## Original article

# Lung Cancer in Renal Transplant Recipients

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## Abstract

**Introduction.** Although the incidence of malignancy has increased after solid organ transplantation, data on lung cancer in this group of patients is scarce. The aim of this study was to determine clinical characteristics and outcome of patients who developed lung cancer after renal transplantation.

**Methods.** Among a cohort of 1658 patients who received a transplant at our institution and were followedup between 1973 and 2014, five patients developed lung cancer. We analyzed risk factors, transplantation characteristics, treatment options and survival.

**Results.** Lung cancer was diagnosed in 5 patients (0.3%). Time to diagnosis after the transplant procedure ranged from 26 to 156 months (mean 115 months). All of them had a smoking history. Tumors were classified as IIB (20%), IIIA (40%), and IV (40%). Histological types included adenocarcinoma (80%) and there was one case of sarcomatoid carcinoma (20%). One patient had concomitant thyroid papillary carcinoma. Radiotherapy was applied in 2 patients, 2 underwent chemotherapy (erlotinib and combination of carboplatinum and etopozide in one patient each), and 2 died within one month after the diagnosis from disseminated malignant disease. Patients with stage IIIA survived 14 and 24 months after the diagnosis. The patient with sarcomatoid cancer underwent thoracotomy with a complete resection, lost his graft function and died 7 months after the diagnosis.

**Conclusion.** Lung cancer is relatively rare malignancy in renal transplant recipients, but associated with high mortality. Smoking is a significant risk factor, thus smoking cessation should be promoted among renal transplant recipients, as well as regular screening for lung cancer.

Keywords: lung cancer, kidney transplantation, smoking

## Introduction

Renal transplantation is a life-prolonging treatment for end-stage kidney disease patients, but it increases risk for developing cancer, mostly because of medications administered to suppress the immune system and prevent rejection of the organ [1-4]. In developed countries most common posttransplant malignancies are skin cancer, Kaposi's sarcoma, renal and thyroid cancer and lymphoproliferative disorders [5,6]. Although the incidence of malignancy has increased after solid organ transplantation, data on lung cancer in this group of patients is scarce.

The aim of this study was to determine clinical characteristics and outcome of patients who developed lung cancer after renal transplantation.

## Materials and methods

In this retrospective study, hospital files of 1658 renal transplant recipients who received renal allograft at the University hospital centre Zagreb between 1973 and 2014 were reviewed. We obtained data about smoking history, dialysis vintage, type of immunosuppression, time after transplantation until development of malignancy, tumor classification, histological type, treatment approach and outcome.

Descriptive statistical analysis was used. Data were compared with results from other countries.

## Results

## Patients' characteristics, treatment and outcome

Among a cohort of 1658 patients who received a transplant at our institution and were followed-up between 1973 and 2014, 5 patients developed lung cancer. Time to diagnosis after the transplant procedure ranged from 26 to 156 months (mean 115 months). All patients who developed lung malignancy had a long-term (more than 20 years) smoking history.

Immunosuppressive protocol included cyclosporine in 3 and tacrolimus in 2 patients, with mycophenolate mofetil and steroids. Three patients received basiliximab induction, two were transplanted without induction.

Tumors were classified as IIB (one patient), IIIA (two patients), and IV (two patients). Histological types included adenocarcinoma (n=4; 80%) and there was one case of sarcomatoid carcinoma (n=1; 20%). One patient had concomitant thyroid papillary carcinoma.

Treatment protocol varied depending on the severity of disease. Two patients were treated with radiotherapy, and two with chemotherapy (erlotinib in one patient, and a combination of carboplatinum and etopozide in the other). The patient with sarcomatoid carcinoma was treated with thoracotomy with complete resection. The outcome was poor. Two patients died one month after the diagnosis. Patients with stage IIIA survived 14 and 24 months after the diagnosis. The patient with sarcomatoid cancer had lost his graft function and died 7 months after the diagnosis.

All patients refused to stop immunosuppressive treatment and undergo graphtectomy. They were switched from cyclosporine or tacrolimus to mTOR-based immunosuppressive protocol.

#### Lung cancer in national registries or studies

Few studies have focused on lung cancer in renal transplant recipients. In Table 1 we present the incidence in transplant population in Croatia and other countries.

 Table 1. Incidence of lung cancer in transplant recipients in different countries [7-10]

Country	Our cohort	Turkey	China	England	Australia	New Zealand
Number of	1.658	4 000	3 462	25 104	3 1 29 083	605 538
recipients	1 050	4 000	5 402	25 104	5 129 085	005 558
Time interval	41	45	40	27	11	11
(years)	11	1,5	10	21	11	11
Incidence (%)	0.3	6	0.8	1.4	1.2	1.3

#### Discussion

The incidence of lung cancer has been particularly increased in recipients of heart and lung transplants, which may be related to the strong influence of cigarette smoking on the development of heart and lung diseases [11]. However, lung cancer may complicate posttransplant course after renal transplantation as well.

This study demonstrates that in our cohort of renal transplant recipients lung cancer is relatively rare malignancy, but has high mortality rate. Patients were diagnosed at advanced stage.

In the general population, non-small cell lung cancer accounts for about 85% of lung cancers and includes: adenocarcinoma which is the most common form of lung cancer among both genders; squamous cell carcinoma which accounts for approximately 25%, and large cell carcinoma which accounts for 10% of non-small cell lung malignancies. The remaining 15% of lung cancers are small lung cancer. Four patients from our cohort had non-small cell cancers and one was diagnosed with sarcomatoid carcinoma.

Significant differences may be noted among different countries. Based on data from the Croatian registry of malignant diseases in the general population, there were 2031 new cases of lung cancer in males and 722 in females in 2013. In the general public, lung cancer is the most common cancer in males, and third in females after breast and colorectal cancer, with the crude rate for males 98.3; for females 32.6, while total crude rate is 64.2 [12]. Thus, lung cancer that is frequent in the Croatian general population is rare in renal transplant population in our cohort of patients. Turkey has a very

high prevalence of lung cancer among renal transplant recipients, while Croatia and China have low prevalence [7,8].

#### Conclusion

All patients who developed lung malignancy continued with smoking after transplantation despite the warnings from nephrologists. Since smoking represents the leading risk factor for development of lung malignancy we should encourage patients to quit smoking, and promote a screening program in this population for early discovery of lung cancer, with annual chest X-rays.

Conflict of interest statement. None declared.

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