригинални рад

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Pneumonia and in-hospital mortality after renal transplantation

Упала плућа и болничка смртност после трансплантације бубрега

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Received: May 26, 2016
Accepted: August 8, 2017
Online First: August 11, 2017
DOI: https://doi.org/10.2298/SARH160526161P

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SUMMARY

Introduction/Objective Pneumonias remain one of the most frequent reasons for morbidity and mortality in the group of kidney recipients.

Objective The aim of this study was to define the factors associated with a higher risk for in-hospital mortality from pneumonia after renal transplantations.

Methods 124 kidney transplants hospitalized with pneumonia for the period of nine years were studied. Different noninvasive and invasive diagnostic tests were used.

Results 41 of the patients died as a result of the pneumonia or related complications during hospital stay. The factors associated with increased risk for in-hospital mortality were development of pneumonia during the early postoperative period (0-1st month) (HR=2.027; p= 0.025) or between 1st and 6th month after surgery (HR=2.303; P= 0.026), dyspnoea (HR=2.184; p= 0.007) and hypoxemia (HR=2.261; p= 0.003). The presence of bilateral infiltrates (HR=2.482; p= 0.001), failure of initial antibiotic therapy (HR=3.548; p<0.001), intubation and mechanical ventilation (HR=4.635; p< 0.001) also increased the risk for a fatal outcome.

Conclusions Knowing the prognostic factors, associated with an increased risk for in-hospital fatal outcome from pneumonia after renal transplantation makes it possible to differentiate a high-risk group of patients, requiring early etiological diagnosis and strict control of the condition, in order to reduce the mortality from pulmonary infections in the group of renal recipients.

Keywords: pneumonia; mortality; recipient; transplantation, solid organ, renal

САЖЕТАК

Увод/Циљ Пнеумоније су један од најчешћих разлога морбидитета и морталитета код прималаца бубрега.

Циљ овог рада је био да дефинише факторе повезане са већим ризиком за морталитет у болници од плућа након трансплантације бубрега.

Методе Анализирано је 124 болесника са трансплантацијом бубрега и пнеумонијом у периоду од девет година. Коришћени су различити неинвазивни и инвазивни дијагностички тестови.

Резултати Због пнеумоније или сродних компликација умро је 41 болесник током боравка у болници. Фактори повезани са повећаним ризиком за морталитет у болници били су: развој пнеумоније током раног постоперативног периода (0-1 месец) (*HR*=2.027; *p*= 0.025) или 1–6. месеца после операције (*HR*= 2.303; *p*=0,026), диспнеја (*HR*=2,184; *p*= 0,007) и хипоксемија (*HR*=2,261; *p*=0,003). Присуство билатералних инфилтрата (*HR*=2.482; *p*=0.001), неуспјех почетне антибиотске терапије (*HR*=3.548; *p*<0.001), трахеална интубација и механичка вентилација (*HR* =4.635; *p*<0.001).

Закључци Познавајући прогностичке факторе, повезане са повећаним ризиком за фатални исход у болници од пнеумоније након трансплантације бубрега, могуће је одредити групу пацијената високог ризика, која захтијева рану етиолошку дијагнозу и строгу контролу стања да би се смањила смртност од плућних инфекција код прималаца бубрега.

Кључне речи: пнеумонија; смртност; прималац; трансплантација, солидни орган, бубрег

INTRODUCTION

The solid transplantation, as a treatment method of the final stage of organ insufficiency, is becoming increasingly significant in recent years. Renal transplantation (RT) is the most frequently performed organ transplant, accounting for approximately 60% of all cases. Of particular significance for the prognosis of the survival rate and the mortality among renal transplant recipients are the pulmonary complications. According to different data in literature, the frequency of post- RT pulmonary complications varies from 5% to 37%. Most complications are caused by pulmonary infections, although their development after renal transplants is the lowest, compared to patients with other organ transplants (frequency 8–16% and mortality rate of 5–8% per annum) [1-3].

