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Araştırma Sunumu | *Research Article*

Düzeltme: *Ağustos 2019 sayısında yayınlanan Comparison Of Elderly Patients With Younger Age Patients Who Were Diagnosed With Non-Small Cell Lung Cancer In Terms Of Operability isimli makalenin Materials and Methods bölümün ilk cümlesi olan; "A total of 288 patients who underwent resection for non-small cell lung cancer in Kocaeli University Medical Faculty Chest Surgery Department between December 31, 2014, and January 1, 2016, were included in this study." cümlesinde yer alan 'December 31, 2014, and January 1, 2016' bölümü 'January 1, 2006, and December 31, 2014' olarak değiştirilmiştir. Yeni cümle " A total of 288 patients who underwent resection for non-small cell lung cancer in Kocaeli University Medical Faculty Chest Surgery Department between January 1, 2006, and December 31, 2014, were included in this study." şeklindedir.*

KÜÇÜK HÜCRELİ DIŞI AKCİĞER KANSERİ TANILI İLERİ YAŞ HASTALARIN OPERE EDİLEBİLİRLİK AÇISINDAN ERKEN YAŞLI HASTALARLA KARŞILAŞTIRILMASI

Comparison Of Elderly Patients With Younger Age Patients Who Were Diagnosed With Non-Small Cell Lung Cancer In Terms Of Operability

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Öz

Küçük hücreli dışı akciğer kanseri nedeni ile opere edilen ileri yaşlı hastaların demografik özellikler, rezeksiyon tipi, sağkalım, erken ve geç post-op komplikasyonlar, hastanede yatış süresi açısından daha genç yaş grubu ile karşılaştırılarak ileri yaşın opere edilebilirlik üzerindeki etkisi araştırılmıştır. Kocaeli Üniversitesi Tıp Fakültesi Göğüs Cerrahisi Anabilim Dalı tarafından küçük hücreli dışı akciğer kanseri nedeni ile rezeksiyon yapılan 288 hasta incelendi. Verileri yeterli görülen hastalar arasından 70 yaş altı (Grup I – Kontrol Grubu) 244 hasta ve 70 yaş ve

üzeri (ileri yaş) (Grup II – Çalışma Grubu) 44 hasta hasta geriye dönük olarak incelendi. Her iki grup arasında hastaların özgeçmişi (p=0.083) ve rezeksiyon tipi (p=0.557) açısından istatistiksel olarak anlamlı fark gözlenmedi. Her iki grup arasında sağkalım açısından istatistiksel olarak anlamlı fark gözlendi (p=0.013). Her iki grup arasında post operatif erken komplikasyon açısından istatistiksel olarak anlamlı fark görülmezken (p=0.514) post operatif geç komplikasyon açısından istatistiksel olarak anlamlı fark gözlendi (p=0.034). Her iki grup arasında post operatif taburculuk süresi açısından istatistiksel olarak anlamlı fark gözlenmedi (p=0.916). Çalışmamızda elde ettiğimiz sonuçlara göre; küçük hücreli dışı akciğer kanseri nedeni ile opere edilmiş ileri yaş hastaların genç hastalar ile benzer demografik özelliklerde olduğu, post-operatif morbidite ve cerrahi tedavi sonuçlarında istatistiksel olarak kısmen anlamlı farklar görülse de büyük oranda benzer olduğu saptanmıştır. Cerrahi tedavi için ileri yaşın tek başına kontraendikasyon teşkil etmediği sonucuna varılmıştır.

Anahtar Kelimeler: İleri Yaş, Akciğer Kanseri, Cerrahi.

