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End-of-Life Health-Care Cost of Patients With Lung Cancer: A Retrospective Study

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Abstract

Introduction: Lung cancer exerts a significant societal and health-care–related economic burden and chemotherapy drugs constitute a major factor of total direct cost. The aim of the present study was to assess the direct health-care cost of lung cancer in Greece by conducting a retrospective analysis on the last 6 months of life.

Methods: The present study was based on both the medical data and costs of treatment of deceased adult patients who suffered from terminal stage IIIB/IV lung cancer (non-small cell lung cancer and small cell lung cancer) during the last 6 months of their life. The study's protocol was approved by the Hospital's Research Ethics Committee. Costs included outpatient (outpatient services) and inpatient (inpatient services) costs. Descriptive statistics were mainly used for statistical analysis.

Results: The files of 144 patients were analyzed. The total cost of health-care services for the study population during the last 6 months of life was attributed by 57% to inpatient services, whereas chemotherapy costs (74%) comprised the largest proportion of the total inpatient cost. The highest expenditure for outpatient services was attributed to concomitant medication (59%), followed by the cost of tests (21%) and radiotherapy (20%).

Conclusions: The results of our study indicate that both inpatient and outpatient costs were substantial. The main inpatient and outpatient cost drivers were chemotherapy and concomitant medication, respectively. A more comprehensive nationwide study would be useful to validate our results and to include also indirect costs of cancer care in Greece.

Keywords

end-stage lung cancer, direct health-care costs, health services, non-small cell lung cancer, small cell lung cancer

Introduction

Lung cancer is the most common cause of death from cancer worldwide and it still remains one of the biggest public health problems.[1] In Greece, it is estimated that 6884 people were diagnosed with lung cancer in 2012, making it the second most frequent form of cancer (responsible for 16.8% of all new cases of cancer for that year[2]) and the most common cause of cancer-related death in Greece (22.59% of all new cancer deaths).[2]

Lung cancer exerts a significant societal and health-care–related economic burden both on a national level and worldwide.[3,4] To quantify the economic burden of cancer, both direct and indirect costs need to be considered.[3-6] Direct costs include all those costs associated with the diagnosis and further treatment of patients, including hospitalizations, pharmacotherapies, and surgical procedures. Indirect costs are mostly a result of loss of productivity due to premature cancer-related disability and death. However, the costs that family incur, during the course of treatment, which are not covered by health insurance also fall into this category. A third category, rarely taken into account, includes all intangible costs linked to the

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What do we already know about this topic?

Lung cancer exerts a significant societal and health-care–related economic burden and chemotherapy drugs constitute a major factor of total direct cost.

How does your research contribute to the field?

This is the first study assessing the end-of-life health-care cost of lung cancer in Greece amid the economic crisis, using real-world data.

What are your research's implications toward theory, practice, or policy?

The direct assessment of the end-of-life health-care costs of lung cancer in Greece constitutes a necessary first step toward achieving rationalization of the utilization of health resources for the treatment of patients with cancer.

loss of well-being of the patient and his close family (psychological distress, pain, and suffering).[6]

A population-based cost analysis estimated that the total economic cost of lung cancer across the European Union for 2009 was €18.8 million, accounting for 15% of overall cancer costs and thus the highest economic burden among the 4 types of cancers studied (colorectal, breast, lung, and prostate cancers).[3] Previous studies have examined the economic burden of lung cancer on a national level in various settings,[7-15] with the first and most ambitious model-based attempt made in Canada.[16,17] However, due to the inherent differences that exist in health-care systems worldwide, results from other countries cannot be easily extrapolated to the Greek context. Moreover, there is a scarcity of data regarding the actual health-care costs of lung cancer in Greece. The studies of Maniadakis et al[18,19] performed economic evaluations of alternative therapies. Recently, a prospective analysis estimated the direct and indirect costs of lung cancer incurred in a Greek University Pulmonary Department with chemotherapy drugs constituting the highest factor of total direct cost.[20] In the latter study, the health-care costs for patients with end-stage lung cancer during the last months of life were not estimated. In 2011, a nationwide study calculated hospital costs for the treatment of smoking-attributable diseases in Greece and demonstrated that lung cancer–related costs for that year were approximately €38.2 million.[21] This study focused solely on hospital-related costs and did not estimate the costs of pharmacotherapy or initial clinic costs. In this era of economic crises and diminished financial reserves, characterizing many economies worldwide and Greece in particular, it is imperative to rationalize the utilization of health resources for the treatment of patients with cancer. The direct assessment of the health-care costs of lung cancer in Greece constitutes a necessary first step toward achieving this goal as could inform policymakers regarding resource allocation for the care of terminally ill patients with lung cancer. We, therefore, conducted a retrospective in-depth analysis of direct health-care costs in patients with end-stage lung cancer treated in the largest general university hospital for chest diseases in Greece. We focused on the last 6 months of life, which constitutes one of the most resource- and cost-intensive periods in cancer treatment.[22]