The risk of infection after transplantation changes in time, especially with the modification of the therapy, and it varies, depending on the immunosuppressive agents used. There are various

therapeutic schemes, differing by drug interactions, side effects, as well as the risk of developing infections [4]. As a result of its inhibiting effects, the immunosuppressive drugs affect the endogenic barrier of the lungs, against the penetration of infectious pathogens [4].The immunosuppressive therapy, used after surgery, defines three sub-periods in the post-transplant period, where different infectious agents, causing pulmonary complications are prevalent – first month after the operation, from the first to the sixth month after the transplantation and late post-transplant period (more than six months after the surgery) [5, 6].

The main challenge when providing care for patients after transplants is to choose the optimal immunosuppression, ensuring balance between the prevention of rejection reactions and the minimization of risk of infections [7]. This can be achieved with a strict monitoring of the immunosuppressive medications [8]. Nevertheless, pneumonias remain one of the most frequent reasons for morbidity and mortality in this group of patients [9, 10].

The aim of this study is to define the factors associated with a higher risk for in-hospital mortality from pneumonia after renal transplantations.

METHODS

A total of 124 post-RT patients diagnosed with pneumonia were included in the study. They were admitted in Clinic of pulmonology, UMHAT "Alexandrovska", during period of 9 years. All patients gave their written informed consent to participate. The protocols conformed to the guidelines of the 1975 Helsinki Declaration. All the patients were after renal transplantation and were at least 18 years of age. Patients with mental disturbances or proven oncological diseases, including pulmonary neoplasms were excluded from the study. Chronic pulmonary diseases like asthma and chronic obstructive pulmonary disease or dysfunctional graft with developed terminal renal insufficiency, and chronic haemodialysis treatment were exclusion criteria. A history of pulmonary tuberculosis successfully treated in the past, does form part of the eligibility criteria. In the cases of a second or subsequent pulmonary complication, only the first complication, registered for the respective patient, was used for the needs of the study and the data analysis.

Detailed medical history was prepared for each patient, and all patients underwent complete clinical examination. When the criteria, responsible for the development of pneumonia were present, the patients were hospitalized for treatment at the clinic. During the hospitalization period the pulmonary and cardiac statuses were followed-up on a daily basis, along with a control of the vital signs – arterial pressure, pulse and respiration rate, body temperature and 24 hour quantity of urine. Haematological and biochemical blood tests were performed: complete blood count with differential leukocyte count, erythrocytes sedimentation rate, C-reactive protein (CRP), creatinine, urea, aspartate aminotransferase (AST), alanine aminotransferase (ALT), potassium, sodium, chlorides, blood glucose, fibrinogen. The tests of all patients included also electrocardiography (ECG) and arterial

blood gases (ABGs) analysis (equipment used – RapidLab 248). Spirometry and in some cases – the diffusion capacity (equipment used was Ganshorn, Germany) were performed in accordance with the requirements of ATS/ERS Guidelines (Miller 2005). Microbiological tests of sputum, pleural effusion liquid or broncho-alveolar lavage (BAL), and blood for aerobic and anaerobic microorganisms, fungi, and Mycobacterium tuberculosis were done. Realquality RQ-Cytomegalovirus (CMV) standart kits of AB Analitica, Italy for the identification and quantitative determination of the CMV deoxyribonucleic acid were used. Posteroanterior radiography of all patients was performed. In cases of diagnostic difficulties, high resolution computer tomography of the thorax (HRCT) was performed (device: Toshiba Aquilion 64-multi-slice, following the Vital Images' Vitrea2 protocol). Some of the patients underwent fiberoptic bronchoscopy with bronchoalveolar lavage, catheter-biopsy, and – if necessary –fibre-clamp biopsy (Olympus BF 1T30). Cytological or histological examinations of the material from the bronchial mucosa or the lung parenchyma were all examined.