Abstract

Elderly patients who were operated for non-small cell lung cancer were compared with younger age patients in terms of their demographic characteristics, resection type, survival, early and late postoperative complications, duration of hospital stay, and effect of older age on operability. A total of 288 patients who underwent resection for non-small cell lung cancer in Kocaeli University Medical Faculty Thoracic Surgery Department were examined. Among the patients with adequate data, 244 patients aged <70 years (Group I, control group) and 44 patients aged >70 years (advanced age) (Group II, study group) were retrospectively analyzed. There were no statistically significant differences between two groups in terms of distribution of medical history of patients (p= 0.083), and resection types (p= 0.557). A statistically significant difference was observed between the two groups in terms of survival (p= 0.013). There was no statistically significant difference between the two groups in terms of postoperative early complications (p= 0.514), but there was a statistically significant difference in terms of postoperative late complications (p= 0.034). No statistically significant difference was observed between the two groups in terms of postoperative discharge time (p = 0.916). This study showed that the demographic characteristics were significantly similar between the elderly and younger patients who were treated for non-small cell lung cancer, although there were partly statistically significant differences in terms of postoperative morbidity and surgical treatment results. It was also observed that advanced age alone does not constitute a contraindication for surgical treatment.

Keywords: Elderly, Lung Cancer, Surgery.

1. Introduction

The increasing incidence of lung cancer has been attributed to several reasons such as passive smoking; air pollution; exposure to arsenic, cadmium, beryllium, radon, and

asbestos; genetic factors; dietary habits; and personal factors, especially smoking (DeMatteis, Consonni & Bertazzi, 2008, p. 34-42; Coultas & Samet, 1992, p. 341-354). Lung cancer is a stealthy disease and causes late symptoms. Therefore, most of the patients are detected in advanced stage and lose their opportunity to undergo surgery. Surgery is the most effective treatment during the early stage (stage 1–2). However, when 5-year survival rate is assessed in patients with early-stage lung cancer who underwent surgery, there are not many optimistic results (LoCicero, Ponn & Benedict, 2000, p.1311-1341). Chronic diseases and malignancy incidence have becoming proportionally increased by the extension of life expectancy among the population. The influence of old age (70 years and older) on the decision of performing a surgical resection has been debated, depending on the increase in lifespan. In this study, elderly patients (aged 70 years and older) who were operated for non-small cell lung cancer were compared with younger age patients in terms of their demographic characteristics, resection type, survival, early and late postoperative complications, length of hospital stay, and the effect of older age on operability. Consequently, the aim of this study was to determine the effect of advanced age on survival after resection.

2. Materials and Methods

A total of 288 patients who underwent resection for non-small cell lung cancer in Kocaeli University Medical Faculty Chest Surgery Department between January 1, 2006, and December 31, 2014, were included in this study. Among the patients with adequate data, 244 patients aged <70 years (Group I, control group) and 44 patients aged >70 years (advanced age) (Group II, study group) were retrospectively analyzed. Both groups were compared in terms of epidemiologic factors, surgical resection types, survival, and postoperative early and late complications. Complete blood counts, biochemistry tests, coagulation tests, ECG, echocardiogram, and pulmonary function test (diffusion) were routinely performed in all patients. Patients with a DLCO value of 60 or more in the respiratory test underwent advanced tests (such as stair climbing and walking test) at FEV-1 values <1.5, lobectomy at FEV-1 values ≥1.5, and pneumonectomy at FEV-1 values ≥2. VO_2 max value was recorded for the

required patients. Patients without pulmonary hypertension (<20 mmHg, detected in the ECO) were preferred for the operation. PET-CT data were removed for cases without PET-CT results. FOB, EBUS, and mediastinoscopy were performed for lymph node sampling of patients with suspected mediastinal lymph nodes on PET-CT. Anesthesia department consultation was provided for all patients before operation. Lobectomy, pneumonectomy, wedge resection, and segmentectomy were performed through posterolateral thoracotomy in the patients. Surgical segmental surgery, lobectomy, and pneumonectomy were performed for patients with appropriate medical condition and PFT, which did not interfere with the operation of the ECO, and in patients who did not reach the desired levels. Follow-up examinations were carried out together with the medical oncology department. Information related to outcome was gathered through phone calls, and hospital file registrations through systems in connection with the National Information System (NIS). Air leaks that extended for more than 7 days were regarded as prolonged air escapes. Complications that occurred in the first 30 days after the operation were evaluated as early complications that occurred after the first 30 days were evaluated as late complications, and deaths that occurred within the first 30 days after the operation were evaluated as surgical mortality. The day of the operation was considered as the start when the hospitalization period was calculated. Statistical evaluation was performed using IBM SPSS 20.0 (SPSS Inc., Chicago, IL, USA). The normal distribution fitness test was assessed using the Kolmogorov–Smirnov test. Numerical variables with normal distribution are represented as mean ± standard deviation, and numerical variables with no normal distribution (median) (25th to 75th percentile) and categorical variables are represented using frequency (percentages). The Kaplan–Meier method was used for survival analysis, and the log-rank test was used for multiple comparisons. Relationships between categorical variables were evaluated by Chi-square analysis. $p < 0.05$ was considered to be statistically significant. The study protocol was approved by the Kocaeli Univercity Ethics Committee.

