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Histological Subtype and Stage Study of Lung Cancers in Patients Referred to Radiotherapy and Oncology Department from Ahvaz Golestan Hospital for the Duration of 2001 to 2011

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Background: Lung cancer is the main leading cause of cancer deaths in men and the second leading cause of cancer death for women in worldwide. This study, explains the subtypes histological study of lung cancers in patients admitted to Ahvaz Golestan Hospital.
Material and methods: Data from the records of all patients with primary lung cancer that their disease was diagnosed during the years of 2001 to 2011 were collected and coded to be analyzed by SPSS software version 20.
Result: Over the 11-year of study a total number of 483 lung cancer cases were identified. Of which, 13% were SCLC and 64.4% NSCLC. A total number of 141 of the patients were female and 372 male. The most common subtype among men was SCC while adenocarcinoma was the most frequent subtype among women. The mean age of patients with SCLC, 63.16 years and in the case of NSCLC was 63 years.
Conclusion: The obtained results from this study showed that there was not a significant relationship for the process of changing in the subtype's frequency, the male and female sex ratio as well as the mean age of patients.

Keywords: Lung Cancer, Subtype, SCLC, NSCLC

Background

Lung cancer that was not a common disease at the beginning of the 20th century, now it has become a major cause of death in the world and now being considered as an epidemic on a global scale. (1,2) The disease is a major cause of cancer death in men and the second leading cause of cancer death in women worldwide. (3,4) The main risk factor for lung cancer is smoking so that, 90% of lung cancer cases are directly associated with smoking; Other risk factors that can be named are as asbestos, radon, ionizing radiation, family history of lung cancer, arsenic, pharmaceutical supplements, beta-carotene compounds (in those who smoke) and low socio-economic status. (5) Lung cancer can be occurred as squamous cell carcinoma, small cell carcinoma, adenocarcinoma, large cell carcinoma, and other less common types that their prevalence varies depending on the type and depends on the difference in the pattern of smoking and exposure to other risk factors for lung cancer. (6) Epidemiology of lung cancer in many parts of the world is changing; as we move forward in the 21st century, it seems unlikely to subside the incidence of lung cancer; however, its load is being displaced from developed countries to less developed countries. (7) In recent years the incidence of 4 major histological types of lung cancer has also changed dramatically. (8) Prognosis is poor because, the most cases are discovered at an advanced stage of disease. Despite significant progress in the medical and surgical treatment in the past decade, there is not a significant decrease in the percentage of patients who survive this deadly disease. In addition, the 5-year survival rate varies from 5% to 15%. However, the most important prognostic factor in lung cancer type is the diagnosis stage of disease that is also important for the survival rate of the patients. (9) In Iran lung cancer is also considered as a very important factor in mortality and disability. Furthermore, according to the study of the burden of disease, cancers are imposed 662.4 Dali per hundred thousand people. In the meantime, lung cancer after stomach cancer with the creation of 53.6 Dali is set in the second position. (10) Due to the large share of lung cancer deaths among cancers, it is also pointed out that the lung cancer is a major health problem worldwide with poor prognosis and the lion's share of deaths from cancer. (2) Therefore, the identification of trends and subtypes of lung cancer in recent years can be a way for prevention and provision to provide needed health cares in terms of lung cancer.

Materials and Methods

In this project the study population included all referred patients with primary lung cancer to the Department of Radiotherapy and Oncology, Ahvaz Golestan Hospital for the period of 2001-2011 years. Information relating to the year of diagnosis, pathology reports, information required to determine the stage of disease, age and sex of the patient were recorded in a special form and after coding, the statistical software was applied. Determining criteria for the year of diagnosis was the diagnosis given in the form of primary pathology. In order to achieve the study objectives, the descriptive statistics and software SPSS v.20 were used to analyze the obtained results. In addition, the annual changes of variables were examined using linear regression.