The statistical data processing was carried out using SPSS vs.16. The adopted level of significance, eliminating the null hypothesis, was $p<0.05$. The statistical analyses included a variational analysis of the quantitative variables – median, standard deviation, standard error of the median and 95% confidence interval of the median, frequency analysis of qualitative variables, graphics. The Chi-square test and the Fisher's exact test were used for establishing the dependency between two qualitative variables, and the Kolmogorov-Smirnov and the Mann-Whitney methods – for testing the normality of distribution of the quantitative variables. Quantitative indicators were assessed, using a ROC-analysis. The probability ratio was calculated, using a logistic regression analysis, and the establishment of the effects of various factors and the risk estimation were carried out, based on the Cox-regression, using Kaplan-Meier survival curves.

RESULTS

A total of 124 kidney recipients with pneumonia were included in the study. The mean age of the patients was 41.23 ± 13.46 years. The male-to-female ratio was 78/46 (62.9% men and 37.1% women). According to the outcome of pneumonia patients were divided into two groups. In the first pneumonia (+) group there were 83 of the patients recovered from pneumonia. The other 41recipients in pneumonia (–) group died as a result of the pneumonia or related complications during hospitalisation. There was no significant difference between the two groups according to main demographic data: age, sex, smoking status, type and length of dialysis treatment before transplantation, immunosuppressive agents used in both patient groups, concomitant diseases ($p > 0.05$ for all).

In the pneumonia (+) group 3 patients became ill during first postoperative month, 36 patients – between 1st and 6th month after transplantation and 44 patients in late post-transplant period (> 6th month after surgery). In the pneumonia (–) group 6 patients became ill during the first postoperative

period, 27 patients – between 1st and 6th month after transplantation and 8 patients in the late period after transplantation. There is a statistically significant dependence between the period of development of the pneumonia and the outcome of the disease (p<0.001).

The effect of the period, during which the pneumonia occurs, on the survival rate of the patients, is shown on figure 1.

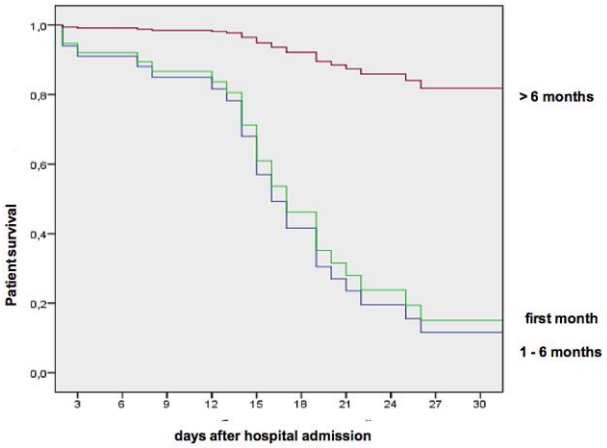
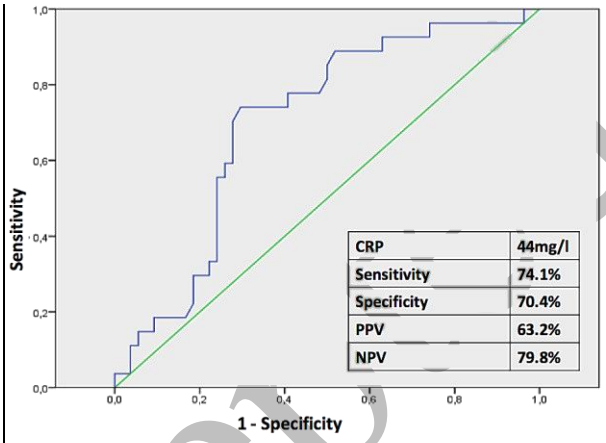


Figure 1. Kaplan – Meier plot – Effect of the period after the transplant on the survival rate in patients with pneumonia.



Graph 2. ROC curve of the CRP as a predictor of a fatal outcome of pneumonia.

The main clinical symptoms are similar in both groups (p>0.05). The only statistically significant difference in clinical features between the two groups is the presence of dyspnoea at admission (p=0.033). This symptom occurs more frequently in the pneumonia (–) group.

Table 1. Comparison of the haematological and biochemical parameters between the two groups.