3. Results

Among our study subjects, 244 (84.7%) were <70 years old and 44 (15.3%) were ≥70 years old. There were 261 (90.6%) males and 27 (9.4%) females. In the <70 years age group, there were 221 (90.6%) males and 23 (9.4%) females. Among those aged ≥70 years, there were 40 (90.9%) males and 4 (9.1%) females. No statistically significant difference was observed in the distribution of age in terms of sex (p = 1.000). The average age of our study subjects was 60.50 ± 8.549 (range: 38–82) years, the average age of the ≥70 years age group was 73.66 ± 3.087 (range: 70–82) years, and the average age of the <70 years age group was 58.23 ± 6.934 (range: 38–69) years. History of cigarette smoking was present in 253 patients (87.8%). Smoking habit was found in 88.11% (215 patients) of those in the <70 years age group and in 86.36% (38 patients) in the ≥70 years age group. No statistically significant difference was detected between the two groups in this regard (p = 0.563). There were also no statistically significant differences between the two groups in terms of the distribution of diseases, including recurrences (p = 0.083); the distribution of pulmonary function test (PFT) and carbon monoxide diffusion test (DLCO) results (p = 0.213 and 0.062), respectively; and the resection types (p = 0.557). The two groups showed no statistically significant differences in terms of postoperative early complications (p = 0.514), but there was a statistically significant difference between the two groups in terms of postoperative late complications (p = 0.034) (Table 1).

The difference of survival between the two groups was significant (p = 0.013), with the median survival of 24 months in the group aged ≥70 years and 33 months in the group aged <70 years, this analysis may have been obscured by the unbalanced number of patients in each group; ≥70 years old group versus the other (Figure 1).

There was no statistically significant difference between the two groups in terms of hospitalization time (p = 0.916). The longest hospital stay was 57 days in the group aged ≥70 years, whereas it was 41 days in the group aged <70 years. Regarding mortality rates, no statistically significant difference was detected between the two groups (p = 0.063), although all deaths were due to cancers, and complications of procedures such as chemotherapy, radiotherapy, cardiac causes, and infections (Table 1).

