Incidence and Mortality by Cancer in Patients After Lung Transplantation in a Brazilian Institution

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ABSTRACT

Background. The first human lung transplantation was performed by James Hardy in 1963 due to lung cancer. Currently, malignancy has its importance in the follow-up of transplanted patients because cancer risk is higher in this population and the main risk factor for this augmentation is immunosuppression. The most common types of cancer are non-melanoma skin cancer and post-transplantation lymphoproliferative diseases. The objective of this study is to measure the cancer incidence and its related mortality in lung-transplanted patients of a Brazilian institution.

Methods. Review of the records of the 263 patients who underwent lung transplantation between April 2000 and April 2016 at the Heart Institute (InCor), focusing on the incidence of cancer, most common types of malignancies, and cancer mortality rate. We compared incidence and mortality with the International Society for Heart and Lung Transplantation (ISHLT) database.

Results. During the 16-year period, the total incidence of cancer was 10.3% with 27 cases diagnosed in 21 patients. The most common types of cancer were non-melanoma skin cancer, prostate cancer, and post-transplantation lymphoproliferative diseases. Comparing the incidences after 1-year, 5-year, and 10-year follow-up with the ISHLT database, they were similar in the first two periods and higher in the third period. As to cancer mortality rate, it was similar to the ISHLT database in both periods analyzed.

Conclusion. The incidence of malignancies was higher in our transplanted patients in comparison with the Brazilian population, and the most frequent types of cancer are in accordance with the literature, except for prostate cancer. Cancer mortality rate was similar to that from the ISHLT database.

THE FIRST human lung transplantation was performed by James Hardy in 1963 on a 58-year-old man with carcinoma of the left main-stem bronchus and secondary obstructive atelectasis [1]. Currently, only 0.1% of pulmonary transplantations are performed due to cancer [2]. In fact, malignancies in transplanted patients are a matter of concern in the postoperative follow-up, whereas national cohort studies have shown an increased risk of cancer in this population [3–5]. There is an increase in both infection-related and unrelated cancers and immunosuppression is the main risk factor. The relation between augmented cancer rate and immunosuppression is also observed in immunosuppressed patients for other reasons, such as HIV infection and acquired immunodeficiency syndrome (AIDS) [6]. The malignancy risk, mainly post-transplantation lymphoproliferative diseases (PTLD), is proportional to the level of immunosuppression and is greater after transplantation of intrathoracic organs [7–9].

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The incidence of cancer on post-transplantation follow-up is approximately 4% to 4.8% in the first 5 years, and the two most common malignancies are non-melanoma skin cancer and PTLDs [2,7]. Lung cancer risk is higher after pulmonary transplantation, especially when performed unilaterally, in the native lung [7].

The objective of this study was to determine the incidence and mortality by cancer in the patients who underwent lung transplantation at the Heart Institute/Brazil (InCor), as well as a brief review of malignancies in the lung transplanted population.

MATERIALS AND METHODS

We reviewed the records of the 263 patients who had undergone unilateral or bilateral lung transplantation at InCor (Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, Sao Paulo, Brazil) from April 2000 to April 2016, regarding its epidemiology, the incidence of cancer in this population, as well as the most frequent types of cancer. We evaluated the total incidence in the 16-year period and the cumulative incidence in 1-year, 5-year, and 10-year follow-up. The cancer mortality rate was measured in the same period. We compared both incidence and cancer mortality with the 2015 International Society for Heart and Lung Transplantation (ISHLT) database.

RESULTS

During the 16-year period from 2000 to 2016, the total cancer incidence measured was 10.3%, with 27 cases diagnosed in 21 patients. The most common types of cancer were non-melanoma skin cancer (14 cases, 51.9%), prostate (4 cases, 14.8%), and PTLD (3 cases, 11.1%). Other less common types of cancer, each one with one case diagnosed, were lung, tongue, colon, acute myeloid leukemia, multiple myeloma, and melanoma (Fig 1). The baseline demographics of our group of transplanted patients are shown in Table 1, containing the distribution of types of transplant and sex, the median age at transplantation, and number of years between the surgical procedure and the first diagnosis of cancer. The median age was higher in the transplanted patients diagnosed with cancer when compared to the total population who had undergone the surgical procedure (median age 43.5 years; range, 6 years to 71 years).

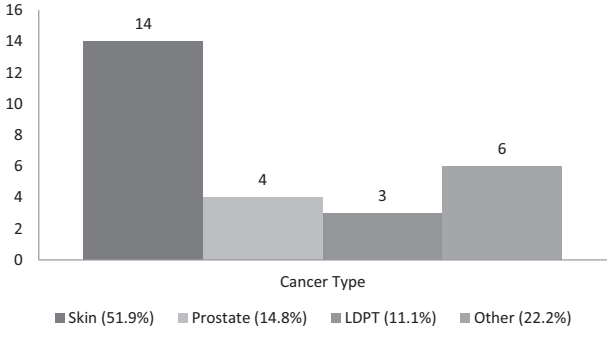

Fig 1. Total number of cases of malignancy in transplant recipients, divided by types of cancer.

Table 1. Baseline Demographics of the Transplanted Population

Characteristic	Number (%)	Median (Range)
Type of transplant		
Unilateral	6 (28.6)	–
Bilateral	15 (71.4)	
Sex		
Male	17 (81.0)	–
Female	4 (19.0)	
Age, years	–	56 (20–65)
Years after transplantation	–	3 (0–10)

Comparing the cancer incidence at our institution with the ISHLT database, it is shown that our data regarding the 1-year and 5-year survivals on follow-up are similar; however, our incidence is higher in the 10-year survival group (Table 2).

As to cancer mortality, we observed two deaths due to malignancy, the first one occurred less than 1 year after the transplantation (247 days) and the second one after 9 years of transplantation. Our cancer mortality rates were compared with the ISHLT database (31 days-to-1-year and 5-years-to-10-years periods), and they were similar in both periods analyzed (Table 3).

DISCUSSION

In the beginning of lung transplantation in 1963, lung cancer was the indication for the procedure. Currently, the performance of transplantations due to lung carcinoma compose a small percentage of cases, in which the main indication of transplantation is multifocal minimally invasive or in situ lung adenocarcinoma [10]. Cancer is now a matter of concern in the postoperative follow-up because its incidence is augmented in the transplanted population, and immunosuppression acts as the main risk factor, whereas higher cancer incidence is observed in immunosuppressed patients for other reasons, such as HIV infection and AIDS.

Several types of cancer, infection-related or not, have their incidence magnified, and the two most common types observed in lung-transplanted patients are non-melanoma skin cancer and the PTLDs. When we parallel cancer incidence in our patients and the 2016 estimated rate of de novo malignancies in the Brazilian population [11], it is remarkable the higher number of cases of cancer in the transplanted population (10.3% versus 0.3%), corroborating with the higher risk of malignancy in immunosuppressed patients described in the literature. As well as this incidence, the most common types of cancer diagnosed in our patients, non-melanoma skin cancer and PTLDs, are also most common according to the literature.

Non-melanoma skin cancer is the most frequent type diagnosed, as observed in our population of transplanted patients, and the risk of skin cancer is higher after lung transplantation when compared with other solid-organ