Laboratory Indicator	Median ± SD Pneumonia (+)	Median ± SD Pneumonia (–)	*p*
CRP	54.60±77.285	94.32±94.100	0.026*
Erythrocytes	51.19±31.688	55.30±26.913	0.530
Leukocytes	9.175±4.6359	9.656±4.3531	0.583
Neutrophils	10.072±11.8294	15.200±21.3843	0.069
Lymphocytes	2.573±3.8850	1.535±2.5872	0.026*
Monocytes	0.965±1.9900	0.777±0.8372	0.301
Eosinophils	0.164±0.4307	0.126±0.1667	1.000
Basophils	1.02±0.136	1.04±0.192	1.000
Thrombocytes	266.59±103.618	236.01±132.407	0.062
Haemoglobin	117.00±23.261	111.22±18.331	0.442
Fibrinogen	5.1842±1.66059	5.9019±1.92601	0.559
Creatinine	205.94±165.943	270.69±210.343	0.321
Albumine	33.75±1.03	32.00±0.96	1.000

The major haematological and biochemical parameters are shown in table 1. Statistical differences between their values in the groups of patients, according to the outcome of the pneumonia were observed for CRP and lymphocytes. The calculated ROC- curve for CRP is shown in figure 2. The area below the curve is 0.702 (95% CI 0.584-0.819), p=0.003.

The ABGs analysis shows that at admission 38 patients (45.78%) of those that subsequently recovered and 35 (85.37%) of the subsequently deceased patients had hypoxemia (p=0.001). Figure 3 shows the ROC curve for PaO_2 in the ABGs at admission. The area below the curve is 0.703 (95% CI 0.591-0.815), p=0.003.

The ABGs analysis, performed on the third day of treatment, revealed hypoxemia in 23 (27.71%) of the subsequently recovered and in 39 (95.12%) of the subsequently deceased patients (p<0.001). Figure 4 shows the ROC analysis, comparing both groups, based on the outcome of the

disease and the PaO_2 values, obtained from the ABGs analysis on the third date of treatment. The area below the curve is 0.884 (95% CI 0.814-0.955, p<0.001).

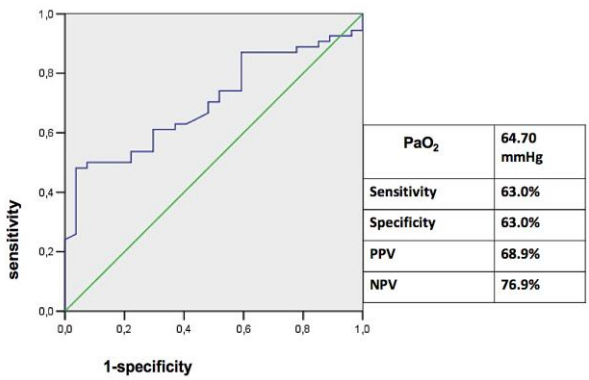


Figure 3. ROC-curve of PaO_2 on the first day, as a lethality predictor.

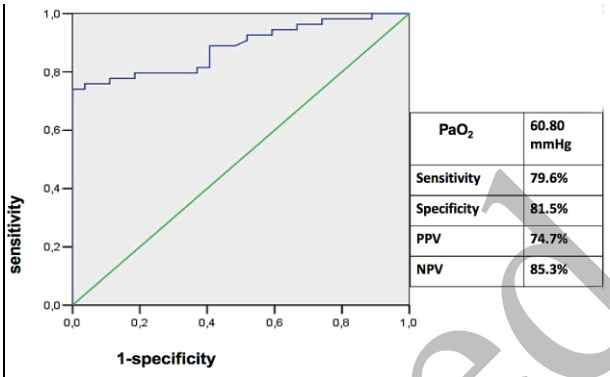


Figure 4. ROC-curve of PaO_2 on the third date, as a lethality predictor.

