CAN G8 SCORING IN PATIENTS WITH GERIATRIC LUNG CANCER HELP TO DETERMINE CURATIVE TREATMENT?

ABSTRACT

Objective: The median age at diagnosis of lung cancer is 70 years and there are limited data in the literature regarding the treatment of elderly patients. In elderly patients, comorbid diseases, poor performance, and toxicity may lead to a surge in physicians' curative treatment and may remain untreated. The aim of this study was to evaluate the results of treatment in patients older than 70 years whose performances were evaluated by using Geriatric 8 score and to find out the response to curative treatment.

Materials and methods: 124 patients over 70 years of age were evaluated retrospectively. 68 patients with early stage or locally advanced non-small cell lung cancer who were inoperable but not suitable for stereotactic radiotherapy were evaluated retrospectively. Geriatric 8 (G8) screening test was used to identify elderly cancer patients who could benefit from curative treatment. Patients received curative chemoradiotherapy or radiotherapy alone.

Results: In all patients(68), overall survival (83% for 1 year, 66% for 2 years) was median 18 months and disease free survival (58% for 1 year, 34.1% for 2 years) was median 14 months. As the G8 score increased, a statistically significant increase was observed in overall and disease free survival. Having weight loss or not, presence of accompanying disease, having good or bad health situation, having body mass index above and below 21, and the usage number of medications below or above 3 affects overall and disease free survival. When only the patients who received radiochemotherapy (n = 43) were evaluated, the mean survival (free of the ECOG performance score) was 12.8 months with G8 score less than 14 and 29.17 months with G8 score 14 and above and were statistically significant (p = 0.000).

Conclusion: When making a treatment decision, clinical evaluation should be performed well in patients older than 70 years with non-small cell lung cancer(NSCLC). In our study, overall survival and disease free survival were found to be better in patients with a G8 score above 14. Therefore, we think that it may be appropriate to use curative concurrent radiochemotherapy in selected patients with high G8 score and not to decide on biological age in elderly patients.

Introduction

While lung cancer frequency has decreased over the last two decades, it is still a commonly diagnosed cancer with the highest mortality rates (1-3). First-line standard treatment in non-small cell lung cancer (NSCLC) is surgery at the early stages or whole-body steriotactic radiotherapy (SBRT) in medically inoperable patients, while simultaneous chemoradiotherapy (CRT) is standard treatment in cases of locally advanced disease (4-7). Mean age at diagnosis is 70 (2). The ratio of geriatric patients (> 70 years old) is 50% in lung cancer patients (3).

Considering only chronogical age when choosing among treatment options reduces the chances for a patient to receive curative treatment. Factors that block the use of standard treatments are comorbidities (8). Definitive treatment results are similar in patients older than 70 without comorbidities and patients younger than 70 years old (9). Comorbidities must be examined closely to detect an effect on the efficacy of oncological treatments.

The most important feature in clinical evaluation of a patient is the performance status and performance is known to be an important prognostic factor in overall survival. Cardiovascular diseases, chronic obstructive pulmonary disease and other cancers are the most common comorbid conditions in lung cancer patients and have prognostic value in overall survival. In addition, the patient's cognitive status, nutritional status, psychological status, social support, and the use of drugs for other diseases are effective in the treatment decision. The G-8 screening tool was developed to identify elderly cancer patients who could benefit from comprehensive geriatric assessment (CGA). G-8 scoring is a screening tool with 8 easy-to-apply questions. Scoring between 0 and 17 is used and a higher score indicates a better health status(10). In our study, we aimed to investigate the results of treatment in patients older than 70 years whose performance was evaluated by using Geriatric 8 score and to find out which group could receive curative treatment.

