

Featuring trends in the epidemiology of lung cancer following the publication of the National Cancer Strategy in the State of Qatar

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Abstract

Introduction

The State of Qatar has witnessed significant reforms in its health care system including the care of cancer patients. In 2011, the National Cancer Strategy, with the aim to deliver a high standard of care to cancer patients across the country, was released. We aimed to investigate the featuring trends in the epidemiological and clinical characteristics of lung cancer in Qatar following the publication of the National Cancer Strategy.

Methods

This was a retrospective cohort study documenting the epidemiological and clinical characteristics of primary lung cancer cases diagnosed during the period from January 1st, 2011 till December 31st, 2018, in the State of Qatar.

Results

The overall age-standardized incidence rate was 8.67 per 100,000 persons (for males and females were 11.64 per 100,000 and 5.36 per 100,000 persons, respectively). The 1, 3, and 5-year overall survival rates were 67%, 48%, and 28%, respectively. The 3-year overall survival rates for stages I, II, III, and IV were 97%, 78%, 52%, and 31% respectively. The 3-year survival rates for males and females were 43% and 64% respectively (P-value 0.029), for Qatari and non-Qatari nationals were 42% and 49% respectively (P-value 0.252), and for smokers and non-smokers were 39% and 69% respectively (P-value ≤ 0.001). The overall age-standardized mortality rate was 5.49 per 100,000 persons. Adenocarcinoma was the most common histologic type.

Conclusion

Despite the low overall lung cancer incidence rate in the State of Qatar, there is a rise in the incidence among females when compared to previous studies. Qatar has favourable 5-year lung cancer survival rates compared to many developed and neighbouring countries. Policymakers in the country should consider the changing patterns in lung cancer incidence when planning future preventive strategies.

Keywords: Lung cancer, epidemiology, Incidence, Survival, Qatar.

Introduction

The incidence and mortality of cancer are rapidly growing worldwide. Lung cancer is not an exception. Despite being a preventable disease, as more than 85% of the cases are caused by smoking, the incidence of lung cancer is increasing in many countries since 1987 due to the increase in smoking prevalence ¹. Globally, lung cancer is the most commonly diagnosed cancer, and the leading cause of cancer death for both sexes combined. It is also the most commonly

occurring cancer in men and the third most commonly occurring cancer in women ². In the year 2018, 2.1 million new lung cancer cases and 1.8 million lung cancer-related deaths (representing close to 1 in 5 (18.4%) cancer deaths) were reported ². The association of lung cancer with smoking is strong, dose-related, and is evident for all types of lung cancer which emphasize the causal nature of the relationship ³. Despite the high prevalence of both cigarette and water-pipe smoking in the Gulf Cooperation Council (GCC) countries, a significant challenge encountered is to obtain accurate data about lung cancer incidence due to the lack of comprehensive, up-to-date population registries ¹. In the State of Qatar, tobacco use remains a significant public health concern with an estimated smoking prevalence of 36.5% ⁴. Furthermore, like in many other GCC countries, the water-pipe smoking epidemic is on the rise in the country and is replacing cigarettes as the most popular method of tobacco use, particularly among youths ^{5,6}. In 2010, Ibrahim et al. reported for the first time, the clinical and epidemiological characteristics of lung cancer in the State of Qatar during the period from 1998 to 2005 ⁷. The age-standardized incidence rate (ASIR) over the study period was estimated to be 8.95 per 100,000 persons for the total population (15.20 per 100,000 for males and 3.95 per 100,000 for females) ⁷. Since then, the State of Qatar has witnessed a significant reform in its health system, including the care of cancer patients. In 2011, the National Cancer Strategy was published with the aim to deliver a high standard of care to cancer patients across the country ⁸. The National Center for Cancer Care and Research (NCCCR), a well-equipped and sophisticated centre, has been established as the premier healthcare facility to deliver such care for all cancer patients in the country. The present study aimed to report the trends in lung cancer epidemiological and clinical characteristics since the publication of the National Cancer Strategy and compare the results with the previously reported data in 2010 ⁷.

Methods

Study design

This was a retrospective cohort study documenting the epidemiological and clinical characteristics of all primary lung cancer cases diagnosed during the period from January 1st, 2011 till December 31st, 2018, in the State of Qatar. Patients with lung metastasis due to primary malignancy originating outside the lungs were excluded.

Data collection and data source

Data related to the epidemiological and clinical characteristics of lung cancer during the study period were obtained from two primary sources; the Qatari National Cancer Registry Database and the extensive search in the patient's electronic medical records. Considering the challenges encountered in many international cancer registries regarding the quality, reliability, and completeness of cancer registration data, we performed an extensive search in patients' electronic medical records to confirm consistency and completeness of the information obtained from the registry. Utilizing the patient's medical records and the cancer registry data, patients in the current study were censored until one of the following happened (a) a patient has died (b) a patient has not yet died by the time of the close of the study, or (c) the time of the last follow up if a patient was lost to follow-up. All data were recorded in a structured data collection sheet.

Quality Assurance

To ensure consistency of the data, all investigators involved in data collection received prior training on how to complete the datasheet. Furthermore, two senior investigators (WI and KS) independently reviewed the data collected by other investigators for accuracy and reliability.

Statistical analysis

Qualitative and quantitative data were expressed as the frequency with percentage and mean \pm standard deviation (SD) with median and range. Descriptive statistics were used to summarize demographic and all other clinical characteristics of the participants. Associations between at least two qualitative or categorical variables were assessed using the χ^2 test. For small cell frequencies, the χ^2 test with a continuity correction factor or the Fisher exact test was applied. Pictorial presentations of the key results were made using appropriate statistical graphs. Incidence and mortality rates were expressed as new cases per 100,000 person-years with 95% confidence intervals (CIs) and age standardization using the World Health Organization (WHO) world standard population 2000–2025. Survival tables and Kaplan-Meier curves were utilized to calculate both 1- and 3-year survival probabilities with log-rank analysis to compare the variables. A Poisson regression model was used to test the time trend in 5-year relative survival. A 2-sided P value less than .05 was considered statistically significant. Statistical analyses related to demographic and subject characteristics were performed using SPSS 22.0 (SPSS, Inc, Chicago, Illinois). Mortality and survival statistics were computed using the StataCorp LP software, version 14.

