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Epidemiological changes in the histological subtypes of 35,018 non-small-cell lung cancer cases in Brazil

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ABSTRACT

Objectives: Regarding the fatality rates stemming from various existing forms of cancers worldwide, lung cancer (LC) is ranked as the main cause of death amongst those who suffer from cancer. Although the epidemiological, clinical, and histological profile of patients with this type of cancer is largely unknown, Brazil has made tremendous efforts to generate data for supporting healthcare policies concerning lung cancer. Taking these factors into account, this study aims to analyse the epidemiological, clinical, and histological profiles of patients with non-small-cell lung cancer (NSCLC) in Brazil.
Material and methods: For this study, a cross-sectional epidemiological study was conducted to nationally analyse patient's data within the cancer hospital registries found in the National Cancer Institute (INCA) and the São Paulo Cancer Foundation (FOSP) between 2000 and 2011.
Results: A total of 35,018 patients diagnosed with NSCLC in Brazil between 2000 and 2011 were analysed. The analysis demonstrated the occurrence of an epidemiological shift, related to the most prevalent histological type of NSCLC in the study population from 2003. The shift resulted in a higher percentage of adenocarcinoma (43.3%) over squamous cell carcinoma (36.5%). Additionally, there was a significant increase in both the number of cases of LC in women and in the rates of patients diagnosed with metastatic disease.
Conclusion: The use of filtered cigarettes since the 60's and the increase in the number of LC cases in women, were one of the causes for the switch in the histological profile of NSCLC in Brazil. Consequently, adenocarcinoma is now the predominant type of cancer detected. Late diagnosis is a hallmark sign.

1. Introduction

When considering the main causes of death among cancer patients worldwide, lung cancer is the leading cause of cancer-related mortality; with an estimated 1.82 million individuals dying annually from this malignant neoplasm [1]. In the United States alone, it is estimated that approximately 221,200 patients were diagnosed with LC in 2015 [2]. In South America, the lowest incidence rates adjusted per age were recorded in Cuenca, Ecuador; constituting 2.2/100,000 for women and 5.0/100,000 for men. The highest incidence rate recorded within the South American context was in Antofagasta, Chile; constituting 19.4/100,000 for women and 55.9/100,000 for men [3]. In Brazil, LC is the second most common type of cancer in males; with 17,330 new estimated cases found in 2016. Moreover, lung cancer is the fourth most common type of cancer found in females; with 10,890 new cases reported within that same year. This form of cancer is responsible for the greatest number of deaths caused by cancer in the country; with 23,501 of them occurring in 2012 [3]. In terms of treatment, cancer treatment is provided free of cost throughout the whole country by the National Health System: the Sistema Único de Saúde (SUS); whilst, some 25% of the population have private health insurance, even if facilities throughout the country are distributed disproportionately.

Consequently, the high LC incidence rates worldwide, is due to tobacco use and its derivatives. A possible explanation for the changes in the number of lung cancer cases by histology could be correlated to changes in smoking habits, the use of filtered cigarettes, a reduction in the number of smokers, and gender differences. In Brazil, a reduction has been noted in the prevalence of smoking. Nevertheless, 16% of the Brazilian adult population

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continue to smoke, in spite of governmental agencies' efforts, through policies to restrict cigarette advertisement and sales [2,4].

Respectively, LC has been divided into two main groups: small-cell lung cancer (SCLC) and non-small-cell lung cancer (NSCLC); with the latter being subdivided into adenocarcinoma (ACA), squamous cell carcinoma (SCC), and undifferentiated/large cell carcinoma (LCC). Changes in histological patterns in smokers and males from predominantly SCC to predominantly ACA, were reported in several countries [5,6,8,9–11]. The histological type plays a role in defining the appropriate type of systemic treatment that should be implemented with the largest therapeutic arsenal being available for ACA; mainly in terms of targeted chemotherapy [7].

However, there is still a considerable lack of highly detailed epidemiological data on LC in developing countries. In Brazil, measures within the Ministry of Health, led by the Brazilian Network for Clinical Cancer Research, were taken to generate data to support healthcare policies regarding LC [12]. Within this context, the objective of the present study was to characterise the epidemiological, clinical, and histological profile of patients with NSCLC in Brazil between 2000 and 2011.

2. Materials and methods

A cross-sectional retrospective study was conducted on LC patients using data from the cancer hospital registries (CHR) found in the National Cancer Institute (INCA) and the São Paulo Cancer Foundation (FOSP) between 2000 and 2011, encompassing a total of 258 hospitals in the 25 states of Brazil and the Federal District (Brasília). In conjunction, these registries cover about 90% of the Brazilian public health system; where they have been progressively implemented through the entire country overtime. However, it is still difficult to estimate exactly how complete the case ascertainment is. By using histologic codes from the International Classification of Diseases for Oncology (ICD-O-3) [13], the following primary incident cancers of the bronchus and lung (ICD 34.0–34.9) were considered for the present analysis: ACA (8140, 8250, 8251, 8252, 8253, 8254, 8255, 8260, 8310, 8323, 8480, 8481, 8490, 8550), SCC (8050, 8070, 8071, 8072, 8073, 8074, 8075), Undifferentiated/LCC (8012, 8020, 8021, 8022, 8031, 8032) and small cell carcinomas (8002, 8041, 8042, 8043, 8044, 8045). From a total of 58954 cases of lung cancer registered in the period, 7512 carcinoma not otherwise specified (NOS), 5385 small cell carcinomas (8002, 8041, 8042, 8043, 8044, 8045), and 11039 cases with other histology types were excluded from this study. The percentage of carcinomas NOS remained practically unchanged throughout the period (12.9% in 2000 to 11.3% in 2012). All cases included in the study were microscopically verified.