Materials and methods:

Records of 124 patients over 70 years of age who were diagnosed and followed by our clinic between 2013 and 2017 were reviewed. 20 were diagnosed with small-cell lung cancer, 23 had metastatic NSCLC, and 13 were patients who received surgery and were admitted for postoperative RT. These records were excluded from the study. Exclusion criterias were: having

the diagnose of small-cell lung cancer or metastatic NSCLC or receiving surgery. Of the remaining patients, 68 with early-stage medically inoperable cancer who were not suitable for SBRT, and those with locally advanced NSCLC who received definitive CRT or RT were evaluated retrospectively.

Age, gender, smoking history, European Cooperative Oncology Group (ECOG) performance state, and comorbidities were evaluated as demographic features from patient recordings. The G8 score was used to provide a detailed geriatric evaluation in terms of digestion, weight loss, mobility, neurophysicological problems, body-mass index (BMI), medication usage, health state, and age. Additionally, the stage of the disease, treatment modalities (consecutive, simultaneous chemotherapy [CT] treatment, agents, etc), presentation of recurrence or metastasis, and survival durations were recorded. Radiotherapy was applied to every patient with 3-dimensional conformal RT at doses of 60 to 66 Gy. Elective nodal irradiation was not used.

Statistical Package for the Social Sciences, (SPSS 16.0 for Windows) was used for statistical analysis. The results were reported using the percent, average, mean, standard deviation, and chi-squared and Mann–Whitney U tests. A p value ≤ 0.05 was considered statistically significant. A Kaplan–Meier test was used for survival analysis, log-rank analysis was used to compare the survival rates of groups, and Cox regression analysis was used for factors that affect survival.

An ethic approval from Health Sciences University, Dr.Lutfi Kirdar Kartal Training and Research Hospital Ethics Cometee was taken at 20.08.2019(2019/514/160/6).

Results:

Sixty of the patients were male (88%) with a mean age of 75 (70–89). Median follow-up was 15 months, (2–54 months). Performance status according to ECOG scale was as follows: 0 for 11 patients (16%), 1 for 44 patients (65%), and 2 for 13 patients (19%). In total, 50 patients (74%) had a history of comorbid diseases. Clinical features are detailed in Table 1.

Table 1. Clinical features

Clinical features	**Number, n (%)**
Age	mean 75 (70–89)
Gender	
Male	60 (88)
Female	8 (11)
ECOG	
0	11 (16)
1	44 (64)
2	13 (19)
Comorbidity	
Hypertension (HT)	12
Diabetes mellitus (DM)	9
HT and DM	10
CHF*	4
COPD**	15
Smoking history	
+	59 (87)
-	9 (13)

** Congestive heart failure*

*** Chronic obstructive pulmonary disease*

Patients' stage during the diagnosis was: Stage 1B in 3 patients (4%), Stage 2B in 6 patients (9%), Stage 3A in 28 patients (41%), Stage 3B in 31 patients (46%). Tumour's median diameter was 5.35 cm (min 1 cm; max 11 cm). Histopathological subtypes were squamous cell carcinoma in 56 patients (82%), adenocarcinoma in 12 patients (18%).

Chemotherapy was applied to 43 patients using carboplatin and paclitaxel (72%) in different regimes between 2–4 cures. It was used concominantly**.** Curative RT alone was applied to 25 patients (28%) who were not able to receive CT.

In all patients, DFS (58.2% per year for 1 year and 34.1% per year) was median 14 months (Graph 1). According to the G8 scores, DFS was grouped as G8 score below 10 (n = 16), G8 score between 10-14 (n = 36) and G8 scores above 14 (n = 16). DFS were: 4 months in G8 scores less than 10, 14 months in G8 scores between 11-14 and 25 months in G8 scores more

than 14. DFS difference between the groups was statistically significant (p = 0.000). According to ECOG status, the mean DFS in patients with ECOG 0-1 (n = 55) was 23.9 months, in patients with ECOG 2 (n = 13), DFS was 8.69 months and the difference between the two groups was statistically significant (p = 0.006).