Results

Tables 1 and 2 show the demographic and clinical characteristics of lung cancer patients. A total of 428 patients were diagnosed with lung cancer during the study period. The mean age at diagnosis was 59.6 ± 12.6 years (59.3 years for males and 60.5 years for females). The median age, minimum age, and maximum age at diagnosis were 60 years, 30 years, and 104 years respectively. Males constituted 78.7% and females 21.3% of lung cancer cases. About 66% of patients had a positive history of smoking. Cough was the most common symptom in 68.6% of cases followed by dyspnea in 46.5%. About 54% of patients had symptoms related to distant

metastasis at presentation, whereas 8% were asymptomatic at the time of diagnosis.

Computerized tomography (CT) guided biopsy was the most common method of confirming the diagnosis in 48% of cases followed by bronchoscopy in 34.2%. The majority of patients (78.7%) were in stage IV at the time of diagnosis (**Figure 1**). Adenocarcinoma was the most common histologic type of lung cancer in 57.3% of cases and the most common in males and females (**Figure 2**). About 23% of patients received surgical treatment, 69% received chemotherapy, and 44% received radiotherapy. Targeted therapy was provided to 44.4% of patients with adenocarcinoma (**Table 2**). There is a significant association between smoking and all the main three histologic types of lung cancer (adenocarcinoma, small cell cancer, and squamous cell cancer) (**Table 3**).

The overall age-standardized incidence rate (ASIR) was 8.67 per 100,000 persons. The ASIR for males and females were 11.64 per 100,000 and 5.36 per 100,000 persons, respectively (**Figure 3**). The median follow-up time was nine months (range 1–89 months). The 1, 3, and 5-year overall survival rates calculated by the Kaplan-Meier method were 67%, 48%, and 28%, respectively (**Figure 4**). The 3-year overall survival rates for stages I, II, III, and IV were 97%, 78%, 52%, and 31% respectively (P-value 1.67) (**Figure 5**). The 3-year survival rates for males and females were 43% and 64% respectively (P-value 0.029) (**Figure 6**), for adenocarcinoma, small cell cancer, and squamous cell cancer types were 55%, 33%, and 48% respectively (P-value 0.088) (**Figure 7**), for patients < 40 years old was 64% (**Figure 8**), for Qatari and non-Qatari nationals were 42% and 49% respectively (P-value 0.252) (**Figure 9**), and for smokers and non-smokers were 39% and 69% respectively (P-value ≤ 0.001) (**Figure 10**). The overall age-standardized mortality rate (ASMR) was 5.49 per 100,000 persons. The ASMR for males and females were 7.55 per 100,000 and 3.13 per 100,000 persons respectively.

Discussion

The current study has demonstrated some striking features related to the epidemiological and clinical characteristics of lung cancer in the State of Qatar. The overall ASIR of lung cancer remains one of the lowest in the world (8.67 per 100,000 persons) with a noticeable rise in ASIR among females (5.49 per 100,000 persons) compared to the previously published data (3.95 per 100,000 persons) ⁷. Data from the Qatari National Cancer Registry revealed that lung cancer ranked the fifth among the most common cancers in the State of Qatar for both sexes during the period from 2009 to 2018, the third for men and the eighth for non-Qatari women resident in the country. It was not among the ten most common cancers for Qatari women. This finding is exciting and may reflect the higher prevalence of smoking among non-Qatari residents in the country ⁴. Lung cancer does show wide geographic variations in its incidence rates across the world. The highest incidence rates are observed in Micronesia/Polynesia, in Eastern Asia (rates are above 40 per 100,000 persons in China, Japan, and the Republic of Korea), and in much of Europe, especially in Eastern Europe, with an ASIR in Hungary as high as 77.4 per 100,000 males. Incidence rates generally remain low in West and Central Africa (ASIRs 2.8 and 3.1 per 100,000 persons, respectively) ². It is a well-known fact that lung cancer incidence and mortality are tightly linked to cigarette smoking patterns. As smoking rates peak, lung cancer incidence and mortality rise in subsequent decades ^{9,10}. The low incidence of lung cancer despite the previously reported high smoking prevalence in the State of Qatar is a fascinating observation in the current study and is difficult to explain. Nevertheless, this finding is not peculiar to Qatar and has also been observed in many other countries of the GCC and the Middle East and North African (MENA) origin. In some of these countries, smoking rates are even higher than in western countries like the United States and the United Kingdom and are comparable with

France and Japan. For example, Kuwait has the highest smoking prevalence of 46% in the region, yet the ASIR of lung cancer is only 7.3 per 100,000 persons. In Egypt, where the use of tobacco products is widespread, and approximately 20 billion cigarettes are smoked annually, the ASIR of lung cancer remains low at 7.6 per 100,000 persons ^{1, 11, 12, 13}. Some of the plausible explanations for this observation are the younger populations in these countries compared to the high lung cancer risk countries, genetic variations, and the inherited susceptibility theory. A fact that supports the theory of genetic and inherited susceptibility is that lung cancer occurs in only a minority of cigarette smokers even though cigarette smoking is the predominant cause of lung cancer. Furthermore, a family history of lung cancer has been observed to be a risk factor for lung cancer in nonsmoking populations ¹⁴. Compared to the previously published data from Qatar in 2010 ⁷, there seems to be a decline in the overall ASIR of lung cancer in men and a rise in women. This finding has also been observed in industrialized countries over the past 40 years. In the United States, the incidence and mortality rates of lung cancer in women have risen markedly and are becoming nearly identical to those of men. Similar trends have also been observed in the United Kingdom, and central and eastern Europe. Such gender trends have been attributed to the rising tobacco epidemic in these countries, the changes in the histologic pattern over time, and the socioeconomic and educational inequalities ^{9, 15, 16}. Similar to previous data ⁷, the current study has shown that adenocarcinoma is the most common histologic type of lung cancer in the State of Qatar. Adenocarcinoma incidence rates have risen and surpassed those of squamous cell carcinoma (historically the most frequent subtype) in many industrialized countries since the 1990s, and its rates continue to increase in populations from other nations. This rise has been in parallel to the increased incidence of lung cancer in women. Different reasons have been postulated to explain the rise in the incidence of adenocarcinoma, including