Methods

Study Design and Population

This retrospective study was carried out at the oncology unit of the Third Internal Medicine University Department of the Sotiria General Hospital for chest diseases from July 2014 through February 2015. The study was based on both the medical data and costs of treatment of deceased adult patients who suffered from terminal stage IIIB/IV lung cancer (non-small cell lung cancer [NSCLC] and small cell lung cancer [SCLC]) during the last 6 months of their life. The study's protocol was approved by the Hospital's Research Ethics Committee.

The population under investigation consisted solely of adult patients, who died between September 2011 and June 2014 and met specific eligibility criteria in order to be included in the study: (i) they had histologically documented terminal-stage lung cancer (ICD-10 C33-C34) during the last 6 months prior to death, (ii) they received at least 2 cycles of chemotherapy, and (iii) they died before the beginning of the study (July 2014).

The starting date of data recording for each patient was considered the date 6 months prior to the date of death and was defined as the "index date." The first, second, third, fourth, fifth, and sixth months referred to in the study represent 6, 5, 4, 3, 2, and last months prior to death, respectively.

Data Source

All available data were entered into Case Registration Forms and were fully consistent with the data from the original hospital documents. Each patient was denoted by the number of his medical file so as to ensure the anonymity of the study population. The following data were recorded: demographic information (gender, age), date of first chemotherapy, date of death, clinical characteristics (type of cancer, staging, comorbidities), and smoker/nonsmoker. Comorbidities were categorized according to disease type, as follows: cardiovascular (ie, coronary heart disease, arterial hypertension, etc), respiratory (ie, chronic obstructive pulmonary disease, etc), metabolic (ie, diabetes mellitus, dyslipidemia, etc), psychiatric (ie, depression, anxiety, etc), and other (ie, gastrointestinal, chronic infections, etc). Also, all available data on outpatient and inpatient services offered during each month of the last 6 months of life of each patient were recorded. The data relating to the administration of chemotherapeutic agents, bisphosphonates, and other medications included the name and number of formulations, the name of the active substance, the dosage form, the route,

and the number of days of administration. Data relating to hospitalizations included, apart from the date, the diagnosis and the duration of hospitalization. All diagnostic and other procedures performed were also recorded. Unit costs for health service interventions were estimated from a number of sources, including the List of Medical Acts of EOPPY-Diagnosis Related Groups-2014 Positive List of Drugs-many Ministerial Decisions, which are presented in Supplementary Table 1.

Cost Estimates

Cost estimates were made in conformity with the National Health Service (EOPYY) in Greece; hence, only direct health-care costs covered by the EOPYY were included. Health-care costs per patient for each month and for the entire 6-month period under investigation, were calculated according to the amounts spent on all medical and pharmaceutical services and were characterized on an overall basis and according to the type of service (outpatient, inpatient) provided. Each month was defined as 30 days. All costs were reported in euros.

Costs included outpatient (outpatient services) and inpatient (inpatient services) costs, but costs for ambulatory care and outpatient visits were not included. Ambulatory care is differentiated from outpatient care as includes anything that happens outside the hospital, that is, primary care office visits or day treatment centers, whereas outpatient care settings are located in a department within a hospital.

Inpatient services included the administration of chemotherapeutic agents and bisphosphonates for bone metastases, the daily hospital fee (incorporating the provision of all medical and nursing services, routine blood tests and relevant expenditure for 1-day hospitalization without overnight stay, 2-day or 3-day hospitalization for the administration of chemotherapy), hospitalization for reasons other than chemotherapy administration, and blood transfusions. Chemotherapeutic agent costs were calculated from the number of vials needed to administer the required dose of each agent throughout each treatment course and the cost of the formulation with the highest concentration of active substance. The daily hospital fee for the administration of all chemotherapy drug combinations was 80€/administration for 1-day hospitalization without overnight stay, and 60€/day for 2-day or 3-day hospitalization. Hospitalization costs were computed by applying the diagnosis-related group (DRG) rate. The DRG rate estimates the cost of a single hospital admission or medical care treatment using as the key variable the ICD-10 code.