4. Discussion

Today, lung cancer is still considered as an important healthcare problem in the society. Smoking has been found to be the most common etiology of lung cancer (DeMatteis, Consonni & Bertazzi, 2008, p. 34-42; Coultas & Samet, 1992, p. 341-354). Consistent with the litterateure, the rate of smoking was found to be 87.8% in our study. Recent developments leading to improvements in the quality of health services, socioeconomic level has extended to the expected life expectancy. Malignant diseases, primarily lung cancer, have increased, and the choice of treatment for malignant cases in advanced age has become an important issue (Melek, Medetoğlu, Demir, Kara & Dinçer, 2011, p. 586-592). The mean age of our study subjects was 60.50 ± 8.549 years. Surgical procedures are the most effective method for the treatment of lung cancer. Although improvements in anaesthesia techniques may increase the number of surgical interventions performed in elderly population, advanced age alone may adversely affect the surgical procedures. According to the third edition of the American College of Chest Physicians (ACCP) Diagnosis and Treatment Guide for Lung Cancer, patients ≥70 years are accepted as advanced elderly group (Detterbeck, Lewis, Diekemper, Addrizzo-Harris & Alberts, 2013, p. 7-37). In our study, it was noteworthy to observe that there were fewer patients who underwent surgical treatment among the elderly. Because of difficulties in reaching a full-fledged health center, sociocultural structure and false beliefs, criteria for the appropriate patient selection of the surgeon. Significant physiological changes occurs in the body with aging, which results in complications and affects the survival of patients after surgery. In particular, physiological changes in the cardiovascular and respiratory systems and comorbidities such as diabetes, kidney and liver diseases, chronic thromboembolism, and nutritional disorders that increase with aging increase the risk of life-threatening complications after surgery (Pagni, McKelvey, Riordan, Federico & Ponn, 1998, p. 40-44 ; Hartz, 2000, p. 989-1000; Ciriaco et al., 2005, p. 1516-1519). In addition, since the majority of lung cancer cases have a long history of smoking, they also have several additional diseases that affect the expected life expectancy and postoperative morbidity rate, especially secondary cardiovascular diseases, COPD, malignancies, and neurological diseases. In a study conducted by Janssen-Heijnen et al. in elderly patients with lung cancer, 23% of patients had cardiovascular disease,

22% had COPD, and 15% had a secondary malignancy (Janssen-Heijnen, Schipper, Razenberg, Crommelin, Coebergh, 1998, p. 105-113). In our study, the most common diseases were those of the cardiovascular system (74 subjects, 25.7%) followed by the respiratory system (72 subjects, 25.6%). The principle prognostic factors affecting the survival in patients with advanced lung cancer include the performance status of the patient (especially cardiac and respiratory functions), the tumor stage, and the histopathologic type.

First of all the mortality rate of the surgeon should be acceptable when surgical decision is made in elderly age patients; 4% for lobectomy and 8% for pneumonectomy (British TS, 2001, p. 89-108). Second, the survival rate must increase after the surgery and not impair the quality of life (Burfeild et al., 2008, p. 597-604). Mortality and morbidity rates vary depending on the surgical technique used. There are studies showing that the mortality rate of pneumonectomies is higher in lobectomy and segmentectomy in elderly patients, and the morbidity rate increases as the resection grows (Ponn, 2005, p. 554-86; Markos et al., 1989, p. 902-910). Although there are studies indicating that the resection types are more limited in the elderly group, there is no significant difference between perioperative mortality and the normal population in elderly cases where lobectomy and segmentectomy have been performed in several studies (Matsuoka, Okada, Sakamoto & Tsubota, 2005, p. 380-383; Dominguez-Ventura et al., 2007, p. 370-374; Okami et al., 2009, p. 1247-1253). Although studies have reported different outcomes regarding mortality and morbidity rates after surgery in elderly patients, the general opinion is that older people are more likely to have a diagnosis than younger adults. However, recent studies have shown that morbidity and mortality rates are at acceptable levels (Pei, Zhou, Han, Liu & Xu, 2014, p. 1230–1238). It has also been reported that age is not a single factor affecting the survival of patients with non-small cell lung cancer (Thomas, Piraux, Jacques, Grégoire, Bédard & Deslauriers, 1998, p. 266-274; Oliaro, Leo, Filosso, Rena, Parola & Maggi, 1999, p. 715-719; Jazieh et al., 2000, p. 1168-1171). In our study, low mortality and morbidity rates were primarily observed in elderly patients, which could be due to careful patient selection and appropriate preoperative and postoperative patient care. Mortality and morbidity rates can be reduced in-elderly patients through