the change in the type of tobacco smoked, genetic predisposition, and environmental exposures ⁹, ¹⁷. One of the most striking findings in the current study is the higher survival rates among patients with lung cancer in the State of Qatar compared to the international figures. The 1, 3, and 5-year overall survival rates in our study were 67%, 48%, and 28% respectively. Recent estimates showed that Japan had the highest 5-year relative survival worldwide at 30%, while Libya, Mongolia, Chile, Bulgaria, and Thailand had the lowest survival rates of less than 10% ¹⁸. The 5-year lung cancer survival rates in the United States, Canada, France, Germany, Italy, and the United Kingdom are 18.7%, 17.3%, 13.6%, 16.2%, 14.7%, and 9.6% respectively ¹⁹. When also compared to the neighbouring GCC countries, the State of Qatar has a higher lung cancer 5-year survival rate. Recent data from Oman revealed a median overall survival of seven months and a 5-year survival rate of 7% for patients with non-small cell lung cancer (NSLC) ²⁰. In the Kingdom of Bahrain, lung cancer 5-year survival is only 3% ²¹. Data regarding lung cancer survival in the Kingdom of Saudi Arabia and the United Arab Emirates are scarce. Nevertheless, the most favourable lung cancer 5-year survival for NSLC reported from one of the tertiary centres in Saudi Arabia is 26% ²². Several factors can explain the better survival rates in the State of Qatar compared to other countries including improved coordination of care of cancer patients at the national level, the timely access to expert opinion and treatment, the utilization of state-of-the-art testing for genetic mutations in NSLC, the availability of sophisticated radiologic investigations, the advanced treatment options that are provided free of charge to all cancer patients resident in the country, and the standardized long-term surveillance of lung cancer survivors.

Study strengths

The current study has described the most recent trends in the epidemiological and clinical characteristics of lung cancer in the State of Qatar and has highlighted some of the outcomes in the care of lung cancer patients following the publication of the National Cancer Strategy in 2011 ⁸. It is the first to describe the details of lung cancer survival and mortality in the country. Among the important points of strength in this study is the extensive search in the patient's medical records that was performed to overcome the deficiency in the cancer registry and ensure consistency and accuracy of the collected data. Furthermore, the results of the present study can be generalized to the whole country as all patients with lung cancer are referred to and treated in the NCCCR from which the study data were obtained.

Study limitations

Nevertheless, the current study has important limitations. Besides the limitations inherited in retrospective studies, one of the major challenges we encountered during data collection was the incomplete cancer registry database that lacks comprehensive and up-to-date information.

Nevertheless, this problem was anticipated at the start, and we decided to search the patient's electronic medical records as well. Another important limitation is the inability to examine the contribution of water-pipe smoking to the burden of lung cancer. As we pointed earlier, the prevalence of this type of smoking is on the rise in the country, and it would be interesting if its contribution to the development of lung cancer, particularly among non-Qatari females, was examined. The retrospective nature of the study did not permit the examination of smoking and other risk factor characteristics among Qatari and non-Qatari patients which, in turn, limited proper characterization of the two populations.

Conclusion

Despite the low overall incidence of lung cancer in the State of Qatar, its incidence in females is rising. Lung cancer has a favourable survival in Qatar when compared to other countries.

Patients in the State of Qatar have good access to standard and advanced cancer care.

Policymakers in the State of Qatar should also consider the changing patterns in lung cancer incidence such as its rise in non-Qatari women, when planning future preventive strategies. Since many lung cancer patients in the country are diagnosed at advanced stages, early detection programs should be considered. Furthermore, an initiative for a cancer registry improvement program is needed in the country. This program should include training of cancer registry staff and can play a crucial role in ensuring good-quality data and adequate data analysis, interpretation, and dissemination.

Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of interest

The authors declare that there are no relevant conflicts of interest.

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Table 1: Demographic characteristics of lung cancer patients

Characteristics	Number of patients (%)	
Age in years (N: 428)		
<40	30 (7.0)	
40-49	64 (15.0)	
50-59	115 (26.9)	
60-69	125 (29.2)	
70-79	71 (16.6)	
80+	23 (5.4)	
Gender (N: 428)		
Male	337 (78.7)	
Female	91 (21.3)	
Nationality (N: 428)		
Qatari	89 (20.8)	
Non-Qatari	339 (79.2)	
Smoking history (N: 387)		
Yes	257 (66.4)	
Number of cigarettes smoked per day for smokers (N: 156)		
Average	26	
1-10	24 (15.4)	
11-20	77 (49.4)	
21-30	7 (4.5)	
>30	48 (30.8)	
Duration of smoking (years) (N: 172)		
Mean±SD	30±13	
Median	30	
Minimum	2	
Maximum	73	
Smoking history by gender (N: 387)/P-value: ≤0.001		
Smoking	Males	Females
Yes	235	22
No	71	59

Table 2: Clinical characteristics of lung cancer patients

Clinical characteristic		Number of patients (%)
Cough (N: 407)		279 (68.6)
Hemoptysis (N: 404)		83 (20.5)
Dyspnea (N: 404)		188 (46.5)
Chest pain (N: 406)		174 (42.9)
Hoarseness of voice (N: 401)		21 (5.2)
Malaise (N: 400)		98 (24.5)
Weight loss (N: 398)		132 (33.2)
Symptoms related to distant metastasis (N: 402)		216 (53.7)
Asymptomatic (N: 404)		31 (7.7)
Finger clubbing (N: 363)		15 (4.1)
SVC obstruction (N: 404)		21 (5.2)
Hypercalcemia (N: 414)		51 (12.3)
Lung involved (N: 418)	Right	237 (56.7)
	Left	150 (35.9)
	Both	31 (7.4)
Method of diagnosis (N: 383)	Bronchoscopy	131 (34.2)
	CT guided biopsy of the lung lesion	184 (48.0)
	VAT lung biopsy	17 (4.4)
	Pleural biopsy	27 (7.0)
	Mediastinoscopy	3 (0.8)
	Biopsy from distant metastasis	17 (4.4)
	Thoracocentesis	4 (1.0)
Treatment received	Surgery (N:375)	86 (22.9)
	Chemotherapy (N:377)	259 (68.7)
	Radiotherapy (N:370)	164 (44.3)
	Targeted therapy (N: 212)	94 (44.4)

Table 3: Associations between the three main histologic types and other variables

Characteristic		Histologic type			P-value
		Adenocarcinoma	Squamous cell cancer	Small cell cancer	
Smoking history	Yes	122	48	25	≤0.001
	No	92	8	5	
Gender	Male	172	61	25	≤0.001
	Female	66	1	6	
Nationality	Qatari	38	19	7	.030
	Non-Qatari	200	43	24	
Lung involved	Right	141	35	12	.172
	Left	73	25	14	
	Both	18	2	3	
Stage at diagnosis	Stage 1	16	3	0	.002
	Stage 2	4	2	2	
	Stage 3A	7	5	1	
	Stage 3B	3	6	1	
	Stage 4	171	31	20	