Outpatient services included all tests (laboratory, imaging, endoscopic, diagnostic) performed privately and those performed in public hospitals during hospitalization and not included in DRGs, radiation therapy, and concomitant medication (adjuvant drugs, drugs for comorbidities, long-term oxygen treatment, best supportive care). In order to calculate the cost of radiation therapy in those cases where the number of sessions and the type of radiotherapy (conventional, 3-D) administered was not specified, we used an average number of 10 sessions of conventional radiotherapy. Furthermore, in cases where there was no available data on the exact dosage of concomitant medication and of supportive care, the number of formulations used were calculated using the average daily dose (Defined Daily Dose [DDD]) as defined by the Anatomical Therapeutic Chemical (ATC)/DDD classification system of the World Health Organization.

A selection of costs for tests, treatment, and hospitalization are shown in Supplementary Table 2.

Statistical Analyses

All demographic and clinical characteristics and data on outpatient and inpatient services and the costs per patient during each of the last 6 months prior to death as well as during the entire 6-month period were recorded in excel files. The database created was used for statistical analysis. To conduct the statistical analysis, the statistical program SPSS v.21 was used. The analysis of direct medical costs was performed by examining costs incurred during each month of the last 6 months of life and during the entire 6-month period under investigation. The results were depicted in bar charts. Percentages were calculated for the presentation of descriptive results relating to demographic and clinical patient characteristics (sex, age, type of lung cancer, smoker/nonsmoker, presence of comorbidities) as dichotomous variables. The descriptive measures of central tendency (arithmetic mean) and dispersion (standard deviation) were used for quantitative variables. The quantitative variables were the costs of tests, radiotherapy, concomitant medication, chemotherapy, transfusions, hospitalizations, and the total costs. Normality was assessed using the Kolmogorov-Smirnov test. Data were not normally distributed and nonparametric statistical analyses were performed for the evaluation of statistically significant differences between all groups with respect to the variables examined in the study. A P value of .05 was considered significant. Differences between monthly costs were examined with the Wilcoxon signed-rank test. Correlation analysis was performed using the Spearman rank correlation coefficient (Spearman ρ) in order to assess the existence or not of a relationship between costs and outpatient and inpatient services and between total costs over 6 months and total costs per month. To examine the associations between dichotomous clinical or sociodemographic variables and the total health-care, impatient, and outpatient costs a series of Mann-Whitney tests was conducted.

Results

Patient Characteristics

In total, the medical files of 230 patients with lung cancer were examined. After applying inclusion criteria, the final study sample consisted of 144 patients, 125 (87%) of whom were male. Sixty-two percent of the patients were older than 65 years. Most patients (78%) were diagnosed with NSCLC and 21% with SCLC. We studied only 1 case with a diagnosis of neuroendocrine tumor of the lung. The majority of patients

Table 1. Patient Characteristics.

Histological Type	NSCLC	SCLC	NET
Number	113	30	1
Gender (M/F)	96/17	28/2	1/0
Age			
65 and older	69	19	1
less than 65	44	11	0
Smokers	103	30	1
Comorbidity (yes/no)	82/31	22/8	1/0
Type of comorbid disease			
Cardiovascular (yes/no)	56/57	19/11	1/0
Psychiatric (yes/no)	13/100	0/30	0/1
Metabolic (yes/no)	34/79	8/22	1/0
Respiratory (yes/no)	17/96	3/27	0/1
Other (yes/no)	23/90	5/25	1/0

Abbreviations: M/F, male/female; NET, neuroendocrine tumor of the lung; NSCLC, non-small cell lung cancer; SCLC, small cell lung cancer.

(72.4%) had comorbidities associated with their lung cancer. Cardiovascular disorders were the most common comorbidities (71%), followed by metabolic (40.2%) and other disorders (27.1%). Ninety-three percent of the patients were smokers. Patient characteristics according to histological type are presented in Table 1.