In terms of body mass index (BMI), the mean DFS in patients between BMI:18.5-21 (n = 37) was 10.9 months, in patients between BMI:21-23 (n = 21) was 20.16 months, in patients with BMI:23 (n = 10) was 33 months. The difference in DFS between the groups was statistically significant (p = 0.000). In all patients, OS (83.2% for 1 year and 66% for 2 years) averaged 18 months (graph 2).Overall survival in terms of G8 scores less than 10 was 6 months (80% for 1 year, 49% for 2 years), 18 months for G8 scores between 11-14, and 35 months for G8 scores more than 14 months (100% for 1 year, 88% for 2 years). p values were less than 0.05 and significant for each group.

ECOG between 0 and 1 did not differ significantly, ECOG 0 was significantly different from ECOG 2 (p, 000), ECOG1 was significantly different from ECOG 2 (p, 007) when we compare ECOG 0,1 and 2 in terms of overall survival. There was a decrease in OS as ECOG increased.

When we rewieved the patients with weight loss (n = 25) compared with patients without weight loss (n = 43) (p = 0.012), patients with neuropsychiatric disorders (n = 43) compared to those without (n = 25) (p = 0.000), patients using more than 3 drugs (n = 17) and those using less than 3 drugs (n = 51) (p = 0.000), patients with reduced food intake (n = 30) and those without reduced food intake (n = 38) (p = 0.000), patients with poor health (n = 17) and patients without good health (n = 51) (p = 0.007); there was a statistically significant difference in terms of OS.

According to BMI status, BMI between 18.5-21 (n = 37) and BMI between 21-23 (n = 21) (P = 0.00) and, BMI between18.5-21 and BMI 23 and above (n = 10). (P = 0.00), showed statistically significant difference in terms of OS.

When only radiotherapy and radiochemotherapy patients were evaluated in terms of age, sex, stage, histological type, receiving chemotherapy or not, tumor size, node status, there was no significant difference in the survey analysis. According to ECOG performance alone, a significant overall survival difference between ECOG 0-1 and 2 was found (p = 0.006).

Discussion:

In the lung cancer mapping project, the incidence of lung cancer was reported to be 41.7 per 100,000 for men and 4.8 per 100,000 for women. Similarly, in our study, male patients were more (88%). Mean age at diagnosis is 70 in that project and 75 in our study(11-13). Smoking is the most important cause of lung cancer (14) and smoking rate is 87% in our study. In studies investigating lung cancer and comorbidity, the rate of at least one comorbidity is high, and in general, approximately 80% of people aged 65 years and over have at least one comorbid disease (15) and this rate is similar (74%) with our study.

Although the majority of the patients diagnosed with lung cancer are elderly patients, information about treatment of elderly patients is limited in the literature. Because of comorbid diseases and poor performance in elderly patients, physicians often avoid curative treatment because they think that treatment toxicity will be higher. For this reason, a group that would benefit from treatment would be left untreated.

In order to provide evidence-based recommendations in elderly patients, the European Organization for Research and Treatment of Cancer (EORTC), Elderly Task Force, and the Lung Cancer group have published a consensus with the International Society of Geriatric Oncology (SIOG). In this consensus: it has been reported that the study data in local advanced lung cancer should be evaluated carefully and life expectancy, concomitant diseases and functional status should be taken into consideration when deciding treatment. According to this consensus, simultaneous or sequential administration of radiochemotherapy should be considered as an option in eligible elderly patients. In a panel in Italy, it was stated that the treatment decision should not be made only by looking at age and that radiochemotherapy could be applied in suitable elderly patients and that the patients would benefit from this treatment modality.

Currently, concurrent radiochemotherapy is the standard treatment for locally advanced lung cancer. It has been reported that chemoradiotherapy increases survival when compared with radiotherapy. However, to date, the results of studies with elderly patients with non-small cell lung cancer are retrospective small series and the results are contradictory (15).