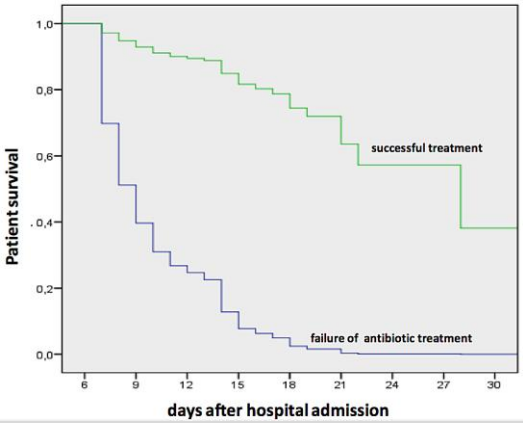


Figure 5. Effect of the adjustment to the antibiotics therapy on the survival rate of the pneumonia patients.

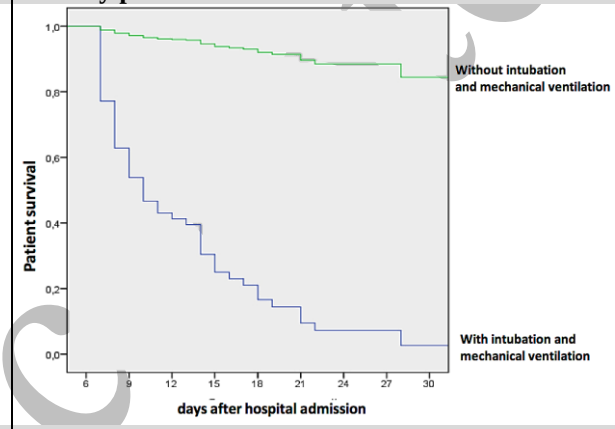


Figure 6. Effect of the mechanical ventilation on the survival rate of the pneumonia patients.

There was a statistically significant difference in the localization of the x-ray alterations between the two groups (p<0.001). The predominant radiological findings in pneumonia (–) group were bilateral changes. They increased the risk of fatal outcome (HR=2.482; 95% CI, 1.439–4.279; p=0.001).

A failure of the antibiotic treatment administered and a need to re-evaluate it was determined in 21(25.3%) of the recipients in pneumonia (+) group and 38(92.68%) of the patients in pneumonia (–) group. The two groups differ statistically (p<0.001) (Figure 5).

In the pneumonia (–) group, 3recipients (7.31%) were subjected to non-invasive ventilation (NIV) and 31(75.61%) –to invasive ventilation. In the pneumonia (+) group 7 patients (8.43%) were subjected to NIV and 2(2.41%) - to invasive (p<0.001). The effect of the need of intubation and mechanical ventilation on the survival rate of the pneumonia patients is shown on figure 6.

Table 2. Indicators for the assessment of the fatal outcome risks.

Indicator	HR	95% CI	*p*
0 month after renal transplantation	2.027	1.092–3.761	0.025
1–6 month after renal transplantation	2.303	1.104–4.803	0.026
Dyspnoea	2.184	1.239–3.849	0.007
Hypoxemia	2.261	1.314–3.890	0.003
Bilateral radiological changes	2.480	1.439–4.279	0.001
Failure of initial antibiotic therapy	3.548	2.418–5.205	< 0.001
Intubation and mechanical ventilation	4.635	2.276–9.437	< 0.001

The risk factors for an in-hospital fatal outcome of pneumonia in patients after renal transplantation are detailed in table 2.

DISCUSSION

The frequency of pneumonia, reported after RTvaries from 2.9% to 30%, as these are the lowest rates, compared to the other organ transplants [11, 12]. The mortality rate, resulting from pneumonia, according to our results is 33.06%. The available literature provides inconsistent data on the mortality of pulmonary infections. Some authors report a rate of 15-20% [13]. Other studies show mortality rates of 21–35%, as there are certain differences between the mortality from pneumonia, acquired in public - 8%, and the Hospital-acquired (nosocomial) cases - 58%, respectively [14, 15].There is a statistically significant dependency between the period of developmentof the pulmonary infection and the outcome of the disease ($p<0.001$). The lethal outcome from pneumonia depends on the period after transplantation, when the infection develops [16]. The mortality rate is higher among patients, acquiring pneumonia in the early post-transplant period or 1^{st}–6^{th} months after surgery. The development of pneumonia during the early postoperative period (0–1^{st} month) increases the lethal outcome risk 2.027-fold (HR=2.027; 95% CI, 1.092–3.761; p= 0.025). The development of pneumonia in the 1^{st} – 6^{th} month after surgery increases the risk of an unfavourable outcome 2.303 times (HR=2.303; 95% CI, 1.104–4.803; p= 0.026). At the same time, most of the successfully treated patients developed pneumonia in the late post-transplant period.

