An overview of mortality & predictors of small-cell and non-small cell lung cancer among Saudi patients

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ABSTRACT

Lung cancer ranks as the top cancer worldwide in terms of incidence and constitutes a major health problem. About 90% of lung cancer cases are diagnosed at advance stage where treatment is not available. Despite evidence that lung cancer screening improves survival, guidelines for lung cancer screening are still a subject for debate. In Saudi Arabia, only 14% of lung cancers are diagnosed at early stage and researches on survival and its predictors are lacking. This overview analysis was conducted on predictors of lung cancer mortality according to the two major cancer types, small-cell lung cancers (SCLCs) and non-small cell lung cancers (NSCLCs) in Saudi Arabia. A secondary data analysis was performed on small-cell lung cancers (SCLCs) and Non-small cell lung cancers (NSCLCs) registered in the Saudi Cancer Registry (SCR) for the period 2009–2013 to estimate predictors of mortality for both lung cancer types. A total of 404 cases (197 SCLC and 207 NSCLC) were included in the analysis, all Saudi nationals. A total of 213 (52.75%) deaths occurred among lung cancer patients, 108 (54.82%) among SCLCs and 105 (50.72%) among NCSLCs. Three quarter of patients are diagnosis with advance stage for both SCLC & NSCLC. Univariate analysis revealed higher mean age at diagnosis in dead patients compared to alive patients for SCLCs (p = 0.04); but not NSCLCs, a lower mortality for NSCLCs diagnosed in 2013 (p = 0.025) and a significant difference in stage of tumor (p = 0.006) and (p = 0.035) for both SCLC and NSCLC respectively. In multiple logistic regression, stage of tumor was a strong predictor of mortality, where distant metastasis increased morality by 6-fold (OR = 5.87, 95% CI: 2.01 – 17.19) in SCLC and by 3-fold (OR = 3.29, 95% CI: 1.22 – 8.85) in NSCLC, compared to localized tumors. Those with NSCLC who were diagnosed in 2013 were less likely to die by 64% compared to NSCLC diagnosed in 2009 (OR = 0.36, 95% CI: 0.14 – 0.93). Age, sex, topography and laterality were not associated with mortality for both types of lung cancer. We observed that the stage of the tumor is the strongest predictor of mortality for both SCLCs and NSCLs. This confirms the impact of diagnostic stage on survival. However, establishing Saudi-specific lung cancer screening guidelines will require further research on the benefits and harms of screening modalities in the Saudi population.

Contents

1. Introduction

Lung cancer is the most commonly diagnosed cancer in the world. According to GLOBACAN, 1.8 million cases of lung cancer were registered during 2012, making up 13% of all cancer deaths [1].

Lung cancer incidence shows a growing trend globally given that in 2002 the number of registered cases was 1.35 million cases which increased to 1.6 million cases by 2008 [2]. This change in incidence contributed to changes in exposure to risk factors, especially smoking, as well as increased lifespan and population size [2,3].

Mortality rate of lung cancer is relatively close to incidence rate, that, global mortality-to-incidence ratio being 0.88 for males and 0.84 for females [3,4]. Lung cancer was responsible for 2.3% of total deaths worldwide during 2004 and ranked as the 8th leading cause of death [5,6].

Saudi Arabia has low incidence rate of lung cancer compared to global incidence. In 2013, age standardized ratio (ASR) was 5.5 per 100,000 for males and 1.8 per 100,000 for females [7]. In contrast, the average global ASR during 2008 was 33.8 per 100,000 for males and 13.5 for females [8]. But, a growing population in Saudi Arabia, along with an expected increase in elderly population size by sevenfold, accompanied by high smoking prevalence; which is gradually increasing by 1.5% for males and 2.0% for females, are all factors that can potentially result in more incidence of lung cancer in Saudi Arabia [9–12].

Lung cancers staging globally shows that only 15% of cases are diagnosed at an early stage [8]. Saudi Arabia falls within the global range, with only 14% of cases diagnosed early with localized tumors [7]. However, in developed countries this percentage is higher. In Canada for example, 20–30% of cases are diagnosed at an early stage [13].

Annual lung cancer screening has been recommended since 2012 by several health organizations and expert panels, which showed a significant decrease in lung cancer mortality by 20.0% (95% CI: 6.8–26.7) (P = 0.004) [14]. However, screening implications are still subject to discussion [15].

Currently, Saudi Arabia does not have national screening guidelines for lung cancer. Developing country-specific screening guidelines requires a strong research base on lung cancer mortality to offer more evidence for decision makers about the value of instituting and implementing national screening guidelines.

The existing gap in detailed knowledge on lung cancer mortality in Saudi Arabia needs to be offset to provide information-for-action for the development of Saudi-customized screening and management guidelines for this malignancy. Hence, main purpose of this paper is focused on the predictors of mortality among lung cancer patients, both small-cell and non-small cell, in Saudi Arabia for the period of 2009–2013.

2. Methods

2.1. Study design

A secondary data analysis was performed on lung cancer cases reported to the (SCR) during the period of 2009–2013 after their permission to use and disseminate the data. Determination of IRB was reviewed by Emory university.

2.2. Setting and data source

Data was requested and readily available from the SCR, as part of their objective is to support dissemination and utilization of registered data.

2.3. Study variables

Data obtained by the SCR includes information on patients demographic data (sex, age, nationality), date of diagnosis, tumor characteristics (topography, morphology, behavior, grade, extension [SEER stage], and laterality), date of last contact (via telephone) and mortality indicators (status and cause of death) [7,16].

2.4. Data management

The dataset included 452 registered cases of lung cancer during 2009–2013, all of which were of Saudi nationality. Diagnoses were restricted to NSCLC and SCLC types of lung cancers. We exclude 48 cases; observations without a valid vital status (N = 1) were excluded as well as unknown cause of death (N = 1) or non-reported data on cancer extension (N = 47; 23 dead and 24 alive). Therefore, the final dataset included 404 observations with a total exclusion of 48 observations.

2.5. Statistical analysis

The distribution of variables was examined by conducting a univariate analysis stratified by SCLC and NSCLC to find differences at each variable within vital status.

To estimate predictors of mortality among lung cancer patients, logistic regression was performed with stratification by histological type. A dichotomous mortality indicator variable was regressed on age, sex, topography, extension, laterality and year of diagnosis. Odd ratios (OR) and 95% confidence intervals (95% CI) were calculated for each predictor. Tumor grade was not included in this study's model due to the large number of missing data (N = 272) and due to the lack of a widely-accepted grading system for lung cancer that is used consistently by all health facilities [17,18]. Tumor behavior variable also was not included in the model due to collinearity, where all observations are recorded as malignant behavior. The level of statistical significance was set at 0.05. Stata (version SE64, Stata Corporation, College Station, TX) was used for analysis.

3. Results

3.1. Demographic and tumor characteristics for overall cases, SCLC and NSCLC

A total of 404 lung cancer cases were diagnosed during the period 2009–2013 and included in the final analysis. SCLC composed 48.8% (N = 197) of the cases, out of which 108 (54.8%) did