In the Japanase Cooperative Oncology Group 0301 phase 3 study, patients older than 70 years were randomized only to RT and concomitant chemoradiotherapy groups, and OS and DFS were reported to be higher in CRT-treated arm (16). Results from 16 phase 2 and 3 data obtained by the National Cancer Institute had evaluated concurrent chemoradiotherapy and with/without

consolidation chemotherapy in patients with stage 3, over/under 70 years of age treated between 1990 and 2012. As a result of this study, OS was reported to be lower and DFS was similar in elderly patients. Other randomised studies have reported that CRT treatments produce similar OS and DFS results in patients both over and below 70 years of age (9). However, these studies are biased due to insufficient numbers of elderly patients. Researchers who conducted a retrospective analysis of Southwest Oncology Group trials 9308 and 9509 reported that only 20% of the patients were over 70 years old (9,15,16). We therefore attempted to determine the proper treatment for individual patients using retrospective, single-centre, limited studies.

As a result of our study, the median OS was found to be 18 months (83.2% for one year) and median 14 months for DFS (58.1% per year, 34.1% per year). The survival rate was higher (29.17 months) in the group treated with radiochemotherapy. And Survival rates were similar to those reported in the literature (17,18). By having prognostic importance in overall survival: performance status, presence of comorbid diseases, cognitive status, nutritional status, psychological status, social support, and drug intake should also be evaluated before making a treatment decision. For this purpose, many scoring methods are used in clinical practice, in which the G-8 screening tool is an easy-to-use screening tool developed to identify elderly cancer patients who can benefit from comprehensive geriatric assessment (CGA). In our study, we used the G8 screening tool for the ease of application when deciding treatment.

Bellera et al. Evaluated the G8 Scoring in elderly patients (10) and suggested that a threshold value at 14 ($\leq$14 versus >14) would provide good sensitivity estimates for the G-8 of at least 80%, without deteriorating the specificity under 60%. In our study, OS and DFS periods were also significantly higher in patients with G8 score over 14.

The majority of diagnosed lung cancer patients are elderly patients. By having a high incidence of comorbid diseases and poor performance in these elderly patients, physicians can avoid curative approaches when making treatment decisions. However, limited studies have shown that elderly patients benefit from radiochemotherapy. Therefore, when making treatment decisions, first of all, clinical evaluation of patients with NSCLC should be performed well.

G8 scoring, which was developed to identify elderly cancer patients that could benefit from geriatric assessment, is an easy-to-use and important screening tool for decision-making in outpatient clinics. In our study, we determined the patients to be treated according to G8 scoring.

And in accordance with the literature, we found that OS and DFS were better in patients with G8 scores above 14. Therefore, the treatment strategy in elderly patients should not be decided according to biological age, and we believe that the standard treatment protocol may be appropriate for concurrent radiochemotherapy in selected patients with high G8 scores.

Conclusion:

Treatment decisions must consider performance and comorbidities in patients over 70 years old diagnosed with NSCLC. Restricting CT to standard-treatment modality ensures survival advantages in a well-chosen group of patients. Our study is one of a few that emphasises the importance of determining treatment protocols in medically inoperable or locally advanced-stage NSCLC patients over 70 years old. Future randomised studies should include more elderly patients and standard treatment protocols must be determined according to performance state and comorbidities.

REFERENCES

1-Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2015;136(5):359-86.

2- Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. CA Cancer J Clin 2013;63(1):11-30.

3-Parkin DM. Global cancer statistics in the year 2000. Lancet Oncol 2001;2(9):533-43.

4-Timmerman R, Paulus R, Galvin J, et al. Stereotactic body radiation therapy for inoperable early stage lung cancer. JAMA 2010;303(11):1070-6.

5-Farray D, Mirkovic N, Albain KS. Multimodality therapy for stage III non-smallcell lung cancer. J Clin Oncol 2005;23:3257-69.

6- Belderbos J, Uitterhoeve L, van Zandwijk N, et al. Randomised trial of sequential versus concurrent chemoradiotherapy in patients with inoperable non-small cell lung cancer. Eur J Cancer 2007;43:114-21.

