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ORIGINAL ARTICLES

Small cell lung cancer treatment and survival: a retrospective study at a brazilian public cancer referral center

Tratamento e sobrevida do câncer de pulmão de pequenas células: estudo retrospectivo em centro público de referência em oncologia brasileiro

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Abstract

Objective: To evaluate the characteristics, treatment received, survival, and prognostic factors of small cell lung cancer patients.

Methods: A retrospective cohort study was conducted at the reference a public cancer-center in Rio de Janeiro, Brazil. A total of 866 small cell lung cancer patients admitted in the period 2000-2020 participated in the study. Comparison between survival curves was performed by the log-rank test; variables whose p < 0.10 entered in the Cox regression models expressed as hazard ratios (HR) with 95% confidence intervals. The association between receiving best supportive care (none treatment) and admission period was evaluated by means of logistic regression.

Results: Median and 12-months survival were 6.2 and 23.7%, respectively. On multivariate Cox regression adjusted for treatment, poor (HR: 1.99; 1.57-2.51) and unknown performance status (HR: 2.79; 2.22-3.49), non-white skin color (HR: 1.25; 1.07-1.46), extensive (HR: 1.62; 1.29-2.04) and unknown staging (HR: 1.33; 1.07-1.65) remained associated with 12-months survival. Patients admitted during the last three admission period were nearly four times more likely to receive best supportive care in comparison to the first period.

Conclusion: The prognosis of small cell lung cancer is poor and the perspective toward increasing their survival is to improve the timely access to diagnosis and treatment.

Keywords: carcinoma, small cell lung, survival analysis, prognosis, retrospective studies.

Resumo

Objetivo: Avaliar características, tratamento recebido, sobrevida e fatores prognósticos de pacientes com câncer de pulmão de pequenas células.

Métodos: Estudo de coorte retrospectivo conduzido em um centro público de referência em oncologia no Rio de Janeiro, Brasil. Participaram 866 pacientes com câncer de pulmão de pequenas células admitidos no período 2000-2020. A comparação entre as curvas de sobrevida foi realizada pelo teste log-rank; as variáveis cujo p < 0,10 foram inseridas nos modelos de regressão de Cox que estimaram *hazard ratios* (HR) e intervalos de confiança de 95%. A associação entre receber o melhor tratamento de suporte (nenhum tratamento) e o período de admissão foi avaliada por meio de regressão logística.

Resultados: A mediana e a probabilidade de sobrevida em 12 meses foram de, respectivamente, 6,2 meses e 23,7%. Na regressão multivariada de Cox ajustada por tratamento, *performance status* ruim (HR: 1,99; 1,57-2,51) e desconhecido (HR: 2,79; 2,22-3,49), cor da pele não branca (HR: 1,25; 1,07-1,46), estadiamento avançado (HR: 1,62; 1,29-2,04) e desconhecido (HR: 1,33; 1,07-1,65) permaneceram

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associados à sobrevida em 12 meses. Pacientes admitidos nos últimos três períodos de admissão mostraram probabilidade quase quatro vezes maior de receber os melhores cuidados de suporte em comparação ao primeiro período.

Conclusão: O prognóstico do câncer de pulmão de pequenas células é ruim e a perspectiva para aumentar sua sobrevida é melhorar o acesso oportuno a diagnóstico e tratamento.

Palavras-chave: carcinoma pulmonar de células não pequenas, análise de sobrevida, prognóstico, estudos retrospectivos.

Introduction

Lung cancer is globally the third most common neoplasm, and it is responsible for most deaths attributable to cancer in the world (1). For therapeutic purposes, lung cancer is divided into two broad groups according to histopathological features: small cell lung cancer (SCLC) and non-small cell lung cancer. Although much advance has occurred in the histological and genomic subclassification of non-small cell lung cancer, SCLC remains a relatively homogeneous group associated with poor outcomes. Histologically, SCLC is a neoplasm of neuroendocrine origin, with typical histological features. On immunohistochemistry there is staining for chromogranin and synaptophysin, and it presents with a pattern of perinuclear staining for cytokeratins (2).

SCLC comprises 15% of all lung cancers and has very aggressive behavior. Most tumors have a central localization, with early involvement of mediastinal lymph nodes and high incidence of distant metastases, being the most common sites the bones, liver, adrenals and the central nervous system (2). The most important risk factor for SCLC is smoking, with over 90% of cases associated with heavy tobacco use (2,3). This behavior is positively associated with social vulnerability and lower educational levels (4). The staging is performed according to the American Joint Committee on Cancer guidelines (5), but for practical reasons most cases are divided into limited stage (a lesion amenable to a single radiation therapy field) or extensive stage (not amenable to a single radiation therapy field).

Despite the large advances in oncology in the last decade, outcomes for SCLC remained stable, with no substantial improvement in survival (6). Due to its aggressive behavior, only a few patients are candidates for curative-intent surgery, most patients are diagnosed with disease involving the mediastinum (locally advanced disease) or with distant metastatic disease. Those patients with limited stage are usually treated with a combination of chemotherapy (CT) and radiotherapy (XRT) (7), and those with extensive stage usually receive CT plus immunotherapy in scenarios where this is available or affordable. Some patients with good response to the initial treatment are candidates for prophylactic cranial XRT, to decrease the frequency and morbidity of brain metastasis.

For decades the mainstay of CT was the combination of cisplatin (or carboplatin) and etoposide. Later, there was the incorporation of topoisomerase I inhibitors in extensive disease (irinotecan replacing etoposide), or as second line treatment (topotecan), with no major improvement in outcomes. The introduction of immunotherapy (anti PD-1) for extensive disease led to some improvement in relapse free survival and overall survival, although the spectrum of patients that derive benefit is still limited and biomarkers failed to adequately select these responsive cases (2,8,9). However, many patients are diagnosed with poor clinical conditions that precludes any SCLC-directed treatment, for whom the only option is best supportive care (BSC).

In Brazil, more than 75% of people rely only on the public health services, organized in the whole country through the Unified Health System (*Sistema* Único *de Saúde*). In this system, individuals have their usual care at the primary care facilities (Family Clinics and Basic Unities of Health), those with conditions that were not controlled at this level are referred to higher-level facilities such as specialized clinics or even high complexity unities. Patients with lung cancer often present symptoms superimposable with those of pulmonary tuberculosis that is very common in this country, in addition, tobacco consumption is around 13% (10), placing Brazil in a position of relatively low consumption. Therefore, it is assumed that there

is some delay in diagnosis and treatment initiation of lung cancer in this country.

