The cost of lung cancer in Turkey

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ÖZET

Türkiye'de akciğer kanserinin maliyeti

Bu çalışmada, Türkiye'de akciğer kanserinin hastalara ve topluma yüklediği bedelleri ortaya çıkarmayı amaçladık. Ocak 2002-Şubat 2003 tarihleri arasında göğüs hastalıkları kliniğine başvuran 103 akciğer kanseri olgusu prospektif olarak çalışmaya alındı. Primer sonlanım ölçütü çalışmanın sonuna veya hastalar ölene kadar hastalıklarının maliyetini ölçmekti. Tüm maliyetler tespit edildiği günkü efektif satış kuru üzerinden dolara çevrilerek kaydedildi. Verilerin değerlendirilmesinde tanımlayıcı istatistikler, ki-kare, Fisher testi, Kaplan-Meier analizi ve nonparametrik Bootstraping yöntemleri kullanıldı. Ortalama sağkalım süresi 6.8 aydı. Direkt tıbbi maliyet toplam 564.960 Amerikan Doları iken, hasta başına ortalama direkt maliyet 5.480 ± 4.088 dolar idi. Akciğer kanseri toplam maliyeti çalışma grubunda 1.473.530 dolar ve hasta başına ortalama 14.306 ± 17.705 dolar idi. Her bir yaşam yılının direkt tıbbi maliyeti ortalama 18.058 ± 25.775 dolar olarak hesaplandı. Cinsiyet, yaş ve histopatolojinin etkisi yokken, hastalık evresi arttıkça direkt tıbbi maliyet de artmaktaydı. Düşük yaşam beklentisi ve kür oranları da düşünüldüğünde, akciğer kanseri ülkemizde özellikle maliyet azaltıcı ve tütünün kontrolüne yönelik önlemlerin önemine işaret etmektedir.

Anahtar Kelimeler: Maliyet analizi, sağlık harcamaları, hastalık yükü, akciğer kanseri.

SUMMARY

The cost of lung cancer in Turkey

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The aim of this study was to evaluate the individual and societal burden of lung cancer in Turkey. A total of 103 cases with lung cancer attended our department between January 2002 and February 2003 were included in our study prospectively. The primary outcome measure was the cost of disease until death of the patients or the end of study. All the costs were exp-

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ressed as United States dollars (USD) and were estimated regarding the effective exchange rate at the time of recording. Descriptive statistics, chi-square, Fisher's exact test, Kaplan-Meier analysis and non-parametric "Bootsraping" tests were performed to evaluate the data. The average survival was 6.8 months. The estimated total direct cost for the entire group was 564.490 USD, and the direct cost per patient was 5.480 ± 4.088 USD. The total cost of lung cancer in the study group was 1.473.530 USD, with a per-patient cost of 14.306 ± 17.705 USD. The average direct cost per life year was 18.058 ± 25.775 USD. Age, gender and histopathology did not affect the cost, whereas direct medical costs were increased with increasing stage. With the low life expectancy and cure rates, lung cancer has been alerting for the cost minimization and disease control measures.

Key Words: *Cost analysis, health expenditures, disease burden, lung cancer.*

Although risk factors for lung cancer have been very well characterized, this disease continues to be one of the major health problems worldwide. In 2004, the number of newly diagnosed cases was approximately 173.700 and the expected number of deaths was 164.400 (1). Lung cancer was the first of all cancer types with 38.6% in males and eleventh with 5.2% in females (2). In a study by Thoracic Society Lung and Pleura Malignancies Study Group, total of 11.849 lung cancer patients were studied between 1994 and 1998 (3).

The resources allocated for lung cancer are growing rapidly due to the advances in the diagnosis and treatment and due to the increases in the incidence of the disease. Economic evaluation has been applied to medical issues, especially in English-speaking countries and has been increasingly employed in oncology since in 1990s (4). The aim of economical analyses is to estimate the burden of the pathology in question, but also, new agents and treatment strategies are compared with this respect. To our knowledge, this is one of the leading prospective studies on economical analysis of cancer in Turkey.

Most of lung cancer patients in Turkey have been managed in university or tertiary state hospitals in Turkey until the mid 2000s. The unit costs are same in these 60 health care centres and the other state hospitals in our country and we think that health costs obtained in our university clinic can reflect the overall of the country average in the working period. Though the aim of this study was to evaluate the individual and societal costs of lung cancer derived from our patient representatives.