Results

In total, in the 11-year of study 483 lung cancer cases were identified in the studied population, of which, 13% (63 cases) related to the small cell cancer (small cell lung cancer) and 64.4 percent (311) related to the non-small cell lung cancer (NSCLC). Furthermore, 22.6 percent (109) of patients diagnosed with lung cancer histological subtype of the disease that were not recorded in medical documents in the pathology form. Among the subtypes of lung cancers for the duration of the study period, 25.1 percent (121 cases) adenocarcinoma, 32.5 percent (157 cases) were the squamous cell carcinoma and 4.3 percent (21 cases) were large cell carcinoma, however, the documents showed that amount of 2.5 percent (12 cases) of patients with NSCLC histological subtype were not traced in the pathology forms. Furthermore, the changing process of frequency for histological subtypes of lung cancer during the study was not significant (Figure 1 and Table 1).

In total, during these 11 years 48.9 percent of studied patients had stage IV disease at the time of diagnosis and to determine the stage of disease for 48% of patients was not possible due to lack of information for their records.

For the SCLC, 46% of patients were in stage IV. However, it was not possible to determine the stage of the disease for 50.8% of the patients. Similarly, 1.6% of patients were recorded with stage IIIb and 1.6 percent in stage IIIa. In the case of NSCLC, 46.6% of the patients were in the IV stage, while for 50.8% of cases it was not possible to set the stage for the patients. It was also documented that 1.6% of patients were in the stage IIIb, 0.6% in stage IIIa and 0.3% in stage Ib, respectively (Figure 2). Moreover, the obtained results showed that the process of frequency changing was not significant for the different stages of the disease in the course of the 11 years of the study. During the study, 141 of the examined patients were female and 372 male. The most common histological subtype among women was adenocarcinoma (Figure 3) and between the men was squamous cell carcinoma (Figure 4). In addition, the process of the frequency changing of the patients with primary lung cancer in both SCLC and NSCLC was not significant (Table 2). The mean age of patients with primary lung cancer for SCLC, 63.16 years and in the case of NSCLC was 63 years. Among the subtype of NSCLC the average age for the patients with adenocarcinoma was 59.81 years while, SCC, 65.8 and for the large cell adenocarcinoma was 63.9 years. However, the mean age for non-small cell cancer (NSCLC) with unknown subtype was documented at 57.33 years. Moreover, the trend of the average age was not significant (p-value = 0.954) for lung cancer patients throughout the study (Figure 5).

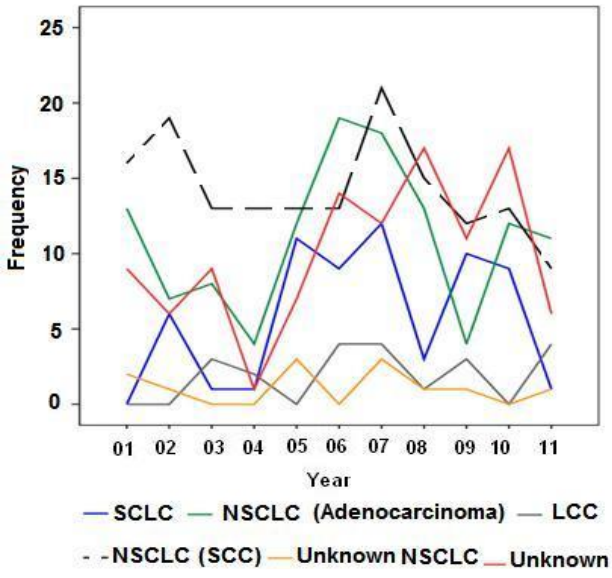

Figure 1. The process of the frequency changing of patients with primary lung cancer referred to Ahvaz Golestan Hospital, 2001-2011 in terms of the disease type.