Cost Characteristics

The total cost of health-care services for the study population during the last 6 months of life was 977 310€, of which 560 180€ was attributed to inpatient services and 417 627€ to outpatient services. Total costs of health-care services in the last 6 months prior to death by cost category were chemotherapy (416 631€; 42%), other/concomitant medication (246 490€; 25%), hospitalizations (94 240€; 10%), tests (86 009€; 9%), radiotherapy (85 135€; 9%), daily hospital fee (43 520€; 4%), and transfusions (6800€; 1%). Notably, chemotherapy comprised the highest percentage of the total cost of care.

No statistically significant association was found between total health-care costs and gender ($P = .622$), age ($P = .062$), smoking habits ($P = .069$), presence of a comorbid disorder ($P = .075$), type of comorbid disorder ($P = .170$ for cardiovascular, $P = .067$ for psychiatric, $P = .287$ for metabolic, and $P = .917$ for other problems), and type of lung cancer ($P = .073$).

Chemotherapy costs (74%) comprised the largest proportion of the total inpatient cost, followed by hospitalizations (17%), daily hospital fee (8%), and transfusions (1%). The highest expenditure for outpatient services was attributed to concomitant medication (59%), followed by the cost of tests (21%) and radiotherapy (20%).

No statistically significant association was found between total outpatient costs and gender ($P = .535$), age ($P = .163$), smoking habits ($P = .300$), and presence of any comorbidity ($P = .968$). The type of comorbid disorder ($P = .802$, .214, .912, .542, for cardiovascular, psychiatric, metabolic, respiratory or other problems, respectively) and the type of lung cancer (NSCLC or SCLC; $P = .203$) did not yield statistical significance either. Following the same line, no statistically significant association was found between total inpatient costs and gender ($P = .345$), age ($P = .081$), smoking habits ($P = .091$), and type of lung cancer ($P = .283$). Having a comorbid disorder ($P = .217$) and type of the comorbid disorder ($P = .182$, .078, .671, .921 for cardiovascular, psychiatric, metabolic, respiratory or other, respectively) were not found to bear a statistically significant association with total impatient costs.

Despite an increasing trend of costs up to the fifth month, costs during the sixth month were found to drop. The main drivers of the 6-month cost were chemotherapy (49 455.14€; 39% of monthly cost) and concomitant medication expenditure (41 131.94€; 32% of monthly cost) along with the cost of hospitalizations (18 054.00€; 14% of total cost). Other costs such as radiation (7035.00€; 6%), daily hospital fees (4660.00€; 4%), laboratory tests (5971.91€; 5%), and transfusions (1400.00€; 1%) had a small impact on total monthly cost. The outpatient, inpatient and total health-care cost by month and service category are presented in Table 2.

The mean monthly costs per patient increased with each passing month toward the end of life, with the exception of the last month of life where a decrease in costs was noted (Figure 1). Significant differences were found between each month from 1 to 5 months ($P \leq .001$), but for the sixth month only between 3 and 6 months ($P = .004$), 4 and 6 months ($P \leq .001$), and 5 and 6 months ($P \leq .001$).

The mean cost per patient by cost category is presented in Figure 2A and B. Statistically significant differences in the mean cost of tests were found only between the sixth month and all the other months of the study ($P \leq .001$). The mean cost of radiotherapy fluctuated around 100€ from 1 to 3 months, rose sharply to its highest value (182€ [standard deviation 464€]) in 4 months and then exhibited a significant downward trend in 5 and 6 months ($P = .047$ and $P = .008$, respectively). The cost of concomitant medication increased continually during the 6-month period and reached its highest value in 5 months, but decreased significantly in the last month before death ($P = .003$). The mean cost of the daily hospital fee increased from 1 to 5 months, but decreased significantly during the sixth month ($P \leq .001$). Statistically significant differences in the mean cost of the daily hospital fee were also found between 1 and 3 months and between 4 and 5 months ($P \leq .05$) as well as between 6 and 2 ($P \leq .05$), 3 ($P \leq .05$) and 4 months ($P \leq .001$). The mean cost of chemotherapy differed significantly between 1, 3, 4, and 5 months ($P \leq .05$), between 2, 4, 5, and 6 months ($P \leq .05$) and lastly between 6, 3 ($P \leq .05$), and 4 ($P \leq .001$) months, showing an increase during the fourth and fifth months and then a decrease in the sixth month. The mean cost of transfusions fluctuated during the 6-month period. Statistically significant differences were only found between 1, 2, 5, and 6 months ($P \leq .05$). The mean cost of hospitalizations decreased between 1 and 4 months and then increased during 5 months, with statistically significant differences between 3 and 4 months ($P \leq .005$) and between 4, 5, and 6 months ($P \leq .005$).