MATERIALS and METHODS

Subjects

A total of 108 consecutive patients with a presumed diagnosis of lung cancer attended the Chest Diseases Department of Faculty of Medicine, Trakya University between January 2002 and February 2003 were included in the study. Five cases in which histopathological diagnosis could not be ascertained were excluded. Follow up was terminated on the 1st of November, 2003. The primary outcome measure was the total cost of the disease until the death of the patients or the end of study period.

Medical history, physical examination, blood and urine tests, two-sided chest X-rays, thoracic and upper abdominal computerized tomography (CT) scans, cranial CT [if symptomatic or in small cell lung cancer (SCLC)], bronchoscopy (when appropriate) and bone scintigraphy were routinely used for staging. This was an observatory study; all the diagnostic and therapeutic decisions were given by the responsible physicians.

Costs

A. Direct medical costs; includes the inpatient and outpatient costs associated with the diagnosis and treatment of lung cancer. The details of the hospital invoices were obtained by using the hospital billing system ®Avicenna. Retail prices were used for the medications and devices obtained from sources other than the hospital pharmacy. All direct medical costs were based on charges and invoices.

B. Additional medical costs; includes inpatient and outpatient costs associated with diagnosis

and treatment arising from causes other than lung cancer that occurred during the timeframe in which lung cancer was an active medical problem (i.e. an associated bladder cancer or diabetes mellitus).

C. Direct non-medical costs; includes costs that are not directly associated with the diagnosis and treatment of the disease, and that were afforded by the patient or his/her caregivers (i.e. transportation). The amount of direct non-medical costs was based on the declarations of the patients and their caregivers.

D. Total direct costs: A + B + C.

E. Indirect costs; Indirect costs included work losses. The age limit for retirement was considered 65 years, and for the patients died earlier than this age, the lost of productivity was calculated based on the monthly income of patients. The lost of productivity calculations were based on the number of days off from work for patients who were still alive and working. The lost of productivity for housewives was not calculated, as there was no clear-cut data about such calculations in the literature.

F. Total costs associated with lung cancer: D + E.

All the costs were expressed as United States Dollars (USD) and were based on effective exchange rate of the Central Bank of the Republic of Turkey at the time of recording (5).

Statistical Analyses

The data were evaluated with MS Excel and MINITAB RELASE 13.32 WCP 1331.00197 (MINITAB INC. USA) program. Descriptive statistics, chi-square, Fisher's exact test, Mann-Whitney U test, Kruskal-Wallis variance analysis, and Student's t-test and ANOVA (if parametric assumptions came true) were performed to evaluate the data. Kaplan-Meier analysis was used for survival analysis. Descriptive statistics, Kolmogorov-Smirnov Test for the consistency with normal distribution, Kaplan-Meier analysis, and non-parametric Bootsraping (with S-Plus program) method were used for cost analyses (6). Mann-Whitney U test, Kaplan-Meier analysis, Student's t-test and the regression analysis were used for the analysis of factors influencing the direct medical costs. In addition, cost per life year was calculated as:

The cost per life year= Direct medical costs/follow up days x 365.

RESULTS

Five (4.9%) patients were female and 98 (95.1%) were male. Mean age was 64 ± 9.3 years, with no significant age difference between the two groups (Table 1).

The minimum duration of follow-up was 30 weeks for surviving patients. Five patients were lost during follow-up; therefore 98 patients were included in the analyses. In the entire study group

Table 1. Distribution of cases by histological subtypes and demographic characteristics.

Characteristic	Female		Male		Total	
	n	%	n	%	n	%
Age (years), mean ± SD	60.6 ± 13.8		64.2 ± 9.1		64 ± 9.3	
Cell type						
SCLC	0	0	26	100	26	100
NSCLC subtypes						
Squamous	2	4.8	40	95.2	42	100
Adenocarcinoma	1	7.7	12	92.3	13	100
Undefined	2	9.1	20	90.9	22	100
NSCLC	5	6.5	72	93.5	77	100
Lung cancer, total	5	4.9	98	95.1	103	100

SD: Standard deviation, SCLC: Small cell lung cancer, NSCLC: Non-small cell lung cancer.

the median [± standard deviation (SD)] survival was 6.8 ± 0.3 (6-7.5) months. There was no survival difference between the SCLC and non-small cell lung cancer (NSCLC) groups in Kaplan-Meier analysis. SCLC patients had similar survival irrespective of their stage, whereas the stage had a significant impact on the survival in NSCLC patients (Figure 1).