In this study, we analysed the following variables: age groups (18–49 years, 50–69 years or ≥70 years), sex (male versus female), smoking (never smokers versus smokers/former smokers), schooling (0–7 years versus ≥8 years of schooling), and place of residence (considering the differences across the North, Northeast, Midwest, Southeast, and the Southern regions of Brazil), year of diagnosis (2000–2011), TNM staging according to the 5th (from 2000 to 2005) and 6th (from 2006 to 2011) editions (early disease – stages IA, IB, IIA and IIB; locally advanced disease – stages IIIA and IIIB; or metastatic disease – stage IV), the first line of treatment implemented (surgery, radiotherapy, chemotherapy or best support care), response to the first treatment, and death by the end of the initial treatment (death or survival).

The therapeutic response at the end of the first course of treatment was classified as either an inadequate response (progressive disease or death) or an adequate response (partial remission, stable disease, or complete response).

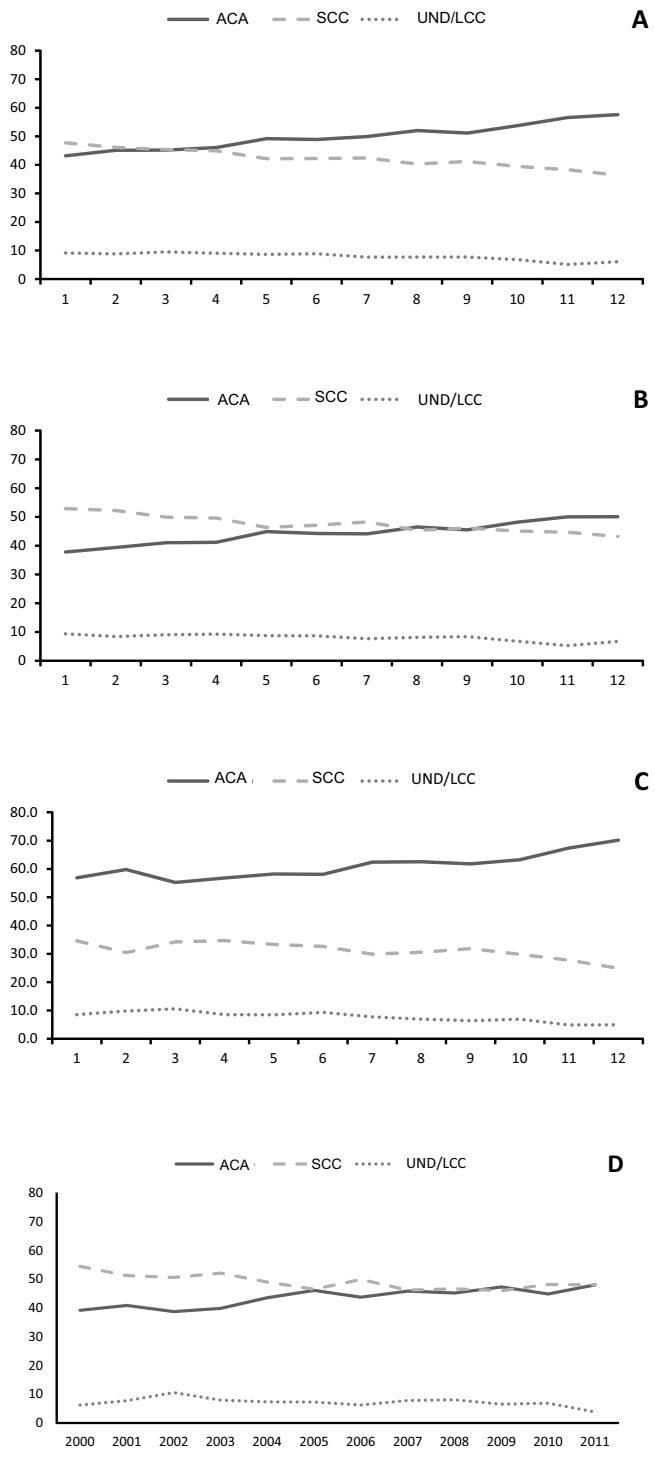

Fig. 1. Distribution of the histological types of non-small-cell lung cancer per year of diagnosis. Brazil, 2000–2011. A) All cases. B) Cases occurring in males. C) Cases occurring in females. D) Cases occurring in smokers/former smokers.

SPSS (Statistical Package for the Social Sciences) software, version 21.0, was used for the data analysis. A descriptive analysis was performed using central tendency and dispersion measures for the continuous variables and to determine the frequency distribution of the categorical variables. The chi-square test was used to compare the frequency of the categorical variables. The coefficient of determination was calculated to identify annual variations. Differences were considered to be statistically significant when the p-values were <0.05.