To comprehensively improve the care of patients with SCLC, it is important to assess the outcomes, the temporal trends related to the frequency of the disease and its presentation, and the impact of the interventions implemented for primary prevention, screening, diagnosis, and treatment. In this study we retrospectively evaluated the characteristics, treatment received, survival, and prognostic factors of SCLC patients admitted at reference a public cancer-center of Brazil, a middle-income country.

Methods

The Research Ethics Committee of the Brazilian National Cancer Institute waived the requirement for informed consent and approved this retrospective cohort study on February 12, 2021 (Protocol Number: 4.538.738). All cases with a histological diagnosis of SCLC (International Classification Disease topographical code C34 (11) and International Classification Disease for Oncology histological codes 8041/3, 8042/3, 8043/3, 8044/3, and 8045/3 (12)) admitted at the cancer-center, located in Rio de Janeiro city, in the period between 2000 and 2020 were included in this study.

Patient information was obtained from the hospital-based cancer registry database. Since Eastern Cooperative Oncology Group (ECOG) performance status (PS) is not systematically collected by the registry, efforts were made to retrieve this information through a review of patients' medical records. The ECOG PS scale is used to assess the functional status of oncology patients, particularly their ability to perform activities of daily living. Scores are assigned based on clinical observation by a healthcare professional, according to the following criteria: 0 = fully active, able to carry out all activities without restriction; 1 = restricted in physically strenuous activity but ambulatory and able to perform light or sedentary work; 2 = capable of self-care but unable to carry out work activities, ambulatory for more than 50% of waking hours; 3 = limited self-care, confined to bed or chair for more than 50% of waking hours; 4 = completely disabled, unable to perform any self-care and totally confined to bed or chair (13).

The hospital-based cancer registry gathers information related to demography (sex, age, declared skin color, school attainment), disease characteristics (topographical and histological diagnosis, staging, date of diagnosis, date of the inscription in the hospital), lifestyle (alcohol and tobacco consumption), patterns of the first treatment (surgery, XRT, CT, or the sequence/combination of treatments, date of the first treatment), and follow-up (relapse, death, last visit). The information was systematically collected from the patients´ files by non-medical professionals in standardized forms and imputed in a prespecified software (SisRHC®). Investigators had access to the data in a .xls format.

All statistical analyses were conducted using R software, version 4.2.2. For analytical purposes, skin color was dichotomized into white vs. non-white, school attainment was categorized as up to eight years vs. nine years or more, staging was grouped as limited disease vs. extensive disease (there were many cases of unknown disease extension). ECOG PS scores were categorized as good (0 - 1), poor (2 - 4), or unknown. Smokers and former smokers were grouped together. Treatment type was categorized as either BSC, any CT, any XRT, or a combination of both. Admission period was categorized into trienniums due to there was a change in the referral of patients to cancer-center starting from 2011, in which referrals began to be predominantly made through the High Complexity Regulation Center of Rio de Janeiro (14).

Overall survival was measured as the interval between the admission of the patient in the cancer-center to the last visit or death, since data on the date of diagnosis were missing in up to 25% of the cases. Survival curves were estimated by the method of Kaplan Meier. Comparison between survival curves was performed by the log-rank test. Variables whose $p < 0.10$ entered in the Cox regression models expressed as hazard ratios (HR) with 95% confidence interval (95%CI) adjusted by

age and treatment status (yes or no).

Since patients who received no SCLC directed treatment have a high risk of death in the first two months from admission in the hospital, and patients who receive any form of treatment have relatively low risk of death in the first two months, but have a higher risk in the following months, the assumption of proportionality of risks will be broken, we performed stratified proportional hazards analyzes according to treatment status. To respect the proportionality principia (Schoenfeld residuals), since most patients died in the first year after diagnosis, follow-up times were trunked at 12 and 24 months.

We also analyzed the association between receiving BSC and triennium of admission by means of logistic regression expressed as odds-ratio (OR); we set statistical significance as $p < 0.05$.

Results

In the period between 2000 and 2020, there were 866 patients diagnosed with SCLC admitted to the cancer-center for staging and treatment. Most patients were males, median age was 63 years, predominance of smokers, and most had low educational attainment (**Table 1**). Four hundred and seventy-one (54.4%) cases were treated until 2009. After 2016 there was a decrease in the referrals of SCLC patients, as well as a decrease in the proportion of patients with limited stage (22.2% of those with known status; n = 21).

TABLE 1 – Characteristics of the patients (N = 866)

Variables	n	%
Male sex	498	57.5
Skin color		
Non-White	277	32.0
White	582	67.2
Unknown	07	0.8
School attainment		
Up to 8 years	612	70.7
9 years or more	238	27.5
Unknown	16	1.8
Alcohol consumption		
Drinker	370	42.7
Former drinker	46	5.3
Non-drinker	267	30.9
Unknown	183	21.1
Tobacco consumption		
Smoker	670	77.3
Former smoker	105	12.1
Non-smoker	42	4.8
Unknown	49	5.8
Staging		
Limited	146	16.8

TABLE 1 – Characteristics of the patients (N = 866) (Cont.).

Variables	n	%
Extensive	284	32.8
Unknown	436	50.4
PS		
Good	151	17.4
Poor	320	37.0
Unknown	395	45.6
Any treatment*	666	76.9

PS, Performance status.
*Any treatment category includes any radiation therapy (n = 387), any chemotherapy (n = 592), any surgery (n = 10), and both radiation therapy and chemotherapy (n = 319).

With relation to PS, among the 471 cases whose data were available, the majority had poor PS. For patients with limited stage, the same proportion of patients had good and poor PS, for extensive stage, there were three times more patients with poor PS than with good PS (**Table 2**).

TABLE 2 – Absolute and relative frequencies of PS according to staging

PS	Limited	Extensive	Unknown	Total
Good	46 (31.5)	47 (16.5)	58 (13.3)	151 (17.4)
Poor	46 (31.5)	124 (43.7)	150 (34.4)	320 (36.9)
Unknown	54 (37.0)	113 (39.8)	228 (52.3)	395 (45.7)
Total	146 (100)	284 (100)	436 (100)	866 (100)

PS, Performance status.

Four hundred and thirty-six (50.3%) patients had histological diagnosis after admission, including 18 (2.1%) who had a biopsy performed on the day of admission. For those patients diagnosed at other facilities the median time between the diagnosis and admission was 14 (IQR: 7-28) days, while the median time from admission to biopsy was 21 (IQR: 12-37) days for those without a prior diagnosis. Until the third admission period (2006-2008), 269 (57.2%) cases were diagnosed only after admission, while 244 (62,0%) had the diagnosis performed before admission in the following periods.