Chemotherapy, radiotherapy and surgery were used in 75 (72.8%), 62 (60.2%), and 11 (10.7%) patients, respectively. Chemotherapy was given 92.3% of SCLC and 66.2% of NSCLC patients.
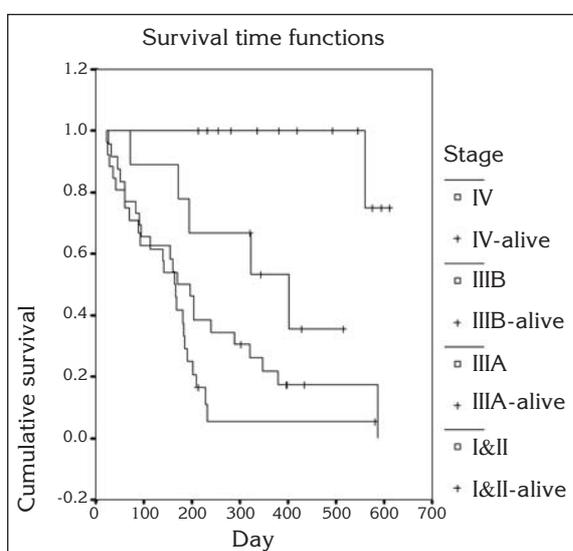
Figure 1. Kaplan-Meier survival analysis in patients with NSCLC.

The total direct medical cost in the study group (n= 103) was 564.490 USD (Table 2, Figure 2). The average cost per patient was 5.480 ± 4.088 USD. The total cost associated with lung cancer in 103 patients was 1.473.530 USD, and the average total cost per patient was 14.306 ± 17.705 USD.

The direct medical cost as calculated by "non-parametric bootstraping" test was 5.471 ± 4.091 USD. In Kaplan-Meier analysis, the average (± SD) and median (± SD) values for direct medical costs until death were 7.198 ± 612 (95% CI: 5.997-8.399) and 6.525 ± 535 USD (95% CI: 5.476-7.574), respectively. Another method for analysing the data is cost per life year (as direct medical cost), and it was 18.058 ± 25.775 USD.

Components of the total direct medical cost (564.490 USD) were 26.303 USD (4.7%) for in-patient hospitalization, 64.501 USD (11.4%) for diagnostic procedures; 314.851 USD (55.8%) for treatments (Figure 3).

Cost components of diagnostic procedures, were 8.902 USD of 78 patients for prior diagnostics (those were performed in other medial centers) (Figure 4). Other invasive procedures included mediastinoscopy, skin biopsy, and transthoracic needle aspiration biopsy etc., with a cost of 2.271 USD in 25 patients.

Table 2. The cost of lung cancer.

Type of the cost	n	Total	Mean ± SD	Upper and lower limits	Normal distribution*	95% CI	Median	Interquartile range
Direct medical costs	103	564.490	5.480 ± 4.088	316-24.574	> 0.05	4.681-6.280	4.614	4.315
Additional medical costs	10	7.755	775 ± 1.097	3-3.316	> 0.05	0-1.560	274	1.198
Direct non-medical cost	103	34.415	334 ± 1.324	5-13.500	0.0000		132	235
Total direct costs	103	606.660	5.890 ± 4.186	436-24.779	> 0.05	5.072-6.708	5.276	4.044
Indirect costs	50	866.870	17.337 ± 19.706	500-99.000	0.042		8.400	22.950
Total cost of lung cancer	103	1.473.530	14.306 ± 17.705	771-104.079	0.000		6.736	12.890