The clinical symptoms of pneumonia do not differ from those in immunocompetent patients. The prevailing complaints of patients with fatal outcome were dyspnoea. A statistically significant dependency between the outcome of the pneumonia and the presence of dyspnoea at admission was determined (p=0.033).The dyspnoea increases the risk of unfavourable outcome 2.184 times (HR=2.184; 95% CI, 1.239–3.849; p=0.007).

The analysis of the laboratory indicators revelead the typical changes in the infection markers, also observed in immunocompetent patients with pneumonia – increased CRP, leukocytosis with neutrophilia, lymphopenia, monocytosis. Also observed are a slight anaemic syndrome, increased levels of creatinine and fibrinogen. Statistically significant differences between the values of the laboratory results in the groups of patients, according to the pneumonia outcome, were observed only to the CRP and lymphocytes. The analysis of the CRP ROC curve shows that CRP at 44mcg/L reveals the highest sensitivity - 74.1% and specificity - 70.4% as fatal outcome predictors. In multivariate analysis, Diadar and al. also found that high CRP is associated with significant risk for death from pneumonia [17].

Patients with post-RT pneumonia show increased rates of hypoxemia. At the same time the low levels of PaO_2 at admission or in the course of treatment, is risk factor for a fatal outcome of the pneumonia [18]. Our results shows that the ABGs analysis at admission revealed hypoxemia in 85.37% of the patients, who subsequently died (p=0.001). PaO_2 values, below the normal range,

increase the risk of a fatal outcome 2.261 times (HR=2.261; 95% CI, 1.314–3.890; p=0.003). According to the ROC-analysis, the PaO_2 level of 64.70mmHg has both the highest sensitivity and specificity (63.0%), as a predictor of a fatal outcome. If PaO_2 is observed dynamically, hypoxemia was determined in 95.12% of the deceased patients (p<0.001) on the third day of treatment. The analysis of the ROC curve on the third day of treatment showed a PaO_2 of 60.80mmHg with very high sensitivity – 79.6% and specificity- 81.5%, as predictors of a fatal outcome. These results coincide with the manuals, prepared so far, where PaO_2 values below 60mmHg are considered a risk factor for a fatal outcome of pneumonia.

Several previous studies showed that multilobar radiographic pulmonary infiltrate were significantly associated with mortality [19, 20]. In our study the x-ray changes have diverse localization, as the presence of bilateral infiltrates increase the risk of a fatal outcome 2.482 times (HR=2.482; 95% CI, 1.439–4.279; p=0.001).

The early initiation of the treatment with appropriate antibiotics is of great importance for the outcome of pneumonia after renal transplantation. In the case of therapy failure risk of mortality increased significantly [21-23].

According our results a failure of the originally started antibiotics treatment and its subsequent revaluation in the course of treatment was observed in 92.68% of the patients in pneumonia (–) group (p<0.001).The need of adjustment to the antibiotics therapy increases the risk of a fatal outcome 3.548 times (HR=3.548; 95% CI, 2.418-5.205; p<0.001).

With view of the occurring complications in the course of the pneumonia, some patients had to undergo non-invasive or invasive ventilation. The mechanical ventilation increases the risk of a fatal outcome in patientswith pneumonia. This fact has been confirmed in numerous studies, carried out previously [15, 24, 25].The prolonged mechanical ventilation is mentioned in a number of publications, as the main risk factor for the development of nosocomial pneumonias [14,15]. At the same time, in recent years a significant volume of data has been accumulated on the role of the NIV in the treatment of acute respiratory insufficiency in immunosuppressed patients [26]. A randomized study of Antonelli and al., involving 25 patients post RT, showed that the NIV, due to hypoxemic respiratory failure, significantly reduced mortality rates (p=0.05) [27]. Hilbert and al. report of a lower rate of use of intubations (46% compared to 77%) and lower mortality rate (50% compared to 81%) (p≤ 0.05for both) among immunocompromised patients with acute respiratory failure and NIV, compared to those observed in conventional treatment [28].