Figure 1: Stage of lung cancer at the time of diagnosis:

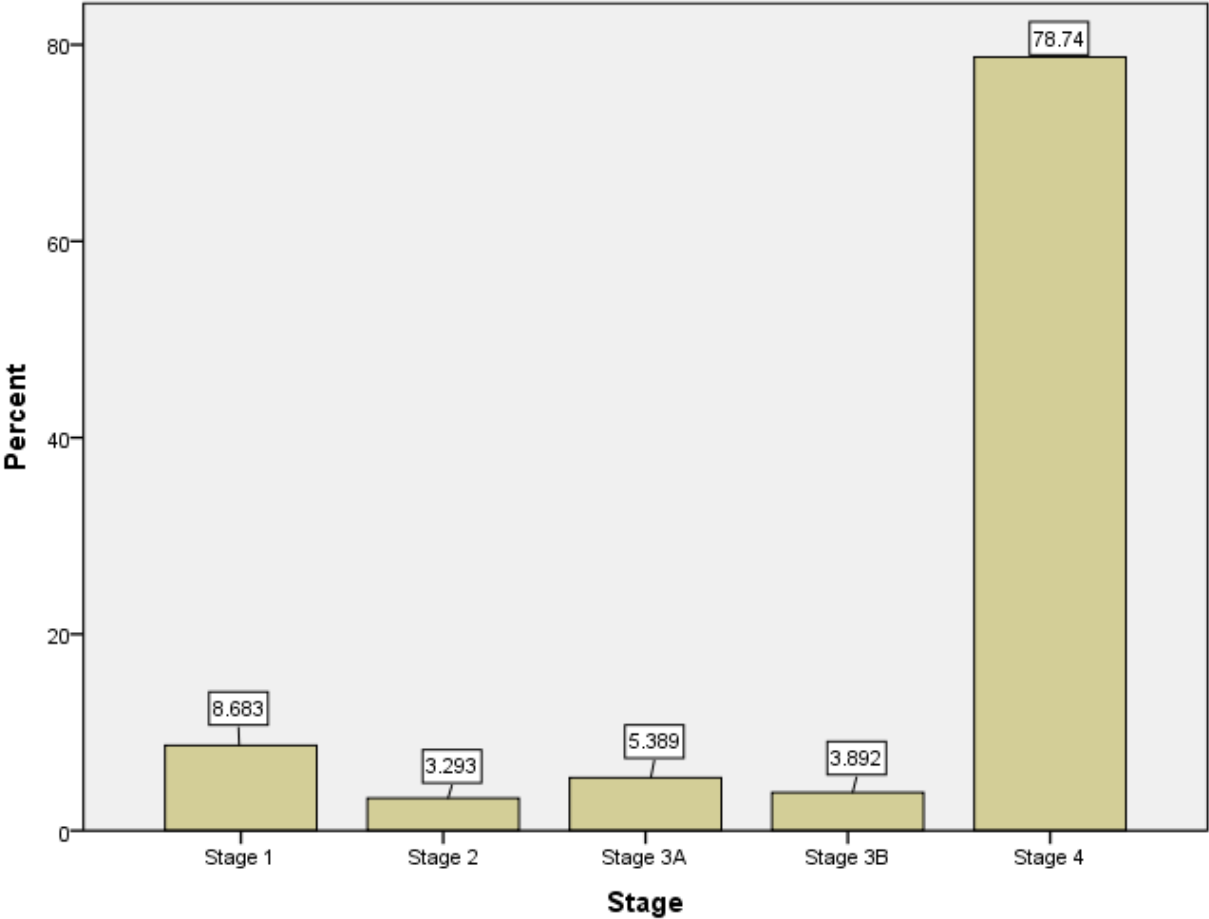


Figure 2: Histologic types of lung cancer

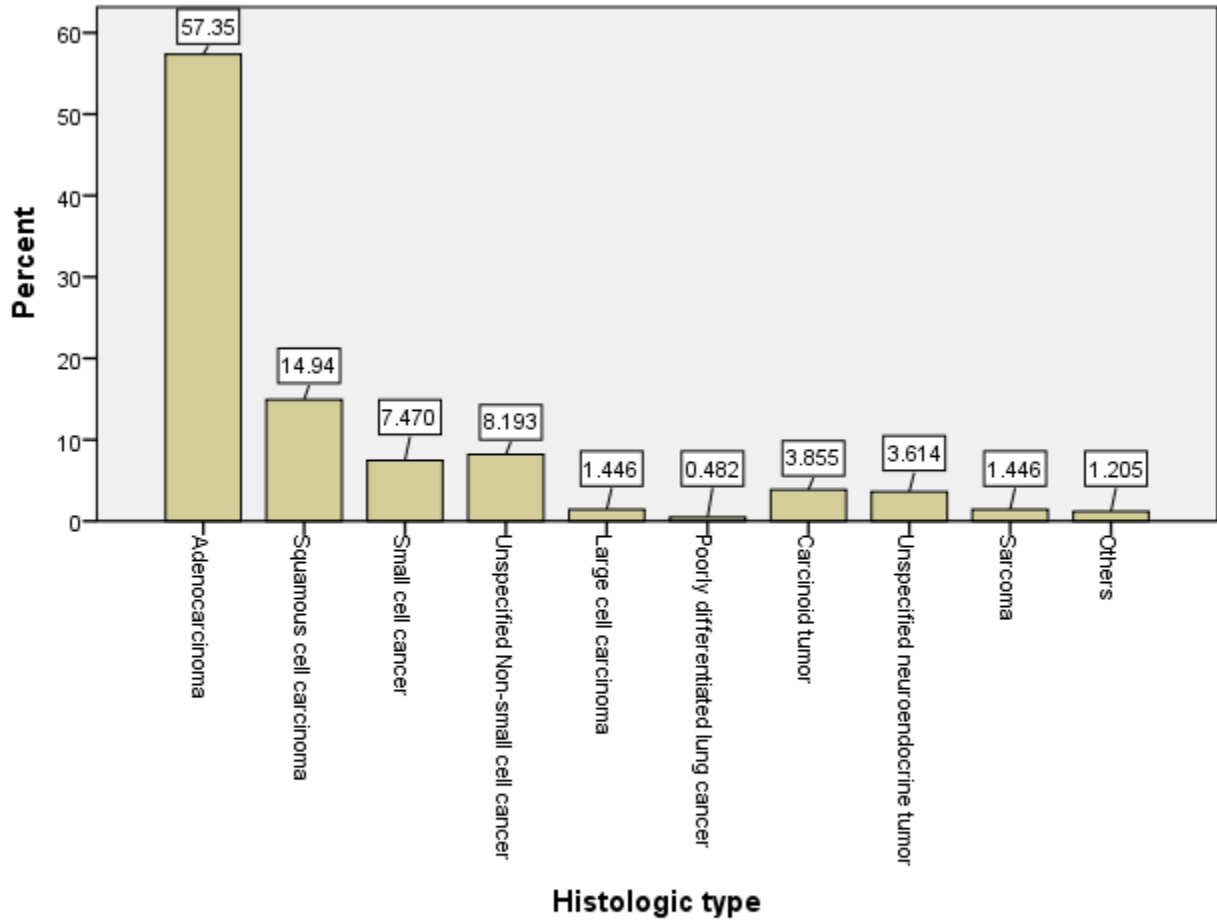


Figure 3: ASIR of lung cancer in Qatar between 2011 and 2018

(per 100,000 person-years)