Table 2. Outpatient, Inpatient, and Total Health-Care Cost by Month and Service Category.

Service Category	Cost by Month (€)					
	1	2	3	4	5	6
Tests	15 886	14 348	20 672	15 299	13 833	5972
Concomitant medication	25 537	32 705	43 371	44 420	59 325	41 132
Radiotherapy	13 444	11 368	14 884	26 186	12 220	7035
Chemotherapy	64 232	63 822	65 057	82 332	91 733	49 455
Daily hospital fee	5760	7080	7920	8740	9360	4660
Hospitalizations	19 580	13 099	16 285	5512	21 710	18 054
Transfusions	200	1600	800	1200	1600	1400
Total OP	54 866	58 422	78 928	85 894	85 378	54 139
Total IP	89 692	85 611	89 262	97 784	124 342	73 489
Total IP + OP	144 141	143 954	168 190	183 678	209 720	127 628

Abbreviations: IP, inpatient; OP, outpatient.

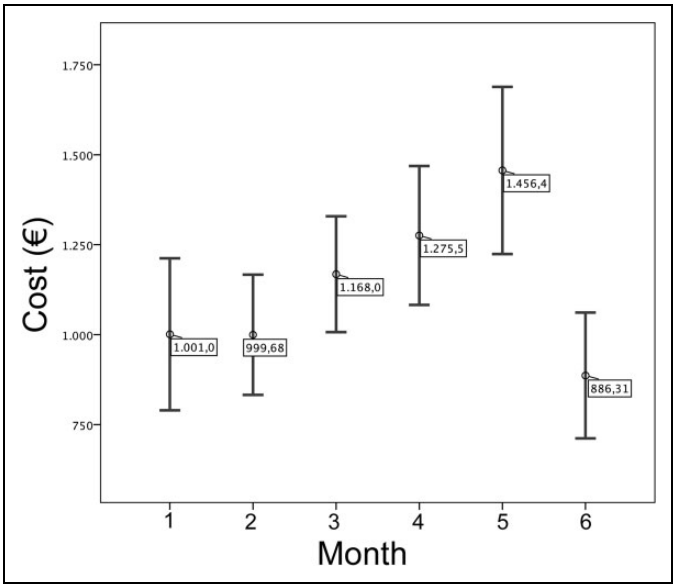

Figure 1. The mean cost per patient per month.

The results of the correlation analysis of total costs per month over the 6 month-study period are shown in Table 3. As shown the total costs of 1, 2, and 3 months were negatively correlated to the costs of 5 and 6 months. In contrast, the total cost of the fifth month was positively correlated to that of the sixth month, as was the fourth month to those of the fifth and sixth months.

The correlation analysis between total outpatient costs and cost of outpatient services showed that total outpatient costs for each month of the study were significantly associated with the cost of concomitant medications (Spearman $\rho = .691$, .726,.726, .652, .839, .873 for 1-6 months, respectively; $P < .01$), the cost of laboratory, imaging, endoscopic, diagnostic tests (Spearman $\rho = .589$, .475, .351, .368, .350, .371 for 1-6 months, respectively; $P < .01$), and the cost of radiation therapy (Spearman $\rho = .418$, .362, .421, .556, .366, .322 for 1-6 months, respectively; $P < .01$).

The correlation analysis between total inpatient costs and costs of inpatient services showed that for each of the 6 months of the study, inpatient costs were highly correlated to the costs of chemotherapy (Spearman $\rho = .809$, .843, .856, .943, .920, .833 for 1-6 months, respectively; $P < .01$), and moderately correlated to the daily hospital fees (Spearman $\rho = .631$, .594, .541, .578,.497, .689, for 1-6 months, respectively; $P < .01$), and the costs of hospitalizations (Spearman $\rho = .396$, .334, .340, .247, .397, .463 for 1-6 months, respectively; $P < .01$). A weaker correlation was found between inpatient costs and the cost of transfusions (Spearman $\rho = .69$, .179, .086, .118, .192, .185, for 1-6 months, respectively; $P < .05$).