With regards to the treatment, 666 (76.9%) patients received SCLC-directed treatment, being 456 (68.4%) any CT, 298 (44.7%) any XRT, and 245 (36.8%) cases received both CT and XRT as first treatment. On the other hand, 200 (23.1%) patients had no specific treatment, that is, received BSC only. The proportion of patients who received neither CT nor XRT increased during the period study, when analyzed according to the triennium of admission. The proportion of patients receiving BSC only was not stable throughout the period analyzed: it increased from 15.3% in 2011 - prior to the implementation of referrals through the High Complexity Regulation Center of Rio de Janeiro - to 35.2% from 2012 onwards, more than doubling over time. **Figure 1** shows that the patients admitted during the last three trienniums were nearly four times more likely to receive BSC in comparison to the first triennium ($p < 0.05$).

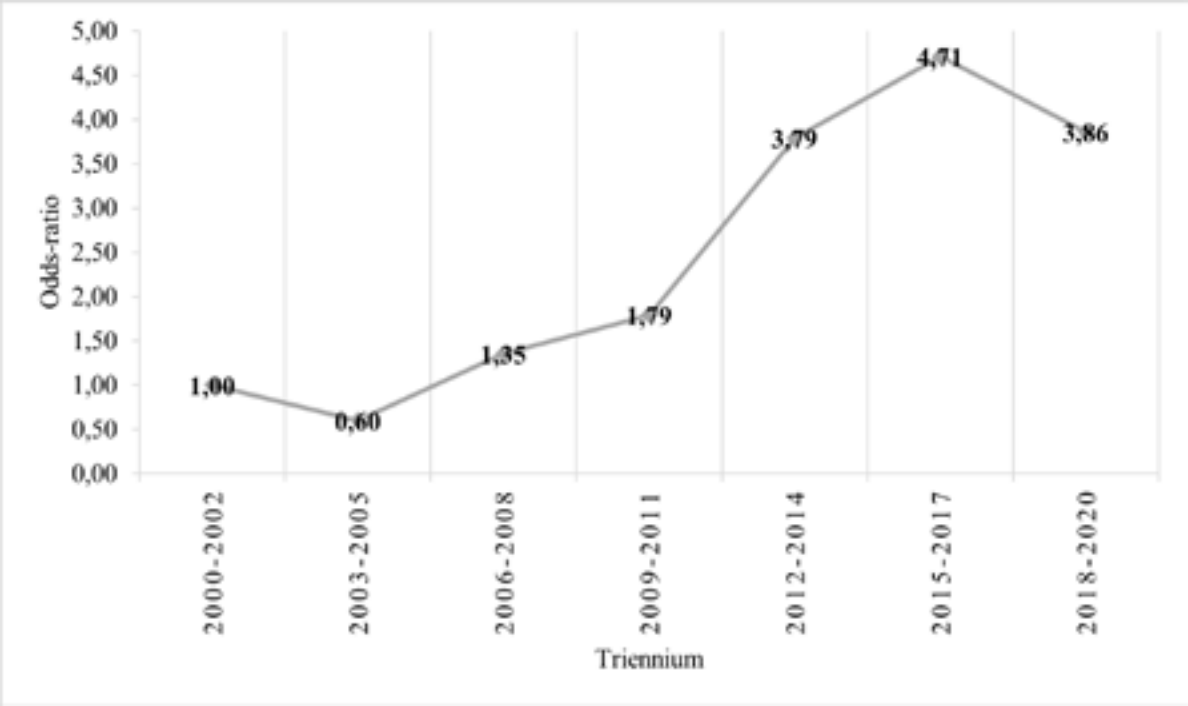


Figure 1 – Odds-ratio of receiving BSC according to triennium of admission. Patients admitted during the last three trienniums were nearly four times more likely to receive BSC compared with the first triennium ($p < 0.05$). BSC, best supportive care.

The median overall survival varied according to the triennium of admission to the cancer center: 8.1 (95%CI: 6.7-9.4) months from 2000 to 2002, 2.3 (95%CI: 1.8-4.3) months from 2012 to 2014, and 4.9 (95%CI: 1.7-7.6) months from 2018 to 2020. Among patients with good PS, the median overall survival was 13.7 months (95%CI: 12.3-16.8), decreasing to 9.3 months (95%CI: 7.0-12.3) among those who received any treatment within the same PS category. As shown in **Table 3**, when stratified by treatment, median survival among patients who received BSC was nearly nine times shorter than among those who received any treatment.

TABLE 3 – Survival according to patients' characteristics

Variables	Median (95%CI), months	12-month (95%CI)	24-month (95%CI)	*p**
All patients	6.2 (5.0-7.0)	23.7 (20.0-25.6)	8.5 (6.6-10.3)	
Sex				0.05
Female	6.5 (5.2-7.9)	29.2 (23.9-33.1)	9.5 (0.6-12.3)	
Male	5.9 (4.2-7.6)	19.7 (16.1-23.1)	7.8 (5.8-10.6)	
PS				< 0.01
Good	13.7 (12.3-16.8)	56.3 (48.5-64.4)	29.1 (21.9-36.4)	
Poor	5.9 (5.0-7.6)	22.5 (17.2-26.3)	5.6 (3.0-8.0)	
Unknown	3.8 (2.8-5.4)	12.2 (9.1-15.5)	3.0 (1.7-5.3)	
Skin color				0.07