7-Curran WJ, Scott CB, Langer CJ, et al. Long-term benefit is observed in a phase III comparison of sequential vs concurrent chemo-radiation for patients with unresected stage III NSCLC: RTOG 94-10. Proc Am Soc Clin Oncol 2003:22;621.

8-Pallis AG, Gridelli C, Wedding U, et al. Management of elderly patients with NSCLC; updated expert's opinion paper: EORTC Elderly Task Force, Lung Cancer Group and International Society for Geriatric Oncology. Ann Oncol 2014;25:1270-83.

9-Blanchard EM, Moon J, Hesketh PJ, et al. Comparison of Platinum-Based Chemotherapy in Patients Older and Younger than 70 Years, An Analysis of Southwest Oncology Group Trials 9308 and 9509. Journal of Thoracic Oncology 2011;6(1):115-20.

10-C. A. Bellera, M. Rainfray, S. Mathoulin-Pélissier, C. Mertens, F. Delva, M. Fonck, P. L. Screening older cancer patients: first evaluation of the G-8 geriatric screening tool. Soubeyran Annals of Oncology. 2012:23(8):2166-72.

11-Parkin DM. Global cancer statistics in the year 2000. Lancet Oncol 2001;2:533-43.

12- Turkish Thoracic Society Lung and Pleural Malignancies Working Group. The relationship between risk factors and histological type in lung cancer. 11th Annual Congress of Turkish Thoracic Society; 2008 April 23-27; Antalya Turkey.

13- Owonikoko TK, Ragin CC, Belani CP, Oton AB, Gooding WE, Taioli E, et al. Lung cancer in elderly patients: an analysis of the surveillance, epidemiology, and end results database. J Clin Oncol 2007;25:5570-7.

14-Alberg AJ, Brock MV, Ford JG, Samet JM, Spivack SD. Epidemiology of lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 2013;143(Suppl 5):1-29.

15- Özgün MA, Karagöz B, Bilgi O, Kandemir GE, Türken O. The prognostic significance of comorbidity in non-small cell lung cancer and its relationship with other prognostic factors. UHOD 2009; 2: 63-8.

16-Weiss J, Langer C. NSCLC in the elderly-the legacy of therapeutic neglect. Curr Treat Options Oncol 2009;10(3-4):180-94

17-Yu HM, Liu YF, Yu JM, Liu J, Zhao Y, Hou M. Involved-field radiotherapy is effective for patients 70 years old or more with early stage non-small cell lung cancer. Radiother Oncol 2008;87(1):29-34. (PMID: 18237795)

18-Atagi S, Kawahara M, Yokoyama A, Okamoto H, Yamamoto N, Ohe Y et al. Thoracic radiotherapy with or without daily low-dose carboplatin in elderly patients with non-small-lung cancer;a randomized,controlled,phase 3 trial by the Japan Clinical Oncology Group(JCOG0301). Lancet Oncol 2012;13(7):671-8.

Figure-1

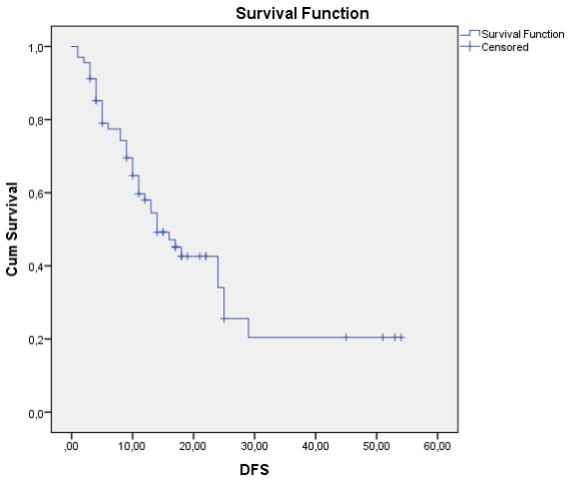

Figure-2