Discussion

This retrospective study is one of only a few studies addressing direct medical costs of current lung cancer management during the last months of life and one of the first attempts to assess the direct costs of managing NSCLC and SCLC in Greece. Analysis of the data showed that the largest monthly expenses came from the provision of inpatient services (57%), the greatest proportion of which was for chemotherapy (42%). A trend toward increasing costs of all services provided in the last 6 months was observed, consistent with the expected increase in applied health-care practices.[23] The cost of both inpatient and outpatient services provided during the last 6 months of life showed an upward trend and reached their highest value during the fifth month and this increase was attributed to the large amounts spent on chemotherapy, concomitant medication, and hospitalizations. A drop in health-care costs was observed in the sixth month; this finding may be attributable to the usage of less aggressive medical care near death, as the cost benefit ratio of these treatments may no longer be considered favorable for the patient at this stage. Previous study on end-of-life patients has shown that the usage of aggressive treatments near death is associated with worse patient quality of life.[24]

The highest values for mean outpatient costs per patient were observed during 4 and 5 months principally because radiotherapy and concomitant medication costs were higher during these

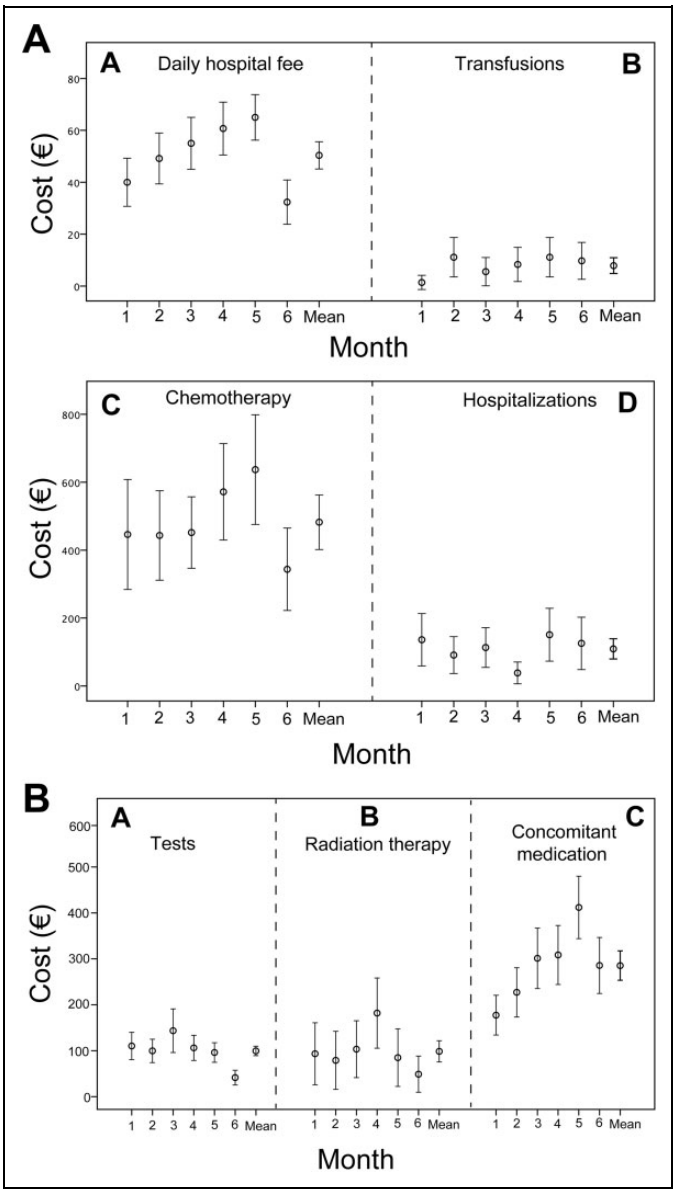

Figure 2. A, The mean inpatient cost per patient by month and cost category. B, The mean outpatient cost per patient by month and cost category.

months. The cost of tests (diagnostic imaging, laboratory, and endoscopy) was higher during 1 to 3 months (maximum) and then decreased gradually until the sixth month, but overall did not contribute significantly to the total health-care cost (9%). This finding was not unexpected, as intensive diagnostic are not carried out at the end of life. The highest cost for radiotherapy was observed during 4 months and decreased thereafter. Radiotherapy may be indicated as either curative or palliative treatment approach for end-stage lung cancer,[25,26] and in our study it was found to be a costly treatment that influenced the outpatient cost. Kutikova et al[11] also found that radiotherapy was a costly cancer treatment during the terminal care phases. The mean cost of concomitant medication per patient, which included drugs for the treatment of adverse effects of chemotherapy, analgesics (opioid or nonopioid), antibiotics, drugs for the control of symptoms of the disease, drugs for comorbidities, and long-term oxygen treatment, rose sharply to its highest value during 5 months. This increase may be attributed to the increasing need for palliative care and symptom control as death approaches.[14] Also, the increased occurrence of side effects due to intensive chemotherapy during 5 months may be partially responsible for this increase.