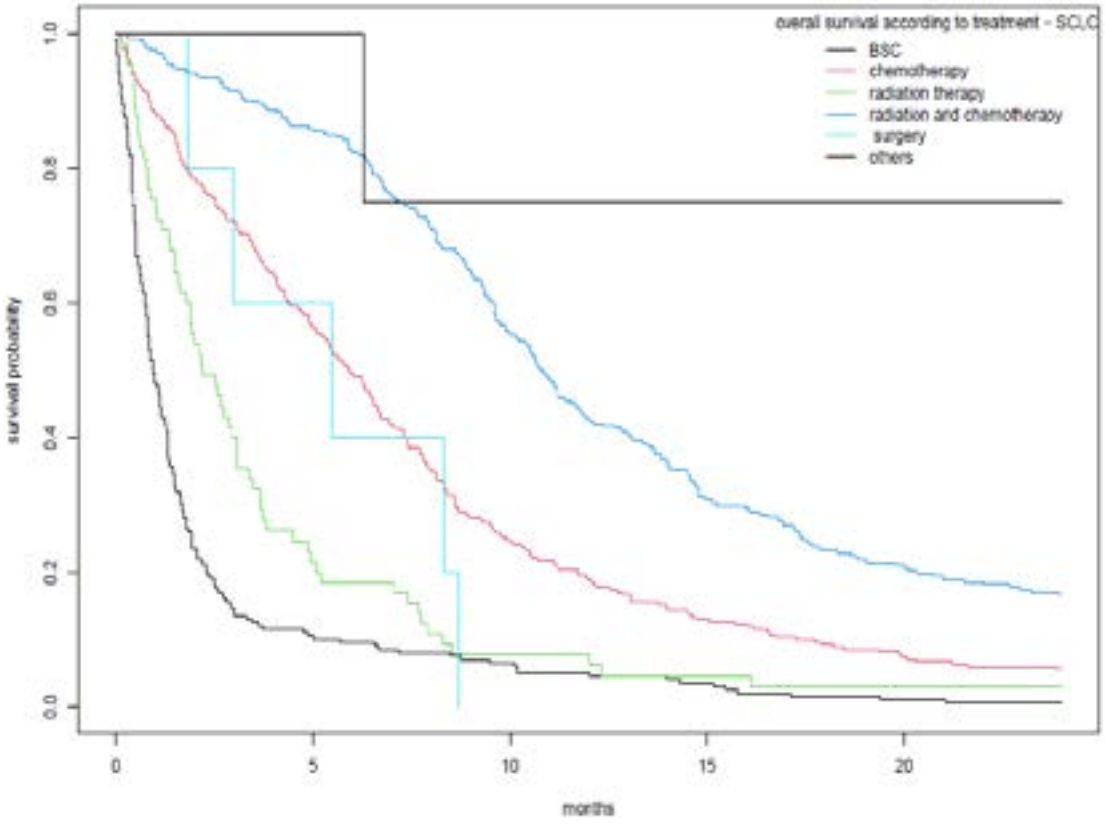
TABLE 3 – Survival according to patients' characteristics (Cont.).

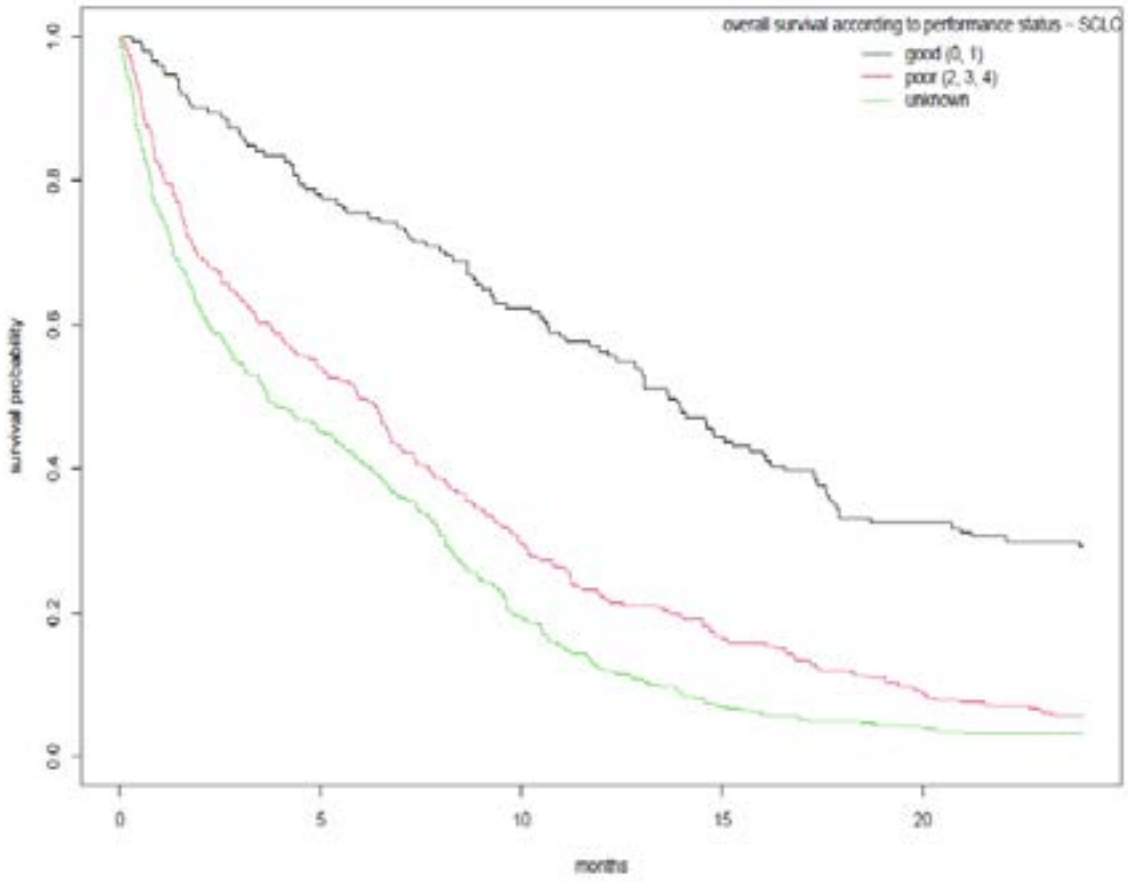
Variables	Median (95%CI), months	12-month (95%CI)	24-month (95%CI)	*p**
Non-White	4.2 (3.0-6.0)	18.5 (15.1-22.1)	6.9 (4.7-10.9)	
White	6.5 (6.0-7.0)	25.9 (20.6-28.6)	9.3 (6.7-11.4)	
School attainment				0.09
9 years or more	7.1 (5.2-9.7)	26.9 (21.7-33.2)	10.1 (6.8-14.6)	
Up to 8 years	5.8 (4.8-6.9)	22.1 (18.2-24.7)	7.8 (5.6-9.9)	
Staging				< 0.01
Limited	8.3 (7.2-10.5)	33.5 (26.9-42.3)	17.1 (12.4-24.9)	
Extensive	4.1 (3.6-5.9)	17.6 (13.3-22.2)	6.7 (3.7-9.4)	
Unknown	6.7 (5.2-7.8)	24.4 (19.6-27.6)	6.9 (4.7-9.5)	
Treatment				< 0.01
BSC	0.9 (0.3-1.8)	4.9 (2.6-9.1)	0.1 (0.1-0.3)	
Any	8.1 (6.5-8.4)	28.6 (25.4-32.3)	10.5 (8.0-13.2)	
Treatment type				< 0.01
BSC	0.9 (0.2-1.4)	5.0 (2.6-9.0)	2.0 (0.2-3.9)	
Any CT	8.7 (7.2-9.8)	31.8 (27.2-34.6)	11.7 (8.9-14.0)	
Any XRT	9.6 (8.7-0.9)	37.0 (31.2-40.8)	14.7 (10.9-17.9)	
CT and XRT	10.8 (9.3-12.4)	42.6 (36.7-47.6)	16.6 (12.2-20.2)	