appropriate patient selection and postoperative care (Ponn, 2005, p 554-86; Spaggiari & Scanagatta, 2007, p. 84-91). The most common complications occurring in the early period after surgery are prolonged air leak, arrhythmia, and atelectasis (Ponn, 2005, p. 554-86; Gebitekin, Gupta, Martin, Saunders & Walker, 1993, p. 653-656; Voltolini, Rapicetta, Ligabue, Luzzi, Scala & Gotti, 2009, p. 147-152). In our study, the most frequent complications that appeared in accordance with the literature were expansion defect, prolonged air leak, and arrhythmia. The postoperative early complication rate was 38.6% in the older age group and 33.2% in the younger age group. There was no statistically significant difference in postoperative early complication rates between the two groups ($p = 0.514$). Surgical complications prolong the length of hospital stay in the treatment process. The mean postoperative hospitalization time was 12.29 ± 6.193 days in the group aged <70 years and 12.98 ± 8.812 days in the group aged ≥70 years, with no statistically significant difference between the two groups ($p = 0.916$). Lobectomy and lymph node dissection is the accepted treatment in Stage 1-2 non-small cell lung cancer (Razi, John, Sainathan & Stavropoulos, 2016, p. 683-689). There are studies suggesting that there is no significant difference in survival between anatomical resection and wedge resection in older ages so long as the patient's respiratory reserve is adequate, but there are also conflicting studies reporting more recurrences and shorter survival in limited resections (British TS, 2001, p. 89-108; Razi, John, Sainathan & Stavropoulos, 2016, p. 683-689). In our study groups, the proportion of sublober resection (wedge-segmentectomy) was 13.9% (Table 1). In a study, there was no prognostic significance of age in elderly patients with lung cancer who were treated surgically; the long-term life expectancy was related to tumor-free factors in patients aged ≥70 years (Melek, Medetoğlu, Demir, Kara & Dinçer, 2011, p. 586-592). It has been reported that life expectancy does not differ between the elderly and younger groups among patients aged ≥80 years, and chemotherapy and radiotherapy could not be applied in full doses in the elderly patients (Melek, Medetoğlu, Demir, Kara & Dinçer, 2011, p. 586-592). In our study, postoperative chemotherapy was administered to 24.1% of patients aged <70 years, whereas this proportion was 36.3% in the group aged ≥70 years, with the difference being statistically significant between the two groups ($p = 0.014$).

5. Conclusion

Our study showed that the demographic characteristics were significantly similar between the elderly and younger patients who were treated for non-small cell lung cancer, although there were partly statistically significant differences in terms of postoperative morbidity and surgical treatment responses. In case of advanced non-small cell lung cancer, resection can be performed, but when the decision of surgery is made, it should not be based upon only the age of the patient but the general performance status of the patient and comorbid diseases should be taken into consideration. We found that advanced age alone does not constitute a contraindication for surgical treatment. Taken together, all the treatment options that can be offered to younger patients should be considered when deciding upon the treatment choice for elderly patients.

