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Does age have an impact on lung cancer survival?

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Abstract:

OBJECTIVE: Lung cancer is the most diagnosed and the most frequent cause of cancer-related deaths in the world. Nonsmall cell lung cancer (NSCLC) prognosis in younger patients is controversial. In this study, surgical survival of young age group with NSCLC was analyzed retrospectively.

MATERIALS AND METHODS: A total of 1043 patients who underwent anatomical lung resection and mediastinal lymph node dissection were analyzed between January 2005 and December 2013. Patients were divided into two groups in terms of age being below 45 years and younger (Group 1) and over 45 years (Group 2).

RESULTS: There were 68 patients in Group 1 and 975 patients in Group 2. Male/female rate was 2.4 and 14, respectively ($P < 0.001$). Adenocarcinoma was more diagnosed in Group 1 (47.1%), and squamous cell carcinoma was more seen in Group 2 (54.7%). The pathological diagnosis was statistically significant ($P < 0.001$). All groups' median survival time was 51 months, and 5-year survival rate was 47.1%. Group 1 and 2 survival rates were 64 and 48 months, respectively, with Group 1 having significantly better results than Group 2 ($P < 0.001$). The 5-year survival rate of female patients included in Group 1 was 73%, whereas it was 44.7% in Group 2 ($P < 0.001$). Age is determined to have remarkable impact on the survival with Cox-regression test ($P < 0.001$, 95% confidence interval).

CONCLUSION: The survival which is significantly better in younger patients may encourage aggressive approaches for these patients. The effect of age on prognosis and survival should be evaluated with multicenter studies.

Keywords:

Surgery, survival, young age lung cancer

Introduction

Lung cancer is the most diagnosed malignity and the most frequent cause of cancer-related deaths in the world.[1,2] Nonsmall cell lung cancer (NSCLC) is accounted for 85% of all lung cancers and often determined in the elder population; however, there is a significant rate (1%–10%) of young patients being diagnosed under the age of 45 or 50 years.[3-6]

NSCLC prognosis in younger patients is controversial. Some authors report that the disease is more aggressive and prognosis is worse; however, others advocate that there is no difference compared to the elder population.[7] Here, we compared patients older and younger than 45 years.

Materials and Methods

In our center, 1188 patients diagnosed with NSCLC who underwent anatomical lung resection and mediastinal lymph node dissection between January 2005 and December 2013 were analyzed, retrospectively. Exclusion criteria of the study are as follows: (1) pathological diagnosis of carcinoid tumors, (2) patients who underwent surgery for only one brain metastasis or adrenal metastasis, (3) unresectable cases, and (4) diagnosis of small cell lung cancer.

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After exclusion of inappropriate cases, 1043 patients were included in the study. Patients were divided into two groups; Group 1 consisted of patients younger than 45 years and Group 2 consisted of patients older than 45 years. Data were recorded with case files and follow-up. Groups are compared for demographic features such as gender and age and histological type, type of operation, smoking, pathological stage, postoperative mortality, and survival. Preoperative chest computed tomography (CT), brain magnetic resonance imaging of metastasis screening, abdominal ultrasound and scintigraphy, and positron emission tomography-CT after 2009 were performed for all patients.

Statistical analyses were made using IBM SPSS 20.0 (PASW Statistics for Windows; SPSS, Chicago, IL, USA). Survival was analyzed with the Kaplan–Meier method and curves were compared using a log-rank test. Multivariate analysis was performed by Cox proportional hazard model. Frequency comparisons were carried out by the Chi-square test between two groups. Results were considered statistically significant if $P < 0.05$.

Results

There were 958 male and 85 female patients whose median age was 61 (28–82) years. Sixty-eight patients were in Group 1 and 975 patients were in Group 2. There were 48 males (70.6%) and 20 females (29.4%) and 910 males (93.3%) and 65 females (6.7%) in Group 1 and Group 2, respectively [Table 1]. Male/female rate was 2.4 and 14 in Group 1 and Group 2, respectively. The ratio between groups was found to be statistically significant ($P < 0.001$). 30 patients (62.5%) in Group 1 and 900 patients (92.1%) in Group 2 were smokers. The number of smokers in Group 1 was statistically lower than the smokers in Group 2 ($P < 0.001$).

The surgical procedures were analyzed for study groups. Lobectomy was performed to 819 patients (78.5%), 203 patients (19.5%) underwent pneumonectomy, and 21 patients (2%) had segmentectomy [Table 2]. In Group 1, 53 (%77.9) patients underwent lobectomy, 15 underwent pneumonectomy (22.1%), and there was no segmentectomy. In Group 2, lobectomy to 766 (78.6%), pneumonectomy to 188 (19.3%), and segmentectomy to 21 (2.1%) were performed. There was no statistically significant difference observed between groups in terms of operation type ($P = 0.502$).

Chest wall resection was performed in a total of 72 patients. Two patients (2.9%) were in Group 1, and 70 patients were in Group 2. There was no statistically significant difference between two groups ($P = 0.135$ – Fisher's exact test). Sleeve resection was performed in seven out of 57 patients (10.3%) in Group 1 and 50 (5.1%) patients in Group 2, and there was no statistically significant difference between two groups ($P = 0.071$ – Fisher's exact test).