BSC, best supportive care; CT, chemotherapy; PS, performance status; XRT, radiotherapy.
***Log-rank test.**

Many patients had missing data on staging and PS. Survival times for patients with missing staging had values intermediary between patients with known staging (limited and extensive disease), suggesting the clinical need for immediate treatment. On the other hand, patients with missing data on PS had poor survival, even worse than that observed in patients with poor PS (**Table 3**).

Individuals classified as non-whites, with extensive or unknown disease, poor or unknown PS, and BSC as the only treatment modality showed significantly worse survival (log-rank test, $p < 0.01$) (**Figure 2** and **Table 3**). The univariate analysis revealed that age, PS, skin color, staging, year of admission and treatment status were associated with 12-month survival. The multivariate analysis, adjusted for age and treatment status, showed that poor or unknown PS, non-white skin color, and extensive or unknown staging remained independently associated with 12-month survival (**Table 4**).


overall survival according to treatment - SCLC
BSC
chemotherapy
radiation therapy
radiation and chemotherapy
surgery
others
survival probability
0.0
0.2
0.4
0.6
0.8
1.0
0
5
10
15
20
months


overall survival according to performance status - SCLC
good (0, 1)
poor (2, 3, 4)
unknown
survival probability
0.0
0.2
0.4
0.6
0.8
1.0
0
5
10
15
20
months

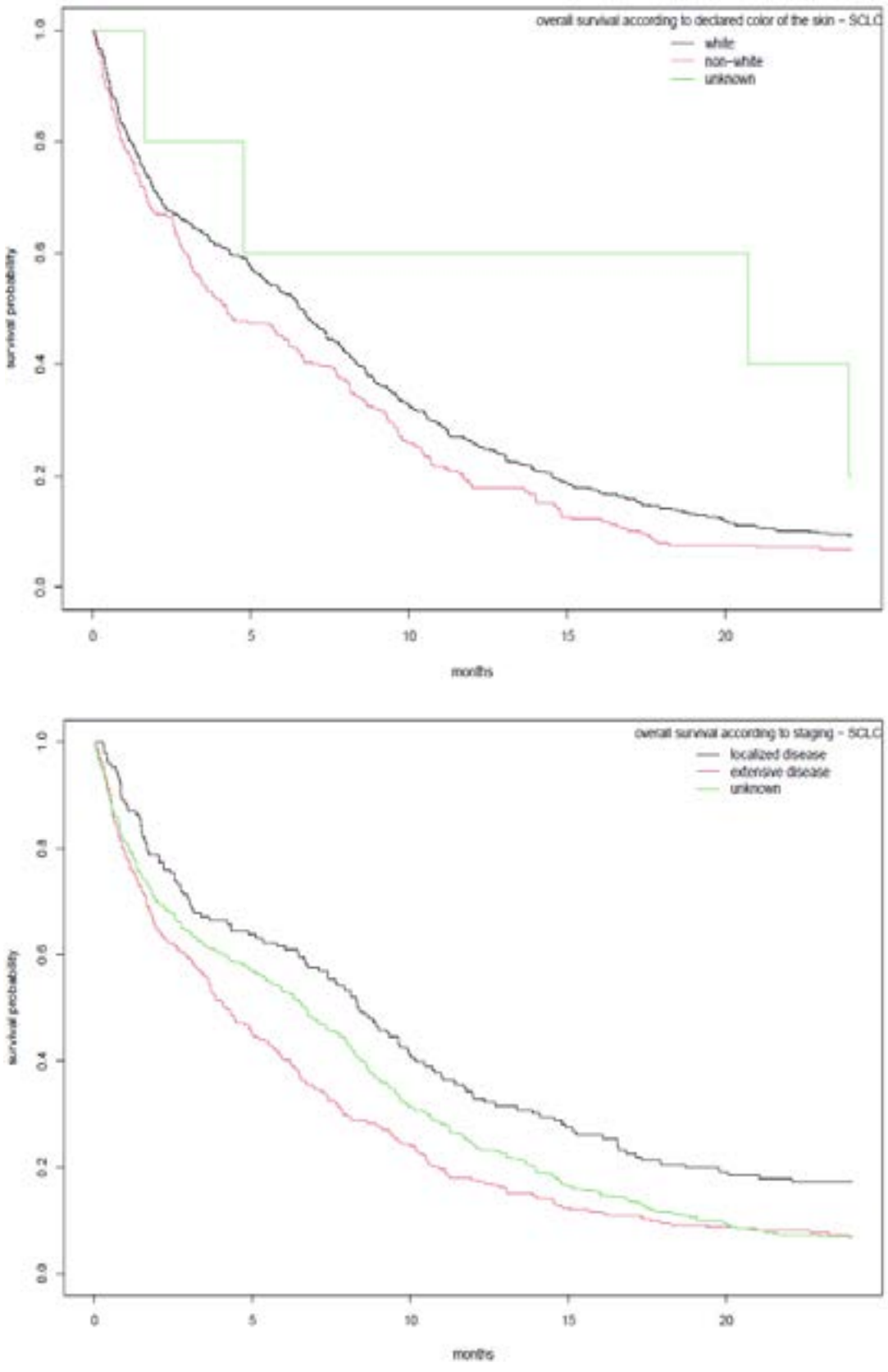


Figure 2 – Kaplan-Meier curves for survival according to treatment, performance status, skin color, and staging (log-rank test, $p < 0.05$).