* Single-sample Kolmogorov-Smirnov Test (p> 0.05) shows normal distribution; confidence intervals were not specified for cases not complying with normal distribution, as it is statistically not meaningful.
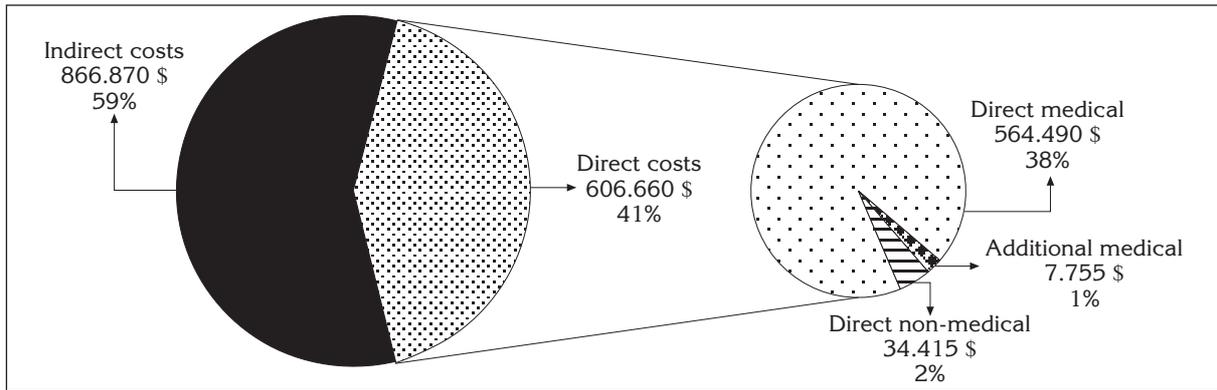SD: Standard deviation.

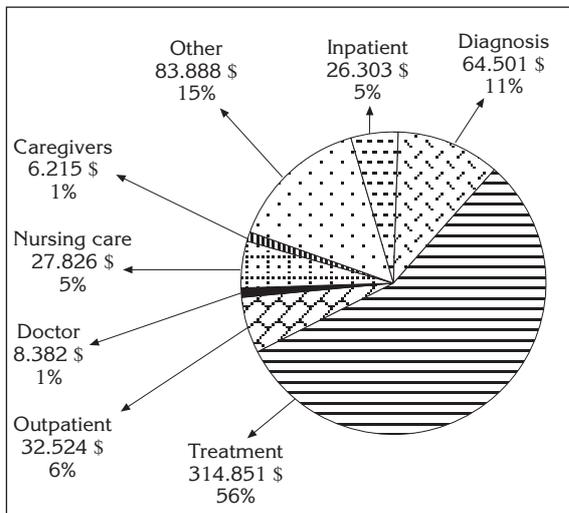**Figure 2. The cost of lung cancer (totally 1.473.530 USD in 103 patients).**

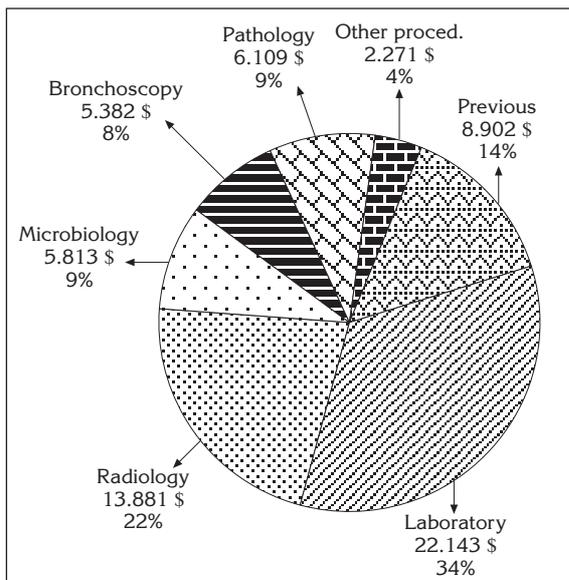**Figure 3. The components of the direct medical costs (totally 564.490 USD).**

Figure 4. The components of diagnostic costs (totally 64.501 USD).

The cost of chemotherapy medications were 162.772 USD in 75 patients (2.170 ± 2.219 USD per patient) and had the highest share (51.7%) in total treatment costs. Standard chemotherapy regimen was cisplatin-etoposide, but other chemotherapy regimens were used rarely (i.e vinorelbine, docetaxel). Total cost for 61 patients who have undergone radiotherapy was 56.148 USD (920 ± 820 USD per patient), comprising 17.8% of treatment costs. Eleven patients were operated, with a total cost of 8.461 USD (769 ± 484 USD per patient), with a small share of 2.7% within the treatment costs. Non-specific medications included those used for side effects of chemotherapy or radiotherapy, and those for non-cancer treatments, with a total cost of 87.470 USD (883 ± 1.047 USD per patient), being responsible for 27.8% of the total expenses for the treatment (Figure 5).