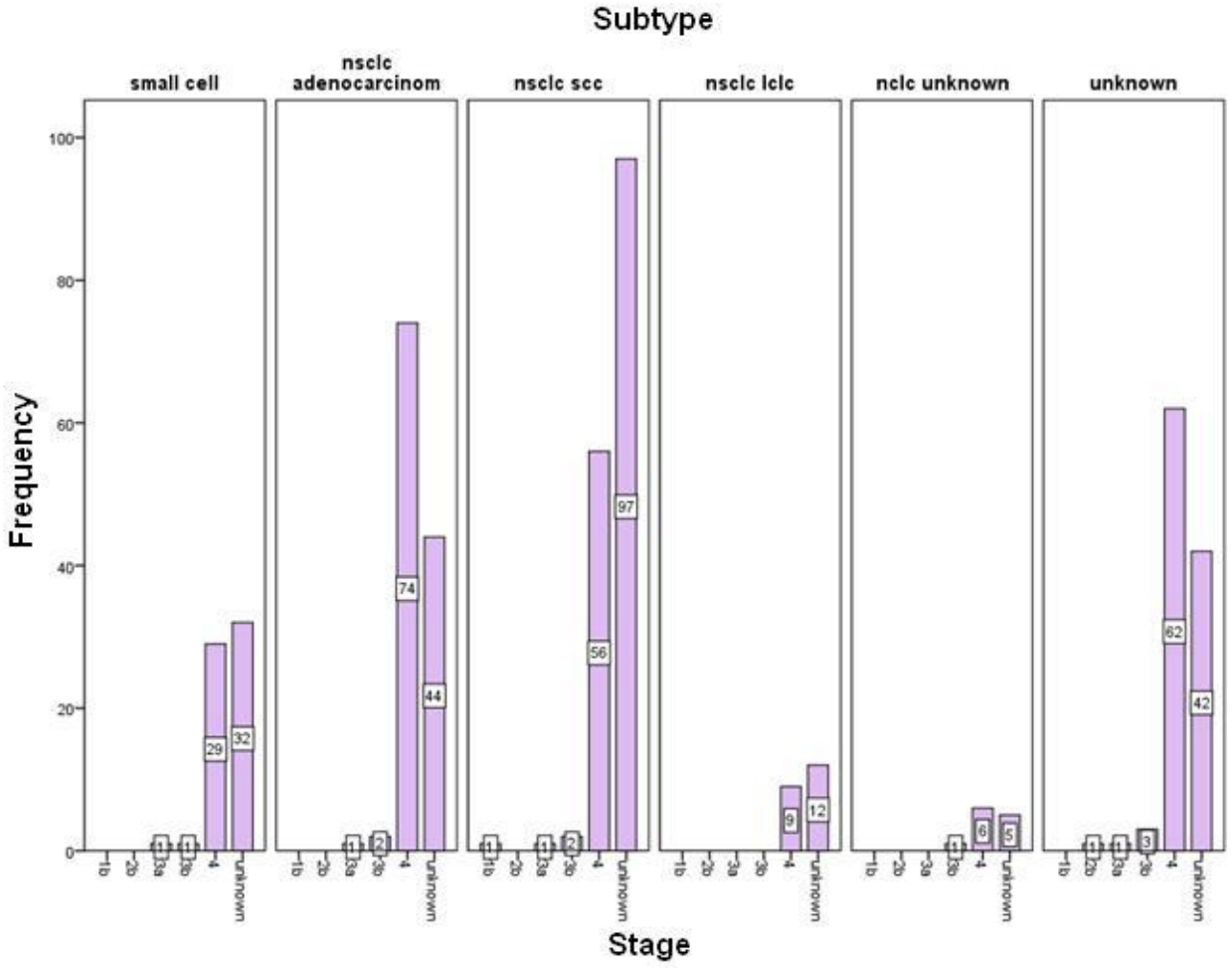

Figure 2. Frequency of lung cancer patients according to the type and stage of disease in patients referred to Ahvaz Golestan Hospital, 2001-2011.

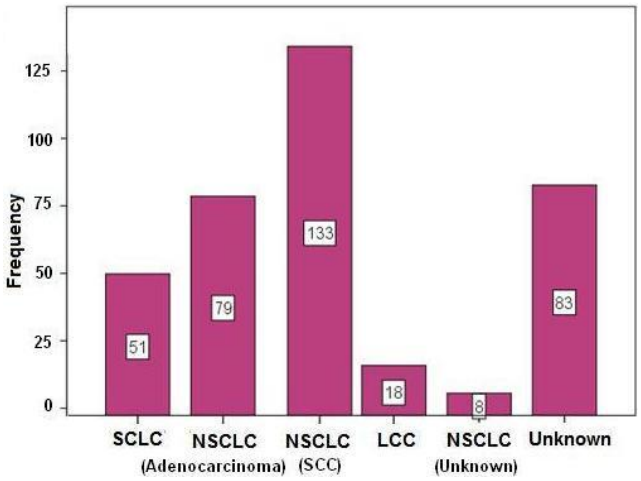

Figure 3. The frequency of the disease with lung cancer in male patients admitted to the Ahvaz Golestan Hospital during the years of 2001-2011.