The cost of inpatient services provided during the last 6 months of life showed an upward trend after 1 month and reached its highest value during 5 months, during which the costs of chemotherapy, daily hospital fees, hospitalizations, and transfusions were higher than the previous months as well as the month before death. Chemotherapy costs, as previously stated, were at a maximum during 4 and 5 months. The majority of lung cancers are typically not diagnosed until they have spread. At the terminal stage, the administration of aggressive chemotherapy becomes urgent, due to the gradual withdrawal of therapeutic agents used to control the underlying disease and due to the patients' wishes to receive such treatments. Since the disease becomes incurable at this stage, the goal of chemotherapy is to prolong the disease-free interval and overall survival, as well as the alleviation of symptoms.[27] Furthermore, during 5 months, an increase in the use of targeted chemotherapeutic agents (bevacizumab, pemetrexed, erlotinib, gefitinib), the costs of which are particularly high, may contribute to the higher costs of chemotherapy. However, during the last month of life, the significant decrease in the cost of chemotherapy ($P \leq .001$) may be attributed to the fact that shortly before death, therapeutic interventions are limited to symptomatic and palliative treatment.[14] It should be mentioned that detailed data on the treatment of patients during 6 months were not available, possibly because of their inability to come to the hospital as the disease progressed or perhaps their choice to stay at home and receive only supportive care. The increased cost of hospitalizations in 5 months was also not unexpected, as oncology patients, at the end of life require hospital monitoring due to exacerbations of the disease (infections, pain-related situations, and myelosuppression), comorbidities, and complications/side effects due to increased administration of chemotherapeutic agents. The largest transfusion costs were observed in 2 and 5 months. Transfusions are widely used as a rapid and effective therapeutic intervention in patients with terminal-stage cancer suffering from anemia as a result of cytotoxic drug-induced myelosuppression. In patients receiving chemotherapy, high transfusion costs are supposedly generated by patients with severe hematological toxicities that may accompany infectious complications.[28] Typically, there is a growing need for blood transfusions in patients with cancer as the number of chemotherapy cycles administered increases.[29] Thus, the extensive use of chemotherapeutic agents during 2 and 5 months could possibly explain the increase in the cost of transfusions, although these did not contribute much to the overall cost.

No statistical significance was found between inpatient costs, outpatient costs, total health-care costs and gender, age,

Table 3. Spearman Rank Correlation Coefficient Between Total Costs Per Month Over 6 Months.

			Total Cost				
			Month 1	Month 2	Month 3	Month 4	Month 5
Total cost	Month 2	Correlation coefficient	0.462[a]				
		Sig (2-tailed)	0.001				
	Month 3	Correlation coefficient	0.215[a]	0.329[a]			
		Sig (2-tailed)	0.010	0.001			
	Month 4	Correlation coefficient	0.003	0.192[b]	0.286[a]		
		Sig (2-tailed)	0.970	0.021	0.001		
	Month 5	Correlation coefficient	−0.203[b]	−0.104	−0.114	0.199[b]	
		Sig (2-tailed)	0.015	0.216	0.174	0.017	
	Month 6	Correlation coefficient	−0.197[b]	−0.110	−0.166[b]	0.061	0.287[a]
		Sig (2-tailed)	0.018	0.189	0.046	0.469	0.001

[a]Correlation significant at the .01 level (2-tailed).
[b]Correlation significant at the .05 level (2-tailed).

smoking habits, presence and type of comorbidities, and the type of lung cancer.