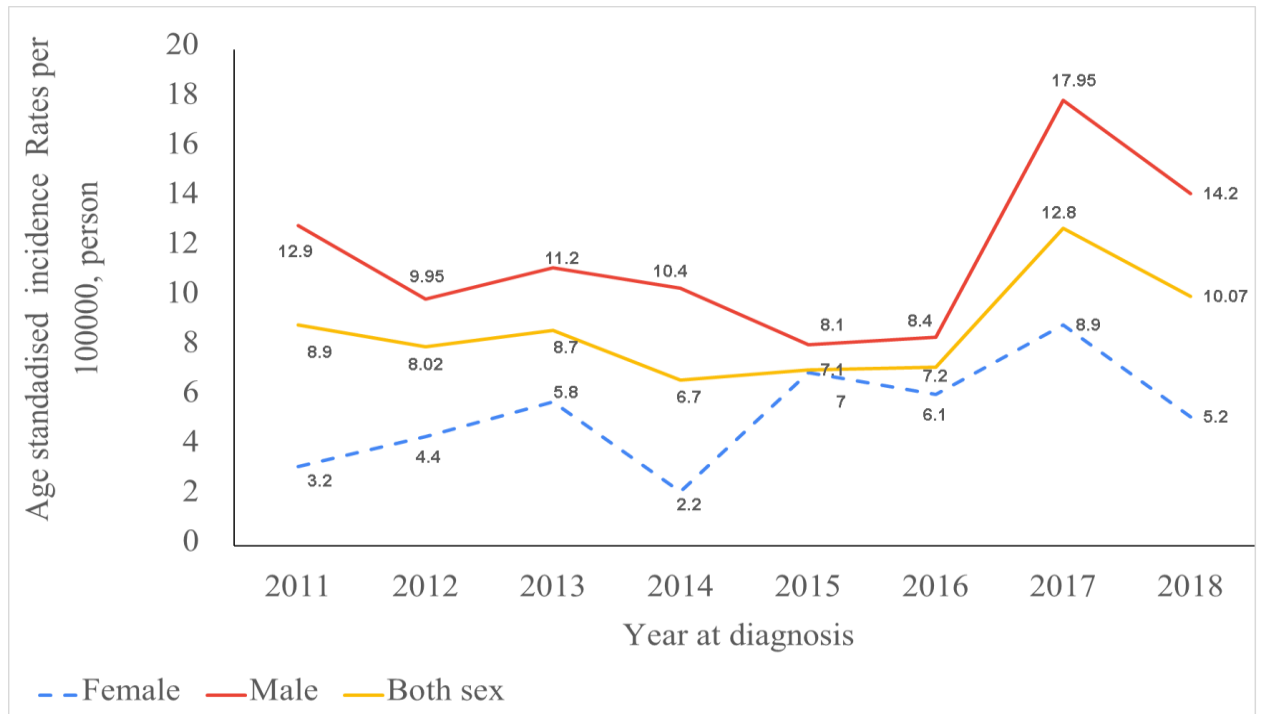


Figure 4: Overall survival of lung cancer patients