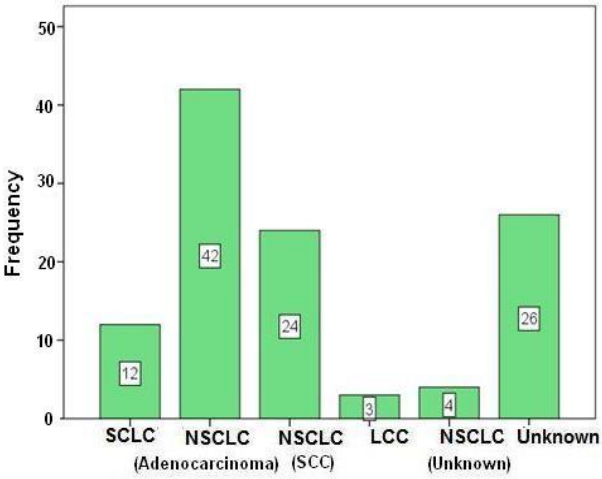

Figure 4. The frequency of lung cancer in terms of disease in female patients admitted to the Ahvaz Golestan Hospital during the years of 2001-2011.

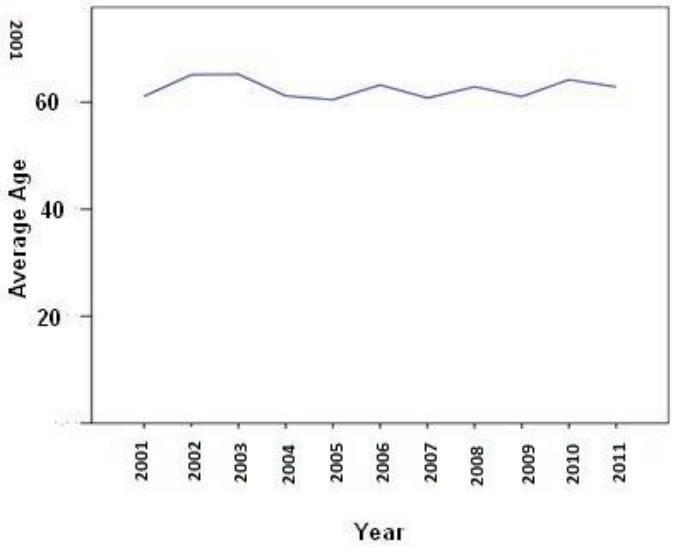

Figure 5. The mean age of the patients with primary lung cancer referred to the Ahvaz Golestan Hospital during the years of 2001-2011.

Table 1. Results of the frequency of variance analysis in patients with primary lung cancer based on thetype disease referred to the Ahvaz Golestan Hospital during the years of 2001-2011.

Disease type	Source Of Variation	Sum Of Squares	Degrees Of Freedom	Mean Square	F-Statistic	P-Value
SCLC	Regression	21.827	1	21.827	1.021	0.339
	Residual	192.335	9	21.373	-	-
	Total	214.182	10	-	-	-
NSCLC Adenocarcinoma	Regression	4.400	1	4.400	0.164	0.695
	Residual	241.600	9	26.844	-	-
	Total	246	10	-	-	-
NSCLC SCC	Regression	22.722	1	22.722	2.287	0.165
	Residual	89.455	9	9.339	-	-
	Total	112.182	10	-	-	-
LCC	Regression	4.400	1	4.400	1.494	0.253
	Residual	26.509	9	2.945	-	-
	Total	30.909	10	-	-	-
NSCLC (Unknown)	Regression	0.145	1	0.145	0.103	0.756
	Residual	12.764	9	1.418	-	-
	Total	12.909	10	-	-	-
Unknown	Regression	47.127	1	47.127	2.166	0.175
	Residual	195.872	9	21.754	-	-
	Total	242.909	10	-	-	-

Table 2. Results of the frequency of variance analysis in patients with primary lung cancer small cell type based on sex referred to the Ahvaz Golestan Hospital during the years of 2001-2011.