With respect to the type of lung cancer, in this study only a small number of patients with SCLC participated, a finding consistent with the epidemiology of lung cancer. Non-small cell lung cancer accounts for more than 85% of all lung cases, approximately 40% of which are first diagnosed at an advanced state.[30] The incidence of SCLC has been decreasing in many countries over the last 2 decades.[31]

From a review of the literature to date, only a limited number of published studies have focused on the costs of terminal-phase lung cancer care. In the Greek context, a recently published prospective study[20] estimated the costs of patients with lung cancer for a period of 32 months from diagnosis to the end of registry and found that the cost of chemotherapy was the main cost driver, a finding consistent with the findings of our study, while the indirect cost was higher for patients than their caregivers. However, the clinical procedures used during treatment of patients with end-stage lung cancer were not recorded and their direct medical costs not estimated.

Direct comparison of our study results with those of studies carried out in other countries is difficult because of differences in patient cohorts, approaches to lung cancer management, health-care systems, funding, study designs, and types of analyses. In this study, we showed that significant costs are generated in the months before death, with chemotherapy and concomitant medication accounting for the highest costs followed by hospitalization fees. This finding is not consistent with the findings of previous studies,[8,10,11,13,15,32] which reported hospitalization fees as the greatest component of cost for the treatment of end-stage lung cancer. Oliver et al[8] showed that the major cost driver in their study was hospitalization and that the direct costs per patient of SCLC care peaked in the months immediately following diagnosis and in the final months of life. Another study examining the patterns and costs of lung cancer management at a Swiss university hospital also found that the major part of the total cost was due to hospitalization costs, but that patients with advanced stages of lung cancer showed the highest cost, mainly due to the costs of chemotherapy.[10] A retrospective study carried out in the Netherlands assessed costs from the initial diagnosis to subsequent death or to the end of the assessment period.[13] The results of that study showed that hospitalization fees were a major contributor to costs (44%-55% of the total cost). The second major cost was due to chemotherapy. Kutikova et al[11] examined the economic burden of lung cancer in the United States and found that during the terminal care phase, with a mean duration 5.6 months, the highest proportion of costs was attributable to inpatient hospitalizations (47%), which may have been due to complications associated with the disease or therapy. Navaratnam et al[15] examined the cost of services provided to patients with NSCLC stage IIIb/IV after completion of chemotherapy until death. They found that hospitalizations accounted for about 80% of the total costs. Approximately 30% of the health services provided were within 28 days of the last date of chemotherapy. It is likely that these were due to chemo follow-up visits and services for the management of chemotherapy complications. A more recent study that analyzed the costs of lung cancer management in South Western Sydney showed that hospitalizations and chemotherapy were the greatest components of cost, constituting 44% and 22% of total costs, respectively.[32]

An explanation for the discrepancy between the findings of the present study and findings of the studies mentioned above may be that the latter were carried out prior to the introduction of targeted therapies as a second/third line option for advanced NSCLC. The targeted therapies account for an 11% increase in treatment costs for lung cancer.[33]

Several limitations of this study should be mentioned. First, we used a retrospective approach to evaluating care at the end of life and this has been debated because of issues relating to selection bias.[34] Some researchers believe that our study design does not give an accurate portrait of all patients living with advanced disease.[35] Nevertheless, retrospective studies are convenient and useful for the identification of patients who may be examined for resource uses and costs within a specified end-of-life period in contrast with prospective studies for

which the selection of such patients is difficult.[36] Second, our study population was derived from just 1 hospital and estimates of direct costs may not be representative of the entire Greek health-care system. Third, we did not record data on indirect costs resulting from the reduced productivity of patients/caregivers, data on patients' costs such as transport costs as well as other intangible costs. All our study patients were covered by the national public health insurance system and as a result we did not include patients without health insurance coverage, patients who utilized private patient care, and the costs of services not covered by the insurance.

Conclusion

The results of our study indicate that the direct medical costs of patients with terminal-stage lung cancer during the last 6 months of their lives are substantial. Both inpatient and outpatient costs peaked during the second month prior to death, with the exception of the cost of tests and radiation therapy that varied considerably throughout the study period. The main inpatient and outpatient cost drivers were chemotherapy and concomitant medication, respectively. These results highlight the need for a new paradigm in the management of these patients. Integration of palliative care in the health-care system in line with the World Health Organization's resolution is of imperative need in the country.[37] However, for this to become a reality a systematic approach is needed. Palliative care settings should be developed in the country and all health-care professionals caring for patients with serious illnesses, including lung cancer, should have the basic knowledge and skills to improve care toward terminally ill patients. A more comprehensive nationwide study would be useful to validate our results and to study other costs, including indirect costs of cancer care in Greece.

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Supplemental Material

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