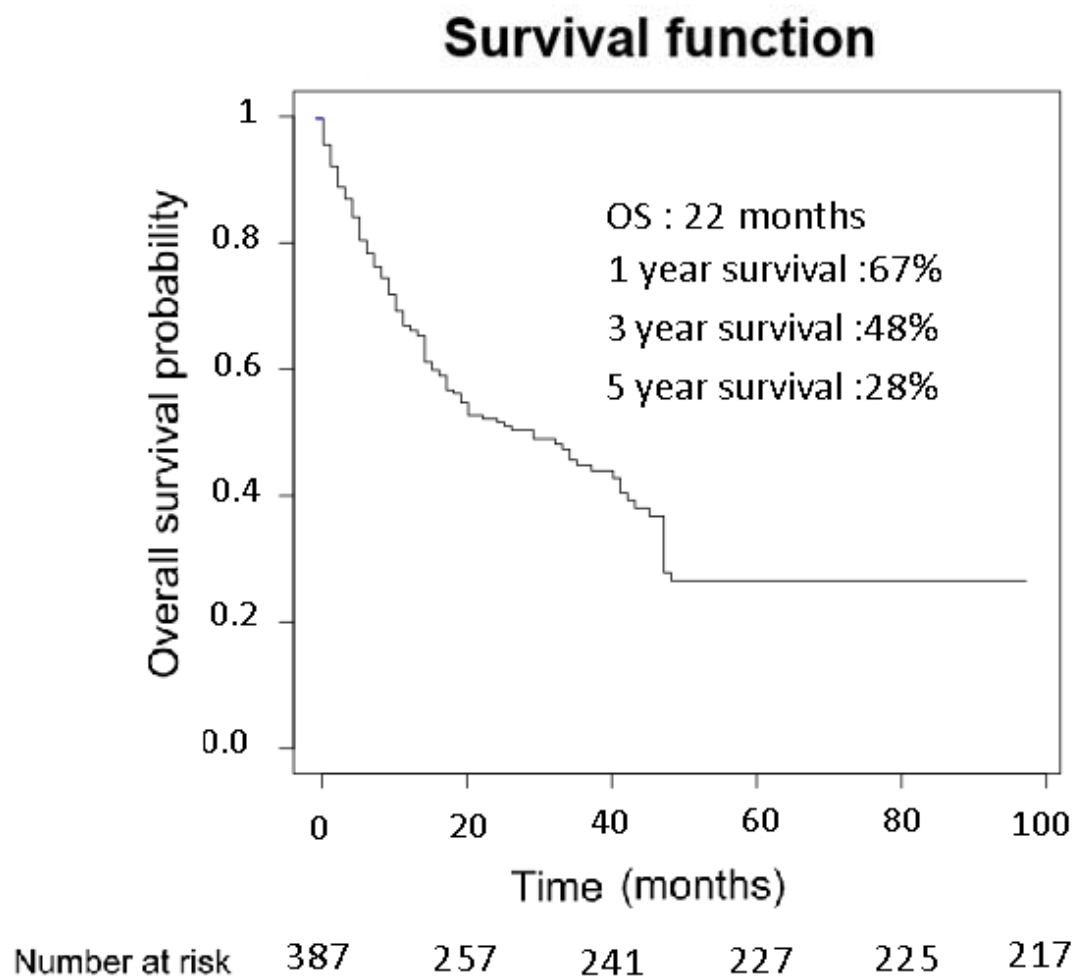
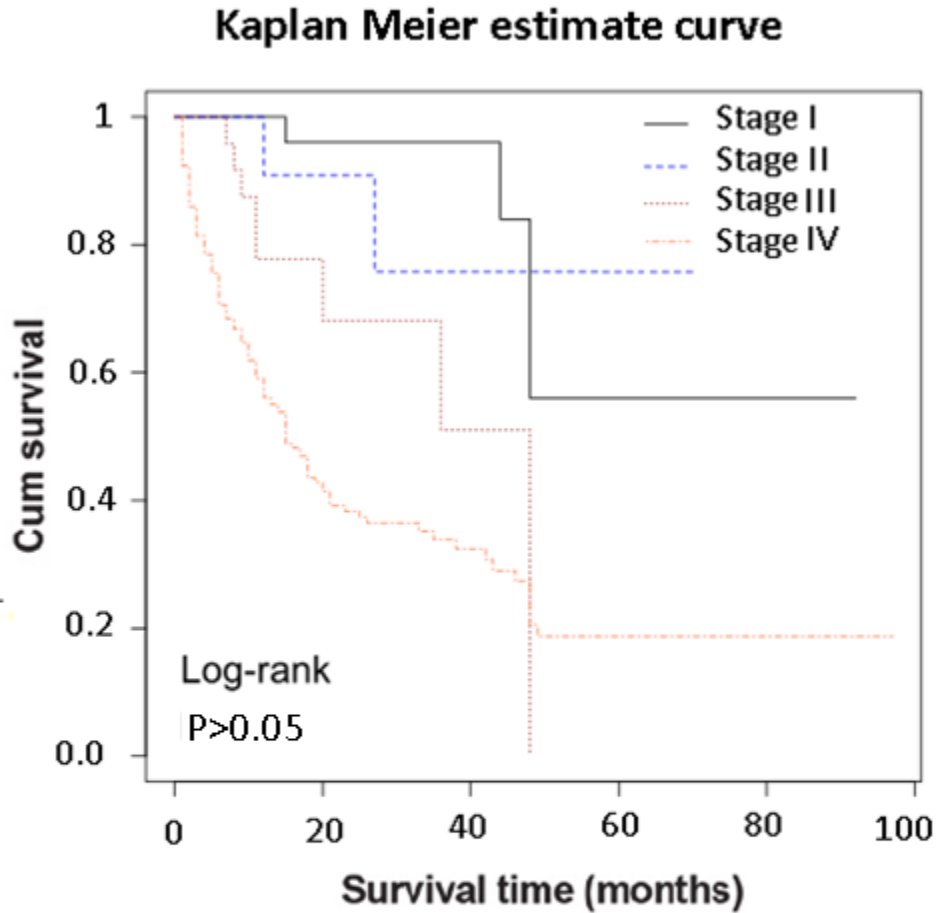
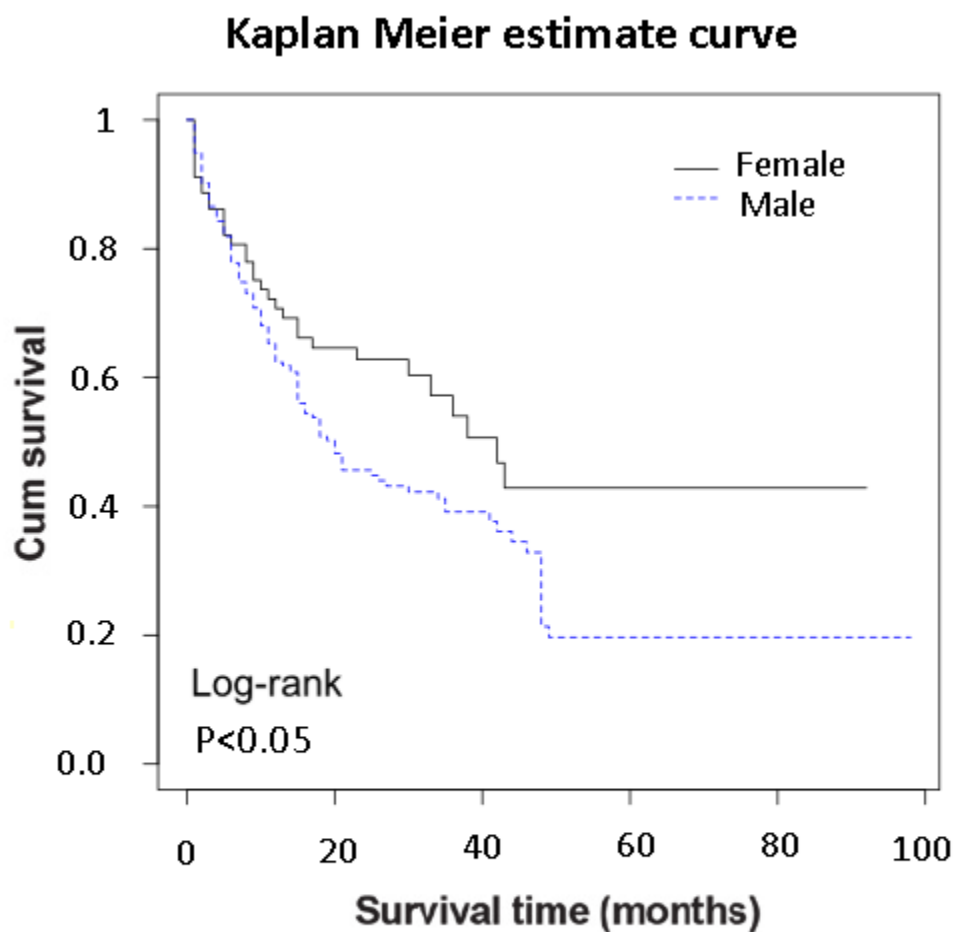