Considering the direct non-medical costs, the cost of transportation in 103 patients was 16.708 USD (162 ± 190 USD per patient), responsible for 48% of direct non-medical costs. The cost of transportation for 50 caregivers was 3.316 USD (66 ± 73 USD per patient), with a share of 10%. One patient spent 13.350 USD for paramedical "alternative medicine" treatment. We could only gather information from 8 patients regarding the "other expenses" category, which included the expenses for hygienic products, newspapers etc. This was equal to 1.041 USD (130 ± 138 USD) and responsible for 3% of the direct non-medical costs.

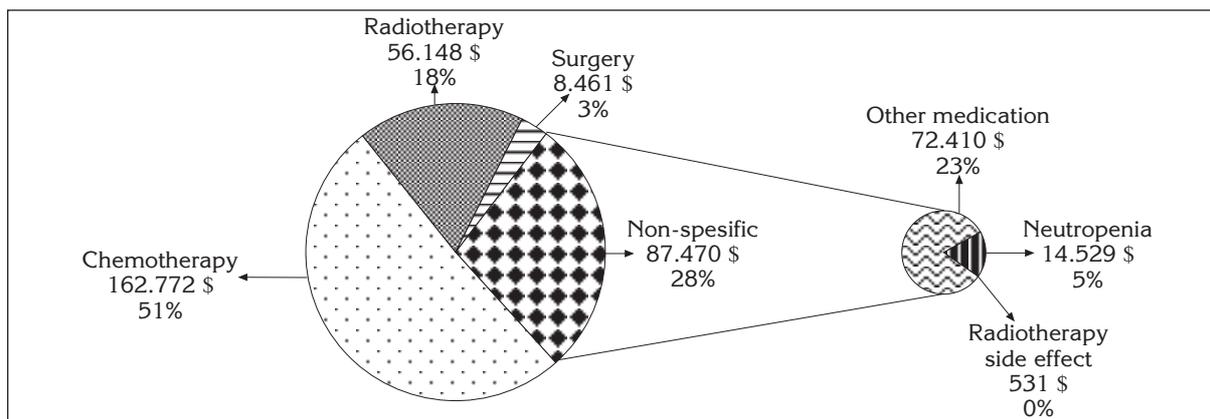No significant association between direct costs and age, gender and histology were observed.

Figure 5. The components of treatment costs (totally 314.851 USD).

The association between the cost and stage of the disease was also explored. The costs in 25 patients with early stage, in 38 patients with Stage IIIB disease, and in 40 patients with Stage IV disease were 3.986 ± 2.683 USD; 5.644 ± 3.974 USD, and 6.240 ± 4.716 USD, respectively, with no significant difference between the groups. However, an association between the stage and cost was observed in Kaplan-Meier analysis. The direct medical costs (median ± SE) were 3.370 ± 454 USD, 4.663 ± 849 USD, and 5.333 ± 832 USD in early stage, locally advanced and systemic diseases, respectively (Log Rank= 6.16, p< 0.05) (Figure 6).
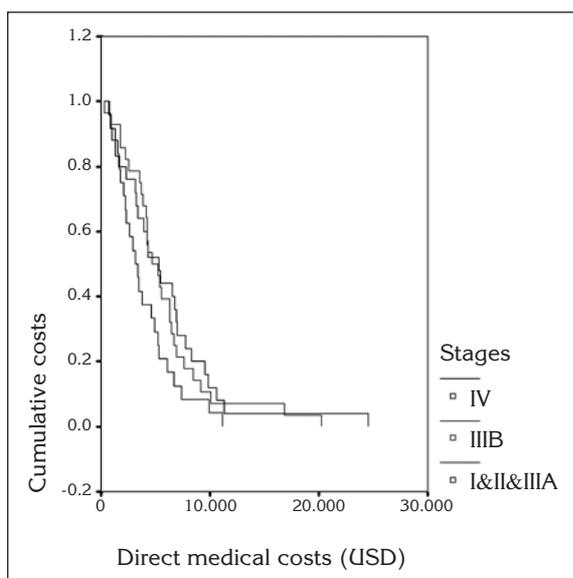

Figure 6. Kaplan-Meier estimates of direct medical costs by the stage of the disease.

When the daily average direct costs were evaluated according to stage groups, the daily average costs increased significantly with increasing stage. The daily average costs in 23 patients with early stage disease, in 36 patients with Stage IIIB disease, and in 39 patients with Stage IV disease were 14 ± 10 USD (95% CI, 9-18 USD), 55 ± 69 USD (95% CI, 32-79), and 65 ± 85 USD (95% CI, 38-93),respectively (p= 0.015).