Table 1: Characteristic of the patients in both groups

	≤45 (*n*=68; 6.5%)	>45 (*n*=975; 93.5%)	*P*
Sex			
Female	20 (29.4)	65 (6.7)	<0.001
Male	48 (70.6)	910 (93.3)	
Smoking			
Yes	30 (62.5)	900 (92.1)	<0.001
No	18 (37.5)	75 (7.9)	

Table 2: Distribution of both groups

	≤45 (*n*=68; 6.5%)	>45 (*n*=975; 93.5%)	*P*
Operation type			
Lobectomy	53 (77.9)	766 (78.6)	0.502
Pneumonectomy	15 (22.1)	188 (19.3)	
Segmentectomy	0	21 (2.1)	
Histopathological type			
Adenocarcinoma	32 (47.1)	333 (34.2)	0.023
Squamous	25 (36.8)	533 (54.7)	
Large cell	3 (4.4)	70 (7.2)	
Other type of NSCLC	8 (11.7)	39 (4)	
N status			
0	44 (64.6)	715 (73.3)	0.299
1	12 (17.7)	134 (13.7)	
2	12 (17.7)	126 (13)	
Stage			
I	24 (35.3)	403 (41.3)	0.091
II	22 (32.4)	367 (37.6)	
III	22 (32.4)	205 (21)	

Histopathological type assessment revealed squamous cell carcinoma in 558 (53.5%) patients (Group 1: 25 [36.8%] and Group 2: 533 [54.7%]), adenocarcinoma in 365 (35%) patients (Group 1: 32 [47.1%] and Group 2: 333 [34.2%]), large cell carcinoma in 73 (7%) patients (Group 1: 3 [4.4%] and Group 2: 70 [7.2%]), and other types of NSCLC in 47 (4.5%) patients (Group 1: 8 [11.7%] and Group 2:39 [4%]). When two groups are compared, adenocarcinoma was found statistically significantly higher in Group 1 whereas squamous cell carcinoma was statistically significant higher in Group 2 ($P = 0.023$).

Analyses of lymph node metastasis revealed that 759 patients (72.8%) were N0, 146 patients (14%) were N1, and 138 patients (13.2%) were N2. The number of N0 patients was 44 (64.6%) and 715 (73.3%); N1 was 12 (17.7%) and 134 (13.7%); and N2 was 12 (17.7%) and 126 (13%) in Group 1 and Group 2, respectively. There was no statistically significant difference between two groups ($P = 0.299$). According to TNM staging, 427 patients (40.9%) were in Stage 1, 389 patients (37.3%) were in Stage 2, and 227 patients (21.8%) were in Stage 3. There was no statistically significant difference between two groups [Table 2].

The median survival of total of patients was 51 months. The 3- and 5-year survival rate was 59.3% and 47.1%, respectively. Median survival of Group 1 was 64 months, and median survival of Group 2 was 48 months [Table 3]. The survival difference between two groups was statistically significant with Kaplan–Meier survival analysis ($P < 0.001$). There was no statistically significant difference in female gender for 5-yeas survival rate; however, 5-year survival rate was statistically significant higher in male patients in Group 1 (73% and 44.7%, respectively; $P < 0.001$). The survival of patients with N0 was statistically significant better in Group 1 than in Group 2 (80.6% and 50%, respectively; $P < 0.001$). Stage-specific 5-year survival analysis showed that Group 1 survival was statistically significant better than Group 2 in Stage 1 (91.7% vs. 55%; $P = 0.007$) and Stage 2 (66% vs. 44.9%; $P = 0.045$); however, there was no statistically significant difference in Stage 3 [Table 3]. The multivariate analysis done via Cox-regression test [Table 4] revealed that only age factor significantly impacted on survival ($P < 0.001$, confidence interval: 95%).

Table 3: All groups' survival

	≤45 median month/5-year rate	>45 median month/5-year rate	*P*
Overall	64/67.4	48/45.6	<0.001
Sex			
Male	66/73	48/44.7	<0.001
Female	52/46.9	58/59.2	0.477
Histopathological type			
Adenocarcinoma	58/59.9	44/42.1	0.043
Squamous	77/74.1	59/49.9	0.014
N status			
0	78/0.6	59/50	<0.001
1	64/56.3	40/39.5	0.361
2	25/33.3	25/33.3	0.508
TNM stage			
I	84/91.7	72/55	0.007
II	64/66	42/44.9	0.045
III	45/45	28/28.6	0.125

Table 4: Multivariate analyses using a Cox-regression model

Variables	OR	95% CI	*P*
Age	1.025	1.016-1.035	<0.001
Histological subtype	0.965	0.855-1.090	0.566
Sex	1.220	0.866-1.719	0.256

OR: Odds ratio, CI: Confidence interval

Discussion

NSCLC is observed more common in the elder population[3] and especially in the sixth and seventh decades.[8] The studies accomplished both in our country and in the world report that the disease is accounted for only 2.7%–12% in the young population.[7-13] In several studies, the disease is encountered mostly after 50 years old.[3,6-13] We determined the young and older patients with the cutoff age as 45 years in our study. The young age group's rate was 6.5% among the study group and this rate was comforted the literature.[7-13]

Smoking is the most remarkable risk factor for lung cancer.[10] Mauri *et al*. declared that smoking was not a statistically significant factor for younger and elder groups.[8] However, in China and India, two studies showed that in younger group, smoking rate was less than elder ones.[14,15] In our study, smoking rate was more significantly higher in elder group than the younger group.