TABLE 4 – Univariate and multivariate analysis for 12-month survival

	Univariate	Multivariate*
Variables	**Hazard ratio (95%CI)**	**Hazard ratio (95%CI)**
Sex		
Male	1	
Female	0.88 (0.76-1.01)	
Age	1.01 (1.01-1.03)	
PS		
Good	1	1
Poor	2.34 (1.87-2.92)	1.99 (1.57-2.51)
Unknown	3.15 (2.53-3.92)	2.79 (2.22-3.49)
Skin color		
White	1	1
Non-White	1.19 (1.03-1.39)	1.25 (1.07-1.46)
School attainment		
Up to 8 years	1	
9 years or more	0.86 (0.73-1.01)	
Staging		
Localized	1	1
Extensive	1.64 (1.33-2.04)	1.62 (1.29-2.04)
Unknown	1.39 (1.14-1.71)	1.33 (1.07-1.65)
Treatment		
BSC	1	
Any	0.24 (0.20-0.28)	
Treatment type		
BSC	1	
Any CT	0.31 (0.25-0.37)	
Any XRT	0.59 (0.45-0.79)	
CT and XRT	0.16 (0.13-0.19)	

BSC, best supportive care; CT, chemotherapy; PS, performance status; XRT, radiotherapy.
***Adjusted by age and treatment status.**

Discussion

We have found in a cohort of patients with SCLC admitted to reference a Brazilian public cancer-center that most individuals present with advanced disease and a large proportion with poor PS, both of which pose a major burden to the poor overall survival found. In fact, about one quarter of patients received BSC only. SCLC represents a considerable proportion of patients with lung

cancer with scarce improvements in treatment. To improve mortality from this disease, the only significant prospects for the next years are to advance in policies against tobacco consumption and improved access to timely diagnosis.

SCLC is not amenable to routine screening, since it has a very aggressive course that poses a major challenge to the health system (15). It is one of the most preventable cancers since its most important cause has been known for a long time: smoking. The incidence of SCLC had a trend of decrease in the last decades (16,17). This may be related to successful strategies of smoking restriction, such as creation of tobacco free places, tax policies, ban of tobacco smoking in public places such as malls, theaters and markets, and restriction of tobacco publicity. Unfortunately, such measures did not eliminated smoking completely, and 13% of adults are still smoking in Brazil (10).

This study illustrates an unmet need for better SCLC patients care. The results of real-life outcomes are far away from data obtained from randomized clinical trials, even those published a decade or two ago. It was shown that socioeconomic markers such as school attainment was not related to the main outcome. This may be related to the fact that a large proportion of patients did not have prompt assess to either the diagnosis, which needs some time to perform, such as chest CT scans, biopsy (either by bronchoscopy or percutaneous), and access to a specialized oncology facility. In fact, many patients spend a long-time receiving treatment for suspected pulmonary tuberculosis (that has a high prevalence in Brazil). Patients also experience delays consulting pulmonologists and thoracic surgeons, and the low availability of CT scans makes the scenario even worse. As a consequence, 67.9% of patients had a poor PS in the current analysis, one half did not have a complete staging (this may be related to the fact that many of such patients needed immediate treatment), and almost one quarter of patients had no treatment at all (even in a hospital devoted to the formation of oncologists, where there is a higher trend to treat patients more promptly) (18).

In this series of cases treated in a single cancer-center, it was observed that 23.1% of patients received BSC. This proportion is in line with other studies that reported the portion of patients which received palliative care, either from single institutions like ours, or from cancer registries. A publication from Portugal revealed that 31% of SCLC patients received BSC in the period between 2015 to 2017 (19). A publication based on the Surveillance, Epidemiology, and End Results database revealed that 22.5% did not receive timely treatment for SCLC (20). In a publication based on the Netherlands Cancer Registry, 13.9% of patients with stage III SCLC received BSC (21).

The proportion of patients receiving BSC was not stable throughout the period analyzed. This may be related to profound changes that occurred in the patterns of patient's referral, as well as in the criteria for cancer-center admission. Until the end of the 2000 decade, patients were admitted according to a local screening to assess the likelihood of receiving specific cancer directed treatment. When this was not the case, these patients were not admitted, and palliative care was provided in other public facilities. However, many patients did not receive adequate palliation. Since the beginning of the 2010s, the regulation of access evolved, so that cases that require a higher complexity care, such as cancer, are directed to specialized facilities through a centralized web-based registry. This change was fully implemented in the cancer-center in 2015, and it is supposed that many patients with advanced disease and poor clinical conditions, such as poor PS, may have been admitted. In this period a publication from this cancer-center evaluated the results of the treatment for patients with poor PS and observed the marginal benefits of CT in that scenario - a poor median survival of 0.97 months was described (18).

It is noteworthy that we had a high proportion of women in this cohort, in contrast with other publications. Franco et al. (22) had 21.4% of women in Spain, Debieuvre et al. (16) had 34.6% for SCLC in France. According to GLOBOCAN statistics,

31.6% of lung cancers arise among females, mostly non-small cell lung cancer (23). In the World Health Organization database (24), the prevalence of tobacco smoking differs according to sex, in Brazil women smoke 42% less than men, while in countries such as France, Germany, Spain, United States and Argentina these figures are 9.9%, 14%, 8.2%, 22% and 26.5%, respectively. Therefore, differences in tobacco smoking may not be attributed to such differences between sexes. In Brazil there is a sustained fall in the prevalence of smoking over the years. From 1989 to 2010, the prevalence fell from 43% to 21% among men, and from 27% to 13% among women (25), and in 2019 the prevalence was 15.9% and 9.6%, respectively (10). In this period, the difference of smoking prevalence rates between men and women ranged from 35.2% to 42.0%. Another possibility may be related to the differential access to the health system between sexes. There is some evidence that men are less likely than women to recognize suspicious symptoms. In a disease with very aggressive clinical course such as SCLC, this may increase the probability of diagnosis delay and treatment referral (26).

Despite the low median survival and 12-month survival probability - reflecting the dismal prognosis of this disease - our data were comparable to those observed in a study conducted with patients registered in the Surveillance, Epidemiology, and End Results database (20), where the median survival was seven months and the 12-months survival was 33%. In a series of cases from the Thoracic Tumors Registry from Spain (22), where more than 94% of patients received any form of treatment, median overall survival was 9.5 months. Our 12-months survival compares with the results observed in the registries of males in New Zealand, Ireland and United Kingdom (27). In a population-based study from Japan (28), it was found that 12-months survival for limited disease was 66.2%, and for extensive disease was 34.8%.