DISCUSSION

In this study, we found that mean total cost per patient was $14.306 and the estimated cost per life year was approximately $18.000. Mean direct medical cost was $5.480; most of which (56%) was due to the expenses of treatment, and chemotherapy had the main share (52%) within treatment costs. In the study by Evans, et al. the direct care costs for diagnosis and treatment of NSCLC ranged from $17.889 for surgery/post-operative radiotherapy treatment of Stage I and II to $6.333 for supportive care for patients with Stage IV disease (7). Direct costs for diagnosis and treatment of SCLC ranged from $18.691 for management of limited stage disease to $4.739 for supportive care of patients with extensive disease (8). The direct costs reported in this study were lower compared to those reported from other countries. In a retrospective study from Turkey direct cost for lung cancer was estimated as $8257 (9). We can explain the low direct medical costs for lung cancer in Turkey by the lower costs of hospitalization, medical examinations, bronchoscopy and surgery

than developed countries. The cost of hospitalization was only 4.6% in our study, whereas it was 30 to 40% in the UK and Canada.

In our series, the percentage of patients treated with surgery was relatively low (approximately 11%), and the percentage of patients treated with chemotherapy was high (73%). However, only 10 to 15% of patients with NSCLC in England and Wales currently receive chemotherapy (10). As expected, the chemotherapy rate was higher in SCLC patients (92%) compared to that in NSCLC (66%). In another study from Turkey, 53% of the patients received chemotherapy, and 17.2% received combined therapy (chemotherapy/radiotherapy and surgery), similar to data reported herein (11).

Overall cost of care in patient with SCLC has been studied by Rosenthal, et al. (12). In this retrospective study, direct health-care costs were calculated from diagnosis to end of treatment in a cohort of SCLC patients. The median cost per patient in 1990 Australian dollars was found to be $14.413. The major cost centers included hospitalization (42%), chemotherapy (18%), and radiotherapy (11%). In a study of 109 patients with SCLC were evaluated retrospectively between 1994 and 1997, and the average total cost per patient was 11.556 (13). Another study from the United Kingdom (UK) in 1993 reported an average cost of 6.150 for NSCLC, and 5.668 for SCLC (14).

In reported studies from Turkey, approximately 10% of the total patient population with lung cancer is women (15,16). In the US, the M/F ratio of deaths due to lung cancer was 7/1 in 1964, and is 2/1 at present (17). In our study, the M/F ratio (19.6%) is higher, compared to the national and the international data. It might be explained that the increase in frequency of smoking in women has not been seen as lung cancer in Thrace region yet (18). Indirect costs may differ due to male/female ratio, for that reason, total costs may be recasted according to male/female ratio.

In a meta-analysis evaluating the economic issues in lung cancer, the treatment was found as moderately expensive. The cost of staging could be minimized through the judicious use of diagnostic and staging procedures (19). On the other hand, Evans, et al. have recommended to reduce the duration of hospitalization, particularly during the diagnostic work-up phase, considering the fact that hospitalization is highly expensive in Canada (7). However, in Turkey costs associated with hospitalization, examinations, and nursing care are much lower compared to these countries, probably at present, rendering such advices is invalid. In our country, costs associated with medications, most of which are imported, are relatively high. Therefore rational use of chemotherapeutic agents may be more beneficial with this respect. However, the most important means of reducing the costs is to emphasize early diagnosis to identify the patients on operable stages.

From a societal perspective, Evans, et al. estimated that for all 15.624 cases of lung cancer diagnosed in Canada in 1988, the total cost of providing treatment and follow-up, and managing relapse over 5 years was $328 million (7). National Cancer Institute estimated that the overall annual cost of cancer diagnosis and treatment was nearly $100 billion in 1990, a figure that includes $27 billion for direct medical costs, $10 billion for morbidity costs (cost of lost productivity), $59 billion for mortality costs (20). Lung cancer cases comprised approximately 20% of all cancers ($20 billion). When this cost is projected to Turkey directly, annual cost of lung cancer foresee $3-4 billion.

As conclusion, the current study shows high individual and societal cost of lung cancer with poor prognosis and detrimental effects on economy of Turkey as a developing country. With the low life expectancy and cure rates, increasing medical technology, and development of newer treatments, lung cancer in our country has been alerting for disease control and the cost minimization measures.

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