Sex	Source Of Variation	Sum Of Squares	Degrees Of Freedom	Mean Square	F-Statistic	(P-Value)
Male	Regression	19.236	1	19.236	1.339	0.277
	Residual	129.309	9	14.368	-	-
	Total	148.548	10	-	-	-
Female	Regression	0.082	1	0.082	0.032	0.861
	Residual	22.827	9	2.536	-	-
	Total	22.909	10	-	-	-

Discussion

Based on the obtained results from this study, a total number of 483 lung cancer cases were identified during the years of 2001-2011. Of which, 13% of cases were correlated to the small cell carcino-

ma and 64.4% were for the non-small cell cancer. In the subtype of NSCLC, The highest relative frequency was recorded for adeno-carcinoma by 25.1 percent and then followed for the SCC by 22.5 percent, large cell carcinoma 3.4 percent, and NSCLC with unspecified pathology types were followed for the next steps. These findings are somewhat similar to the study of Japan (11) where the adenocarcinoma was also the most common subtype among the lung cancer subtypes. Besides, in the Japan study the SCC was in the second position. However, a similar study was conducted in Kermanshah (2) and the SCC was revealed as the most frequent subtype and then were ranked next, the small cell carcinoma and adenocarcinoma subtypes, respectively. In a study in India (12) SCC was also the most common subtype and anaplastic carcinoma and adenocarcinoma were placed in the the next ranks. In a study in South Asia (13) the trend of lung cancer was increased in the course of the study. This study indicated that the changes in the lung cancer rate in South Asia and non-South Asian populations were due to the caused by changes in smoking habits. In a study conducted in Hong Kong (1) the incidence of lung cancer was generally decreasing. However, in the subtype's analysis, the incidence of squamous cell carcinoma and large cell carcinoma were in the reduced form as well. Additionally, the incidence of adenocarcinoma for the duration of the study period was placed horizontally. This study assumed that the decline in smoking in the population resulted in for the reduction of incidence of squamous cell carcinoma. This study also confirmed the relatively horizontal trend of the adenocarcinoma due to the important heredity-environment conflict role or the use of filtered cigarette with low-tar. Also in the study of Kermanshah (2) the annual change trend for the incidence of lung cancer was examined that it was in the reduced form however, this reduction was not statistically significant. This study alleged that this intangible reduction in the incidence of lung cancer was due to the existing of the problems and changes in the cancer records. In our study the overall trend of lung cancer for each subtype was not statistically significant for the duration of 11 years study, which might be due to an intangible change in the habits of smoking during the study period, and the role of race and environment in the development of the lung cancer. Among the 483 identified patients during the study 141 cases were women and 372 men. The most frequent subtype among men was SCC and among women was the adenocarcinoma. Furthermore, the trend of the change frequency of subtypes in terms of the sex in the case of any subtypes of the lung cancer for men and women was not significant.

In Kermanshah study (2) it was revealed that the incidence rate of lung cancer in the all years of study in men was more than women.

In addition, in the Greek study (14), the incidence of lung cancer in men was more than women. Likewise, the most common subtype in women was adenocarcinoma and the most common in the male was the subtype of SCC which was consistent with the present study. Moreover, in the Greek study (14), a significant decrease in the percentage of squamous cell carcinoma and an increase in the percentage of adenocarcinoma among men were observed in the second decade and in women, the relative incidence of adenocarcinoma was decreased and squamous cell carcinoma increased, however, this was not significant. At any rate, these results were not consistent with the present study results. In addition, in the Greece study a significant change in the prevalence of small cell carcinoma was not observed. In Swedish study (9), the relative frequency of lung cancer in men was more than women and adenocarcinoma was the most common subtype found among women and the squamous cell carcinoma was the most common subtype among men which these results were consistent with the present study.

In a study from the South Texas, it was documented that the Adenocarcinoma was the most common subtype among men and women. The Devasa's study (6) suggested that the adenocarcinoma among men and women has increased for the duration of the study period. This study also showed that the squamous cell carcinoma and small cell cancer were vertically reduced in the examined women. Additionally, the SCC incidence had fallen among men in North America and some European countries indicating the results were inconsistent with the present study. Based on the results of this study, despite the decline in smoking in many Western countries and the use of filtered low-tar cigarette, the increase of adenocarcinoma cancer among women and men still continues. In a study conducted in the Ireland (5) the total incidence of lung cancer was scrutinized and it was cleared that the men were more involved than women. This study also confirmed that a declining trend in the incidence of lung cancer in men (one percent annually) and an increasing trend in the prevalence of the lung cancer was observed among women which were not in agreement with the findings from the present study.