Figure 5: Lung cancer survival by cancer stage



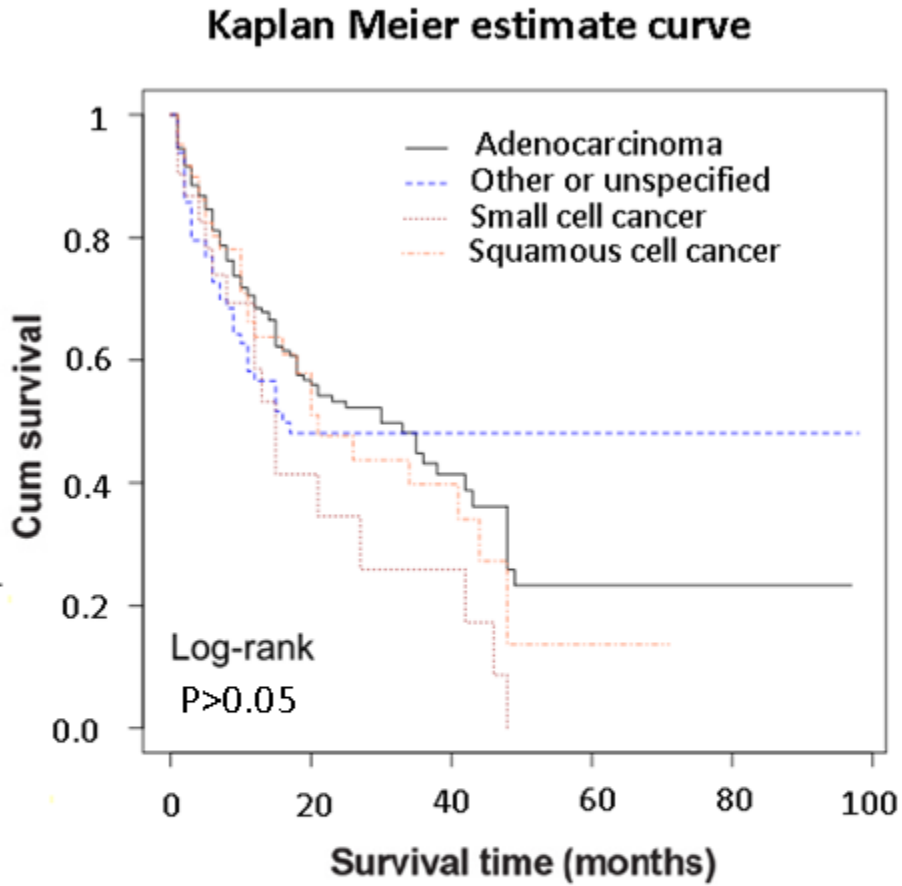
	Median OS	1-year survival	3-year survival	P-value
Stage I	Not reached	100%	97%	P>0.05
Stage II	Not reached	100%	78%	
Stage III	31 mos	79%	52%	
Stage IV	18 mos	68%	31%	

Figure 6: Lung cancer survival by gender



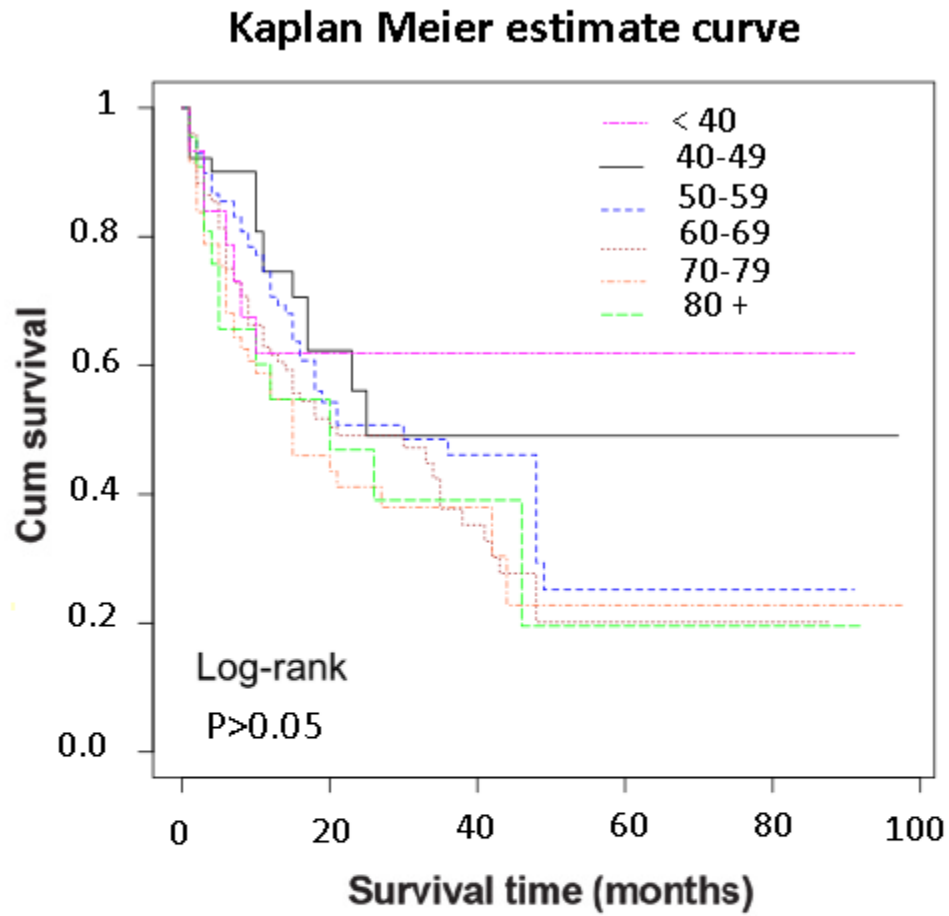
	Median OS	1-year survival	3-year survival	P-value
Male	21 mos	79%	43%	P<0.05
Female	41 mos	81%	64%	