In the multivariate analysis it was found a higher risk of death for patients characterized as non-whites. This finding is worrisome since it may pose relevant issues related to delayed assessment according to skin color, different treatment response, or distinct biological disease behavior. As a matter of fact, although there could be potential genetic differences to indicate differential response or survival, these explanations seem so unlikely. The same may be said about the behavior of the disease. Unfortunately, skin color is a marker of socioeconomic status in Brazilian society, even after adjusting for school attainment and marital status. This may be related to difficulties of non-white persons in access to the health system, delayed diagnosis, cultural issues. Some studies identified that black patients were less likely to receive CT in the United States of America (29,30), as well as uninsured, elderly and people living in rural areas. There are issues related to the promptness of the treatment beginning according to the skin color in a few situations (31). In this cohort there was no difference in the time to begin treatment according to skin color (data not shown).

This study has several strengths. It was possible to identify all cases of SCLC admitted to the cancer-center, irrespective of treatment, with pathological diagnosis reviewed by an expert pathologist: a cohort that provided an appropriate sample size to allow major precision to the estimates. Patients were treated by a constant group of physicians, following the same guidelines. Over the period study, there was no major shifts in SCLC treatment, hence the "time effect" may reflect true issues related to the characteristics of patient referral and hospital admittance. Lastly, the retention of cases with unknown staging and unknown PS in the stratified Cox models was a strength, as it minimized potential anticipation bias (32) and did not penalize the power of the analyses due to sample size reduction (33).

On the other hand, this study also has some limitations. It is a hospital-based cancer registry study on such a way no information about the CT regimen or details on the XRT (either thoracic, prophylactic cranial irradiation, palliative) was collected. There is no information on the number of cycles of CT, successive lines of treatment, or if combined treatments were either concomitant or

sequential. Furthermore, the hospital-based cancer registry does not collect data related to co-morbidities which interfere with outcomes data. Although the primary information was abstracted by a specialized technician in cancer registry in a standardized fashion, there were many missing data in relation to staging and PS, which may preclude evaluation of treatment results among these groups. It should be considered that most patients had not complete baseline staging due to many reasons, including poor PS that required prompt treatment, or lack of resources.

In conclusion, this study represents a real effort in the analysis of clinical data on lung cancer in Brazil. We found in a cohort of patients with SCLC admitted to reference a public cancer-center that the probability of receiving BSC only was increased over the years. Furthermore, we found evidence that poor or unknown PS, non-white skin color and extensive or unknown staging are associated with poor survival.

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Conflicts of interest disclosure

The authors declare no competing interests relevant to the content of this study.

Authors' contributions

All the authors declare to have made substantial contributions to the conception, or design, or acquisition, or analysis, or interpretation of data; and drafting the work or revising it critically for important intellectual content; and to approve the version to be published.

Availability of data and responsibility for the results

All the authors declare to have had full access to the available data and they assume full responsibility for the integrity of these results.

References

1. Mattiuzzi C, Lippi G. Current cancer epidemiology. J Epidemiol Glob Health [Internet]. 2019 [cited 2025 Sep 26];9(4):217–22. Available from: https://doi.org/10.2991/jegh.k.191008.001.

2. Rudin CM, Brambilla E, Faivre-Finn C, Sage J. Small-cell lung cancer. Nat Rev Dis Primers [Internet]. 2021 [cited 2025 Sep 26];7(1):3. Available from: https://doi.org/10.1038/s41572-020-00235-0.

3. Pesch B, Kendzia B, Gustavsson P, Jöckel KH, Johnen G, Pohlabeln H, et al. Cigarette smoking and lung cancer relative risk estimates for major histological types from a pooled analysis of case-control studies. Int J Cancer [Internet]. 2012 [cited 2025 Sep 26];131(5):1210–9. Available from: https://doi.org/10.1002/ijc.27339.

4. Özmen MU. Causal effect of education on tobacco use in low-and-middle-income countries. Nicotine Tob Res [Internet]. 2023 [cited 2025 Sep 26];25(8):1474–80. Available from: https://doi.org/10.1093/ntr/ntad056.

5. Lim W, Ridge CA, Nicholson AG, Mirsadraee S. The 8th lung cancer TNM classification and clinical staging system: review of the changes and clinical implications. Quant Imaging Med Surg [Internet]. 2018 [cited 2025 Sep 26];8(7):709–18. Available from: https://doi.org/10.21037/qims.2018.08.02.

6. Howlader N, Forjaz G, Mooradian MJ, Meza R, Kong CY, Cronin KA, et al. The effect of advances in lung-cancer treatment on population mortality. N Engl J Med [Internet]. 2020 [cited 2025 Sep 26];383(7):640–9. Available from: https://doi.org/10.1056/NEJMoa1916623.

7. Bogart JA, Waqar SN, Mix MD. Radiation and systemic therapy for limited-stage small-cell lung cancer. J Clin Oncol [Internet]. 2022 [cited 2025 Sep 26];40(6):661–70. Available from: https://doi.org/10.1200/JCO.21.01639.

8. Tariq S, Kim SY, Novaes JMO, Cheng H. Update 2021: management of small cell lung cancer. Lung [Internet]. 2021 Nov [cited 2025 Sep 26];199(6):579–87. Available from: https://doi.org/10.1007/s00408-021-00486-y.

9. Rudin CM, Awad MM, Navarro A, Gottfried M, Peters S, Csőszi T, et al. Pembrolizumab or placebo plus etoposide and platinum as first-line therapy for extensive-stage small-cell lung cancer: randomized, double-blind, phase III KEYNOTE-604 study. J Clin Oncol [Internet]. 2020 [cited 2025 Sep 26];38(21):2369–79. Available from: https://doi.org/10.1200/JCO.20.00793.

10. Malta DC, Gomes CS, Andrade FMD, Prates EJS, Alves FTA, Oliveira PPV, et al. Tobacco use, cessation, secondhand smoke and exposure to media about tobacco in Brazil: results of the National Health Survey 2013 and 2019. Rev Bras Epidemiol [Internet]. 2021 [cited 2025 Sep 26];24(suppl 2):e210006. Available from: https://doi.org/10.1590/1980-549720210006.supl.2.

11. World Health Organization. International statistical classification of diseases and related health problems. 10th ed. São Paulo: Universidade de São Paulo Press; 2012.

12. World Health Organization. ICD-O – International classification of diseases for oncology. 3rd ed. São Paulo: Universidade de São Paulo Press; 2013.

13. Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, McFadden ET, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol [Internet]. 1982 [cited 2025 Sep 26];5(6):649-55. Available from: https://doi.org/10.1097/00000421-198212000-00014.