The results of our study are similar to the previous publications. We have established a statistically significant relation between the outcome of the disease and the type of ventilation administered (p<0.001). The group of the recovered patients is dominated by those with non-invasive ventilation- 7 kidney recipients (8.43%). In the pneumonia (–) group 75.61% (31 patients) had been intubated and mechanical invasive ventilation had been administered to them. The need of intubation and mechanical ventilation increases the risk of a fatal outcome 4.635 times (HR=4.635; 95% CI,

2.276–9.437; p<0.001). Most patients on NIV recovered. At the same time the NIV is not statistically significant for the outcome of the disease. The results are probably due to the small number of patients, treated with NIV.

The markers of inflammation, hypoxemia and hypocapnea from the ABGs analysis, as well as the bilateral infiltration changes, shown by the radiological tests of the lungs may be used as predictors for the outcome of the disease and the occurrence of complications. The need of revaluation of the antibiotics treatment in the course of the disease is an independent risk factor for the developmentof complications and a fatal outcome. That fact may be used when determining the high-risk groups of renal recipients with pneumonia, requiring increased attention and strict control in the course of treatment.

Our study has not determined any factors, associated with increased risk of development of pneumonia. No comorbidities, which may have an aggravating effect on the course of the pneumonia, have been taken into account. No long-term evaluation of the survival rate after pneumonia in this group of patients has been made. We studied only in-hospital death and did not analyse the mortality after that.

CONCLUSIONS

Based on the results that we have obtained, it is possible to prepare an algorithm with prognostic factors, associated with more severe course of the pulmonary infections and an increased risk of the occurrence of complications and a fatal outcome. This makes it possible to differentiate a high-risk group of patients, requiring early etiological diagnosis or strict control of the condition, in order to reduce the mortality from pneumonia after renal transplantation.

REFERENCES

1. Dupont LJ, Verleden GM. Pulmonary Manifestations of Systemic Diseases. European Respiratory Society Monograph 2006; 34: 202–19.
2. Edelstein CL, Jacobs JC, Moosa MR. Pulmonary complications in 110 consecutive renal transplant recipients. S Afr Med J. 1995; 85: 160–163.
3. Caetano MP, Vaz AP, Castro FI, Bustorff M, Damas C. Lung and renal transplantation. Rev Port Pneumol. 2009; 15: 1073.
4. Duncan MD, Wilkes DS. A Review of Immunosuppression and Pulmonary Infections. Proc Am Thorac Soc. 2005; 2(5):449–455.
5. Fishman JA. Infection in Solid-Organ Transplant Recipients. N Engl J Med 2007; 357: 2601–14.
6. Vinod PB, Sharma RK. Opportunistic infections (nonCMV) in live related renal transplant recipients. Indian J Urol. 2009; 25: 161–8.
7. Parasuraman R, Yee J, Karthikeyan V, del Busto R. Infectious Complications in Renal Transplant Recipients. Adv Chronic Kidney Dis. 2006; 13(3): 280–94.
8. 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(2): 551–3.
9. Ingsathit A, Avihingsanon Y, Rattanasiri S, Premasathian N, Pongskul C, Jittikanont S et al. Different etiologies of graft loss and death in Asian kidney transplant recipients: a report from Thai Transplant Registry. Transplant Proc. 2010; 42(10): 4014–6.
10. Sousa SR, Galante NZ, Barbosa DA, Pestana JO. Incidence of infectious complications and their risk factors in the first year after renal transplantation. J Bras Nefrol. 2010; 32(1):75–82.
11. Gavalda J, Len O, San Juan R, Aguado JM, Fortun J, Lumbreras Cet, al. Risk factors for invasive aspergillosis in solid-organ transplant recipients: a case-control study. Clin Infect Dis. 2005; 41(1): 52–9.