Figure 7: Lung cancer survival by histologic type of the cancer



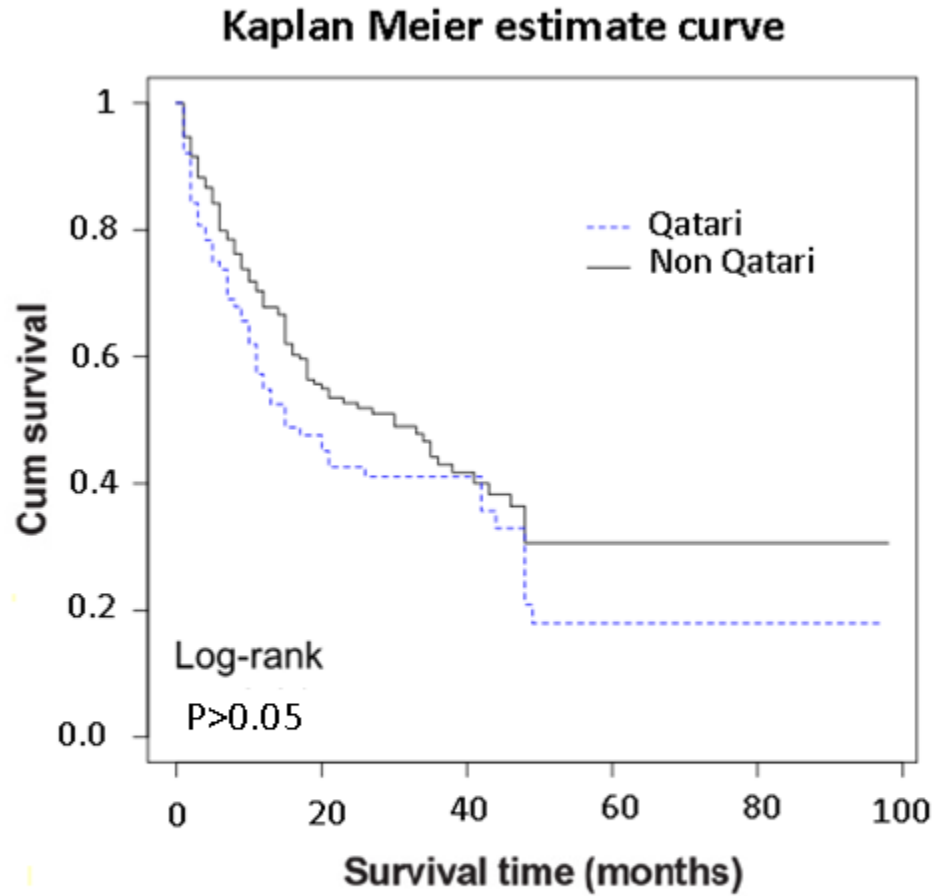
	Median OS	1-year survival	3-year survival	P-value
Adenocarcinoma	38 mos	71%	55%	P>0.05
Other and unspecified	18 mos	63%	51%	
Small cell cancer	16 mos	60%	33%	
Squamous cell cancer	21mos	61%	48%	

Figure 8: Lung cancer survival by age at diagnosis



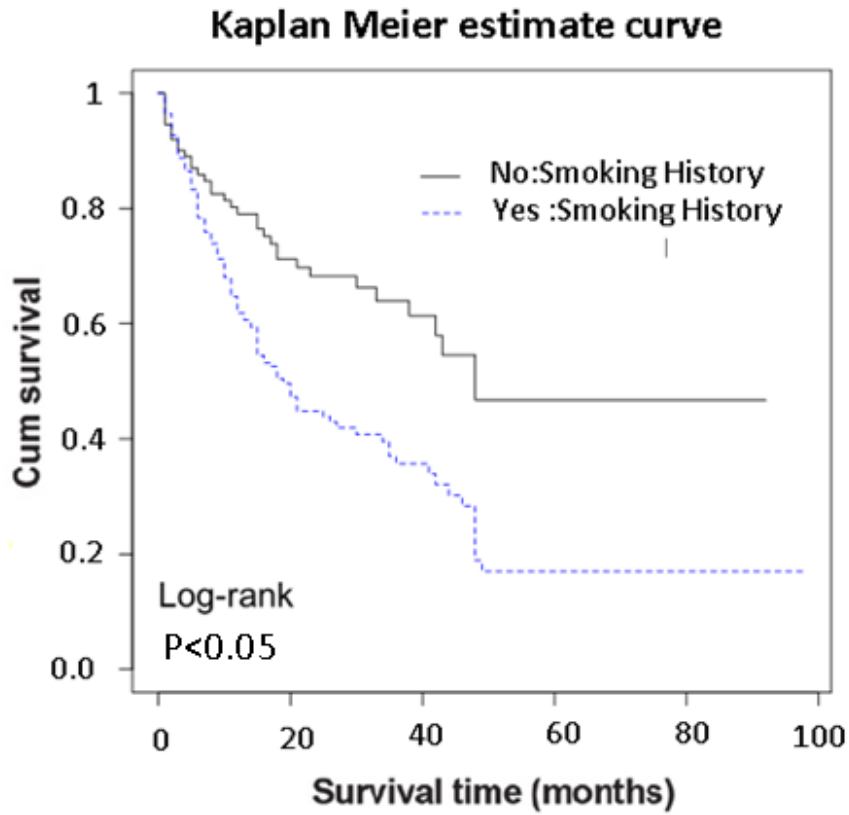
	Median OS	1-year survival	3-year survival	P-value
<40	Not reached	64%	64%	P>0.05
40-49	25mos	86%	51%	
50-59	30mos	79%	46%	
60-69	33mos	63%	40%	
70-79	15mos	58%	37%	
80+	20mos	54%	36%	

Figure 9: Lung cancer survival by patient's nationality



	Median OS	1-year survival	3-year survival	P-value
Qatari	15mos	57%	42%	P>0.05
Non -Qatari	33mos	74%	49%	

Figure 10: Lung cancer survival by smoking history



	Median OS	1-year survival	3-year survival	P-value
Yes- smoking history	15mos	75%	39%	P<0.05
No- smoking history	33mos	88%	69%	