Correspondingly, in the study of South Asia (13) a significant increase in the incidence of lung cancer was observed in men in the course of the study years however, the increase was not significant in women.

A study from Japan documented that the adenocarcinoma was the most common subtype among both sexes, and then the SCC was ranked in the second position for the both sexes as well.

A Chinese study emerged that there was a pattern changing of histology in the form of increase for the adenocarcinoma percentage and a decrease in the percentage of squamous cell carcinoma in men. Additionally, there was also a decrease in the percentage of adenocarcinoma in women that was not consistent with the present study.

The mean age of patients with small cell cancer was 63.6 years while, non-small cell cancer was 63

years. For the subtype of NSCLC cases the mean age of patients with adenocarcinoma was 59.81 years, the SCC, 65.8 and for the large cell adenocarcinoma were 63.o9 years. As well as, for non-small cell cancer (NSCLC) with unknown subtype this figure was 57.33 years.
In a study from Turkey (15) the mean age of patients with lung cancer at diagnosis stage was 59.4 which was less than the average age of the disease in the present study.

Also in the study of South Texas (8) the average age of disease was evidenced at 59 years. The mean age for adenocarcinoma was 58 years, large cell carcinoma 57 years, for small cell cancer 59 years and for SCC was recorded 61 years.
Nevertheless, the results of this study were more consistent with the Swedish study (9) in which the average age of disease was also recorded at the 6th decades. For the duration of this study, no significant change was observed in the mean age of patients with lung cancer. However, in the North West of Italy (16) a significant increase was observed in patients' age with lung cancer at the 65 to the 68 years.

In the study of Greece (15) during the second decade of the investigation a significant increase was verified for the mean age of the patients with the lung cancer.

In terms of the disease stage at diagnosis time the whole patients with primary lung cancer referred to the Department of Radiotherapy and Oncology, Ahvaz Golestan Hospital, for the duration of 11 years of study 48.9 percent disease at diagnosis time were in the stage IV. Also, for 48% of patients it was not possible to determine the stage due to incomplete information in the patients' files. In general, 1.9% of patients were in stage IIIb, 0.8 percent stage with IIIa and 0.2 percent in stage Ib. In the histological subtypes of lung cancer, for small cell carcinoma, 46% of patients were in stage IV and for 8.5% of the patients the stage determining was not possible.

The percentage of patients with NSCLC in the stage IV was 46.6 while, for 50.8% of patients the probability of determining the stage of disease was not possible.

In the subtypes of NSCLC for the SCC subtype, 35.7% patients were in the stage IV however, 61.8% were classified in unknown group stage.
In the subgroup of large cell carcimoma, 42.9% were in stage IV and 57.1% of patients were classified as unknown stage. In the Irish study (5) the percentage of recognized patients in the phase III for the period of 2000-2003 was 23% and in 2004-2008, was 26 percent. In addition, the relative percentage of identified patients in 1996-1999 for the stage IV was 26%. The relative percentage of patients identified in 2000-2003 was recorded for 23 percent, and in 2004-2008, was 38 percent. Comparing the above results for the examined patients in this study they were showing a higher stage at diagnosis time. However, according to the achieved results from this study despite advances in diagnostic and treatment methods, there was no significant decrease for the stage of diagnosis.

In the Swedish study (9) 68% of patients diagnosed with stage IIIb (27.2) or IV (40.8 percent) which were largely inconsistent with the present study results.

Additionally, in the North West of Italy study (16) 77% of patients were documented with locally advanced stage (41%) or metastatic stage (36 percent).

Conclusion

The results showed that the frequency of lung cancer in the total in both sexes and in all studied lung cancer subtypes did not show a significant change. This can be due to impalpable changes in the culture and lifestyle of the people especially in the case of smoking and exposure to other lung carcinogens.
For the duration of the study also the average age of patients for the lung cancer in the community, no significant change was observed that this can be of confirmation of above issue.

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