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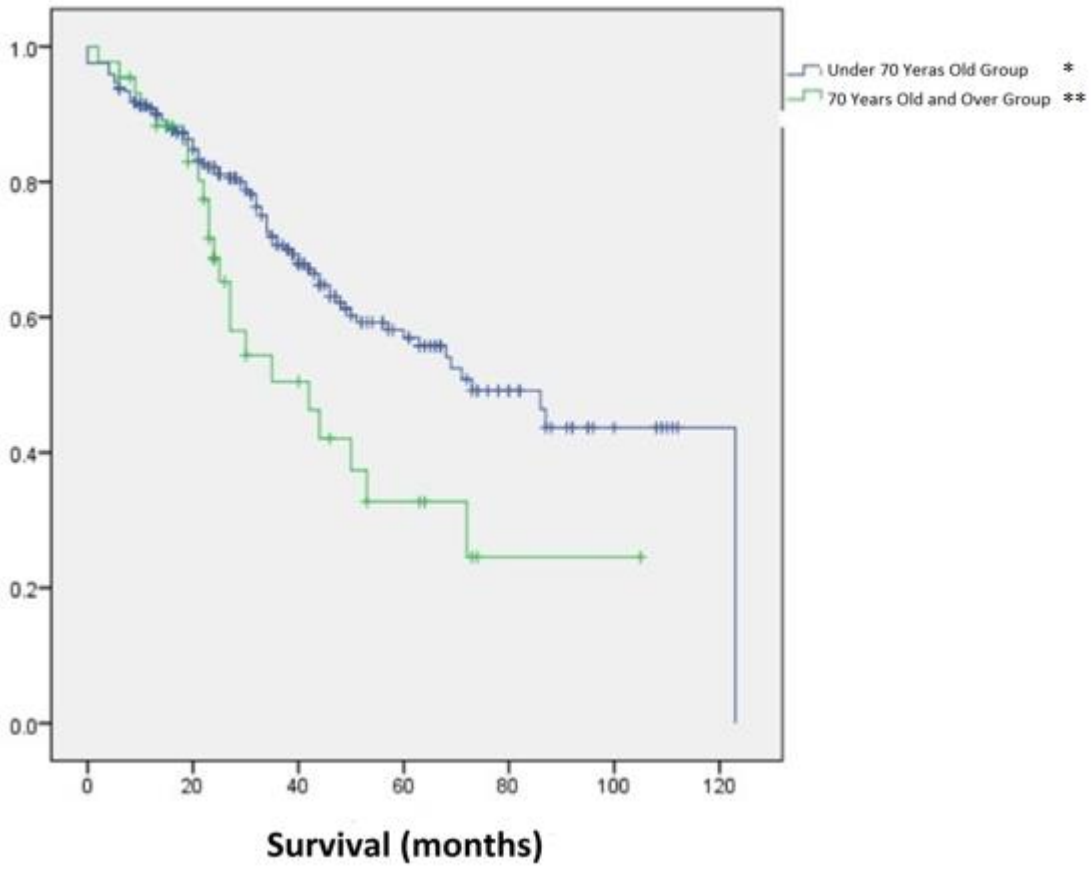

Figure 1. Survival by age group (comparison of the age group of 70 years and above and the age group of 70 years).

*The median value of the group aged <70 years was 33.00 (range: 16.25–50.00) months.

** The median value of the group aged ≥70 years was 24.00 (range: 16.50–43.50) months.

Figure 1 shows a statistically significant difference in survival between the two groups (p = 0.013).

Table 1. General Characteristics of the Study Groups

				Group 1		Group 2		
		Total(288)		Under 70 years old (n:244)*		70 years old and over (n:44)*		p**
Epidemiology		Number	Percent	Number	Percent	Number	Percent	
Average Age		60,5		58,23		73,66		
Sex								1
	Male	261	90,6	221	90,6	40	90,9	
	Famale	27	9,4	27	9,4	4	9,1	
Smoking		253	87,8	215	88,11	38	86,36	0,563
Disease History								0,083
	Absent	84	29,16	46	18,85	10	22,72	
	Respiratory system	72	25	59	24,18	13	29,54	
	Cardiovascular system	74	25,7	56	22,95	18	40,9	
Pathological Tumor Type								0,011
	Adenocarcinoma	128	44,4	110	45,08	18	40,9	
	Squamous cell carcinoma	130	45,1	108	44,26	22	50	
	Others	30	10,4	26	10,65	4	9,09	
Features Connected to Surgery								
Operation Type								0,557
	Anatomical	223	77,4	186	76,22	37	84,09	
	Wedge	32	11,1	22	9,01	3	6,81	
	Segmentectomy	8	2,77	14	5,73	1	2,27	
	Extended	21	7,3	19	7,79	2	4,55	
	İnoperabl	4	1,4	3	1,22	1	2,27	
Early Post Op Complication								0,514
	Absent	190	66	163	66,8	27	61,4	
	Respiratory system	64	22,2	53	21,7	11	25	
	Cardiovascular system	19	6,6	14	5,7	5	11,4	
	Resp+ Cardio	2	0,7	2	0,8	0	0	
	Others	13	4,5	12	4,9	1	2,3	
Late Post Op Complication								0,034
	Absent	279	96,9	239	98	40	90,9	
	Respiratory system	9	3,1	5	2	4	9,1	
Discharge Time (Day)		12,4		12,29		12,98		0,916

*n: number, ** p: significance value