Studies which carried out in Italy[12] and Kuwait[10] showed that male/female rates did not differ between older and younger age groups. On the other hand, some studies published in Japan[7] and Canada[10] showed that the number of female patients was higher in younger age group. In the study of Thomas *et al*., male/female rate was lower than 1 in the United States.[3] The male/female rate was 2.4 and 14 in Group 1 and Group 2, respectively, and is found statistically significant ($P < 0.001$).

Several studies for young age group showed that adenocarcinoma is the most common histopathological subtype in lung cancer.[1] Thomas *et al*.,[3] Ramalingam *et al*.,[4] Bryant and Cerfolio,[6] Sekine *et al*.,[7] Mauri *et al*.,[8] McDuffie *et al*.,[11] and Decaro and Benfield[13] reported that adenocarcinoma was the most common subtype of lung cancer [Table 5]. Yet, some studies have revealed opposite data. For instance, Misirligil *et al*.[9] and Roviaro *et al*.[12] reported that squamous cell carcinoma was the most common histopathological subtype in young age group. There are differences in elderly group in several studies. Decaro and Benfield,[13] Misirligil *et al*.,[9] Ramalingam *et al*.[4] and Kreuzer *et al*.[16] reported that squamous cell carcinoma was seen more frequently in the elderly group while Sekine *et al*.,[7] Mauri *et al*.,[8] and Thomas *et al*.[3] reported that adenocarcinoma was the most common subtype in the elderly group. In our study, squamous cell carcinoma was more common in Group 2 whereas adenocarcinoma was the most seen in Group 1. In various studies, adenocarcinoma was more observed subtype in young age, nonsmokers, and females.[17,18] We assume that since smoking was detected less in Group 1, adenocarcinoma is more commonly seen in Group 1 in our study.

Bryant and Cerfolio compared the surgical procedures between two groups and they did not find any difference.[6] However, in Tian *et al*.'s study, pneumonectomy was

Table 5: Results of the studies that published in the literature

	Study time	Age	Male/female ratio		Histopathology		5-year survival (%)	
			Young	Old	Young	Old	Young	Old
Thomas *et al*.[3]	2015	40	0.9	1.2	AC	AC	NA	NA
Ramalingam *et al*.[4]	1998	50	1.5	2.2	AC	SCC	16.1	13.4
Bryant and Cerfolio[6]	2008	45	1.5	1.5	AC	SCC	51	62
Sekine *et al*.[7]	1999	40	1.5	2.6	AC	AC	20	20
Mauri *et al*.[8]	2005	45	4.5	7	AC	AC	NA	NA
Misirligil *et al*.[9]	1988	40	2.9	11.7	SCC	SCC	NA	NA
McDuffie *et al*.[11]	1989	50	1.2	3.5	AC	SCC	NA	NA
Roviaro *et al*.[12]	1985	45	13	13.6	SCC	SCC	20.8	25
DeCaro and Benfield[13]	1982	40	1.5	5	AC	SCC	8	7.8
Kreuzer *et al*.[16]	1998	45	2.6	5.6	AC	SCC	NA	NA
Current study	2015	45	2.4	14	AC	SCC	67.4	45.6

SCC: Squamous cell carcinoma, AC: Adenocarcinoma, NA: Not available

significantly higher in younger group.[19] Our study's results are similar to Bryant and Cerfolio's studies. Mauri *et al*. reported that Stage 3 was observed more common in Group 1.[8] Bryant and Cerfolio[6] and Roviaro *et al*.[12] found no significant difference in both groups for staging in their studies. In our study, there was no significant difference in the stage distribution of both groups.

In some studies, younger group's prognosis is better than elderly groups.[4,10,20,21] In Roviaro *et al*.'s study, 5-year survival rate was 36% and 42.2% in Group 1 and Group 2, respectively.[12] Tian *et al*. reported that there was no difference for 5-year survival rate between two groups.[19] Conversely, Bryant and Cerfolio issued that younger group's 5-year survival rate was significantly worse than elderly group, with a rate of 51% and 62%, respectively.[6] Median survival and 5-year survival rate of Group 1 were significantly better in our study.

As a result, surgeons are encouraged for more aggressive procedures for younger patients since they have significantly higher survival rates. The effect of age on survival and prognosis can be better evaluated with a larger number of patients in multicenter trials.

Conclusion

As a result, surgeons are encouraged for more aggressive procedures for younger patients since they have significantly higher survival rates. The effect of age on survival and prognosis can be better evaluated with a larger number of patients in multicenter trials.

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Conflicts of interest
There are no conflicts of interest.

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