14. Brasil. Instituto Nacional de Câncer (INCA). Mudanças no procedimento de primeira avaliação no INCA [Internet]. Informe INCA. 2013 Aug 7 [cited 2025 Sep 03];(314). Available from: https://ninho.inca.gov.br/jspui/bitstream/123456789/14059/1/Informe%20INCA%20314-3-Mudancas-no-procedimento.pdf.

15. The National Lung Screening Trial Research Team. Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med [Internet]. 2011 [cited 2025 Sep 26];365(5):395-409. Available from: https://doi.org/10.1056/NEJMoa1102873.

16. Debieuvre D, Molinier O, Falchero L, Locher C, Templement-Grangerat D, Meyer N, et al. Lung cancer trends and tumor characteristic changes over 20 years (2000-2020): results of three French consecutive nationwide prospective cohorts' studies. Lancet Reg Health Eur [Internet]. 2022 [cited 2025 Sep 26];22:100492. Available from: https://doi.org/10.1016/j.lanepe.2022.100492.

17. Barta JA, Powell CA, Wisnivesky JP. Global epidemiology of lung cancer. Ann Glob Health [Internet]. 2019 [cited 2025 Sep 26];85(1):8. Available from: https://doi.org/10.5334/aogh.2419.

18. Baldotto CS, Cronemberger EH, de Biasi P, Zamboni M, Sousa A, Zukin M, et al. Palliative care in poor-performance status small cell lung cancer patients: is there a mandatory role for chemotherapy? Support Care Cancer [Internet]. 2012 [cited 2025 Sep 26];20(11):2721-7. Available from: https://doi.org/10.1007/s00520-012-1392-0.

19. Soares M, Antunes L, Redondo P, Borges M, Grimson F, Hermans R, et al. Small cell lung cancer treatment and survival in Portugal: a retrospective analysis from the I-O Optimise initiative. Eur J Cancer Care (Engl) [Internet]. 2021[cited 2025 Sep 26];30(6):e13496. Available from: https://doi.org/10.1111/ecc.13496.

20. Wang S, Tang J, Sun T, Zheng X, Li J, Sun H, et al. Survival changes in patients with small cell lung cancer and disparities between different sexes, socioeconomic statuses and ages. Sci Rep [Internet]. 2017 [cited 2025 Sep 26];7(1):1339. Available from: https://doi.org/10.1038/s41598-017-01571-0.

21. Evers J, Hendriks LEL, De Jaeger K, Wijsman R, De Ruysscher D, Terhaard C, et al. Trends and variations in the treatment of stage I–III small cell lung cancer from 2008 to 2019: a nation-wide population-based study from the Netherlands. Lung Cancer [Internet]. 2021 [cited 2025 Sep 26];162:61–70. Available from: https://doi.org/10.1016/j.lungcan.2021.10.011.

22. Franco F, Carcereny E, Guirado M, Ortega AL, López-Castro R, Rodríguez-Abreu D, et al. Epidemiology, treatment, and survival in small cell lung cancer in Spain: data from the Thoracic Tumor Registry. PLoS One [Internet]. 2021 [cited 2025 Sep 26];16(6):e0251761. Available from: https://doi.org/10.1371/journal.pone.0251761.

23. World Health Organization. International Agency for Research on Cancer. Global Cancer Observatory. Cancer Today [Internet]. [cited 2025 Sep 03]. Available from: https://gco.iarc.fr.

24. World Health Organization. The Global Health Observatory. Estimate of current tobacco use prevalence. Distribution [Internet]. [cited 2025 Sep 03]. Available from: https://www.who.int/data/gho/data/themes/topics/sdg-target-3_a-tobacco-control.

25. Levy D, Almeida LM, Szklo A. The Brazil SimSmoke policy simulation model: the effect of strong tobacco control policies on smoking prevalence and smoking-attributable deaths in a middle-income nation. PLoS Med [Internet]. 2012 [cited 2025 Sep 26];9(11):e1001336. Available from: https://doi.org/10.1371/journal.pmed.1001336.

26. Sarma EA, Rendle KA, Kobrin SC. Cancer symptom awareness in the US: sociodemographic differences in a population-based survey of adults. Prev Med [Internet]. 2020 [cited 2025 Sep 26];132:106005. Available from: https://doi.org/10.1016/j.ypmed.2020.106005.

27. Araghi M, Fidler-Benaoudia M, Arnold M, Rutherford M, Bardot A, Ferlay J, et al. International differences in lung cancer survival by sex, histological type and stage at diagnosis: an ICBP SURVMARK-2 Study. Thorax [Internet]. 2022 [cited 2025 Sep 26];77(4):378–90. Available from: https://doi.org/10.1136/thoraxjnl-2020-216555.

28. Oze I, Ito H, Nishino Y, Hattori M, Nakayama T, Miyashiro I, et al. Trends in small-cell lung cancer survival in 1993–2006 based on population-based cancer registry data in Japan. J Epidemiol [Internet]. 2019 [cited 2025 Sep 26];29(9):347–53. Available from: https://doi.org/10.2188/jea.JE20180112.

29. Tapan U, Furtado VF, Qureshi MM, Everett P, Suzuki K, Mak KS. Racial and other healthcare disparities in patients with extensive-stage SCLC. JTO Clin Res Rep [Internet]. 2020 [cited 2025 Sep 26];2(1):100109. Available from: https://doi.org/10.1016/j.jtocrr.2020.100109.

30. Roof L, Wei W, Tullio K, Pennell NA, Stevenson JP. Impact of socioeconomic factors on overall survival in SCLC. JTO Clin Res Rep [Internet]. 2022 [cited 2025 Sep 26];3(7):100360. Available from: https://doi.org/10.1016/j.jtocrr.2022.100360.

31. Massignam FM, Bastos JLD, Nedel FB. Discriminação e saúde: um problema de acesso. Epidemiol Serv Saúde [Internet]. 2015 [cited 2025 Sep 26];24(3):541–44. Available from: https://doi.org/10.5123/S1679-49742015000300020.

32. Jansen RJ, Alexander BH, Anderson KE, Church TR. Quantifying lead-time bias in risk factor studies of cancer through simulation. Ann Epidemiol [Internet]. 2013 [cited 2025 Sep 26];23(11):735–41. Available from: https://doi.org/10.1016/j.annepidem.2013.07.021.

33. Kwak SK, Kim JH. Statistical data preparation: management of missing values and outliers. Korean J Anesthesiol [Internet]. 2017 [cited 2025 Sep 26];70(4):407–11. Available from: https://doi.org/10.4097/kjae.2017.70.4.407.

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