12. Kutinova A, Woodward RS, Ricci JF, Brennan DC. The incidence and costs of sepsis and pneumonia before and after renal transplantation in the United States. Am J Transplant. 2006; 6(1): 129–39.
13. Briggs JD. Causes of death after renal transplantation. Nephrol. Dial. Transplant. 2001; 16 (8): 1545–9.
14. Alangaden G, Thyagarajan R, Gruber S, Morawski K, Garnick J, El-Amm JM et al. Infectious complications after kidney transplantation: current epidemiology and associated risk factors. Clin Transplant. 2006; 20(4):401–9.
15. Bonatti H, Pruett TL, Brandacher G, Hagspiel KD, Housseini AM, Sifri CD, et al. Pneumonia in solid organ recipients: spectrum of pathogens in 217 episodes. Transplant Proc. 2009; 41(1): 371–4.
16. Aguilar-Guisado M, Givaldá J, Ussetti P, Ramos A, Morales P, Blanes M, et al. Pneumonia After Lung Transplantation in the Resitra Cohort: A Multicenter Prospective Study. Am J Transplant. 2007; 7(8): 1989–96.
17. Diadar OS, Ersoy A, Akalin H. Pneumonia after kidney transplant: incidence, risk factors, and mortality. Exp Clin Transpl. 2014; 12 (3): 205–11.
18. Sanz F, Restrepo MI, Fernández E, Mortensen EM, Aguar MC, Cervera A, et al. Hypoxemia adds to the CURB-65 Pneumonia severity score in hospitalized patients with mild pneumonia. Respir Care. 2011; 56: 612–618.
19. Fine MJ, Smith MA, Carson CA, Mutha SS, Sankey SS, Weissfeld LA, et al. Prognosis and Outcomes of Patients With Community-Acquired Pneumonia A Meta-analysis. JAMA. 1996; 275(2): 134–41.
20. Cisneros JM, Muñoz P, Torre Cisneros J, Gurgui M, Rodriguez Hernandez MaJ, Aguado Jma, et al. Pneumonia After Heart Transplantation: A Multiinstitutional Study. Clinical Infectious Diseases. 1998; 27: 324–31.
21. Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, et al. Infectious Diseases Society of America, American Thoracic Society; Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis. 2007; 44 Suppl 2: S27.
22. Menéndez R, Torres A, Zalacaín R, Aspa J, Martín Villasclaras JJ, Borderías L, et al. Risk factors of treatment failure in community acquired pneumonia: implications for disease outcome. Thorax. 2004; 59(11): 960.
23. Oster G, Berger A, Edelsberg J, Weber DJ. Initial treatment failure in non-ICU community-acquired pneumonia: risk factors and association with length of stay, total hospital charges, and mortality. J Med Econ. 2013; 16(6): 809–19.
24. Cervera C, Agusti C, Angeles Marcos M, Pumarola T, Cofan F, Navasa M, et al. Microbiologic features and outcome of pneumonia in transplanted patients. Diagn Microbiol Infect Dis. 2006; 55(1): 47–54.
25. Liu H, Ye QF, Wan QQ, Zhou JD. Predictors of mortality in solid-organ transplant recipients with infections caused by Acinetobacter baumannii. Ther Clin Risk Manag. 2015; 11: 1251–7.
26. Garpestad E, Brennan J, Hill NS. Noninvasive ventilation for critical care. Chest. 2007; 132: 711–20.
27. Antonelli M, Conti G, Bufi M, Costa MG, Lappa A, Rocco M, et al. Noninvasive ventilation for treatment of acute respiratory failure in patients under-going solid organ transplantation: a randomized trial. JAMA. 2000; 283: 2239–40.
28. Hilbert G, Gruson D, Vargas F, Valentino R, Gbikpi-Benissan G, Dupon M, et al. Noninvasive ventilation in immunosuppressed patients with pulmonary infiltrates, and acute respiratory failure. N Engl J Med. 2001; 344: 481–7.

