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A retrospective review of patients over 70 years of age undergoing pneumonectomy for non-small cell lung cancer: 10 years of experience, a cross-sectional study

Küçük hücreli dışı akciğer kanseri nedeniyle pnömonektomi uygulanan 70 yaş üzerindeki hastaların incelemesi: 10 yıllık deneyim, kesitsel çalışma

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Ethics Committee Approval: The study was approved by the Ethic Committee of Ankara City Hospital (28/05/2020-18979). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.
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Abstract

Aim: Future projections suggest that more older people will be affected by non-small cell lung cancer (NSCLC) over the next years due to longer life expectancy and aging global population. Chronological age is used to define elderly. 70 years of age is the most commonly accepted lower limit of senescence since the majority of physiological changes occur after this age. The aim of the current study was to review demographic, epidemiological and clinical characteristics of patients over the age of 70 diagnosed with NSCLC who underwent pneumonectomy at our clinic in a retrospective manner.

Methods: This cross-sectional study involved a retrospective assessment of 21 patients over 70 years of age who were diagnosed with NSCLC and underwent pneumonectomy between January 2010 and January 2020. Demographic data, symptoms, tumor types, localization of tumors, postoperative complications and stages of cancer were recorded in the database and statistically analyzed.

Results: All 21 patients were male and had a mean age of 72.5 years. The presenting symptom was dyspnea in 23.8% of the patients, cough in 28.6%, hemoptysis in 19%, chest pain in 14.3% and weight loss in 4.8% of the patients and 9.5% of the cases were detected incidentally. The tumor types included squamous cell carcinoma (57.1%), adenocarcinoma (23.8%), adenosquamous carcinoma (14.3%) and large cell carcinoma (4.8%). Tumor site was the left lung in 81% and right lung in 19% of the patients. Early postoperative complications occurred in 5 (23.8%) patients. Three of these patients developed atrial fibrillation and two patients suffered hemorrhage. Postoperative tumor stages of the patients were stage 3a (47.6%), stage 2b (19%), stage 2a (14.3%), stage 1b (9.5%) and stage 1a2 (9.5%). Multidimensional scaling analysis showed an association between the type of tumor and smoking but no association was found between tumor type and family history (P=0.024, P=0.586, respectively).

Conclusion: It should be kept in mind that surgical resection and even pneumonectomy which is associated with high mortality and morbidity can be successfully performed in older cancer patients through a good preoperative workup, tumor staging, assessment of the risk of mortality and the effects of comorbid conditions.

Keywords: Lung cancer, Surgery, Pneumonectomy, Age

Öz

Amaç: Uzayan yaşam süresi ve yaşlanan dünya nüfusu ilerleyen yıllarda daha fazla sayıda yaşlı küçük hücreli dışı akciğer kanserli (KHDAK) hastanın ortaya çıkacağını göstermektedir. Yaşlılık tanımlaması için kronolojik yaş kullanılmaktadır. 70 yaş fizyolojik değişikliklerin giderek artmaya başladığı dönem olması nedeniyle en çok kabul gören sınır olmuştur. Çalışmamızda; kliniğimizde KHDAK tanısı nedeniyle pnömonektomi uygulanmış 70 yaş üstü hastaların demografik, epidemiyolojik ve klinik özelliklerinin geriye dönük olarak incelenmesi amaçlanmıştır.

Yöntemler: Kesitsel tipteki bu çalışmada, Ocak 2010 ile Ocak 2020 arasında KHDAK tanısı alan ve pnömonektomi yapılan 70 yaş üstü 21 hastanın retrospektif olarak değerlendirilmesi yapıldı. Demografik veriler, semptomlar, tümör tipleri, tümörlerin lokalizasyonu, postoperatif komplikasyonlar ve kanser evreleri veri tabanına kaydedildi ve istatistiksel olarak analiz edildi.

Bulgular: Çalışmamızda yer alan 21 hastanın tamamı erkek ve ortalama yaş 72,5 idi. Hastaların %23, 8'i dispne, %28,6'ı öksürük, %19'u hemoptizi, %14,3'ü göğüs ağrısı, %4,8'i kilo kaybı şikayeti ile başvururken %9,5'i insidental olarak saptanmıştır. Tümör tipi %57,1 squamöz hücreli karsinom, %23,8 adenokarsinom, %14,3 adenosquamöz karsinom ve %4,8 large cell karsinom olarak tespit edilmiştir. Tümör %81 sol, %19 sağ akciğer yerleşimliydi. Postoperatif erken dönemde olguların 5'inde (%23,8) komplikasyon görülmüştür. Erken dönem komplikasyon görülen olguların 3'ünde atrial fibrilasyon, 2'sinde kanama olduğu görüldü. Hastaların postoperatif evreleri; %47,6'ı evre 3a, %19'u evre 2b, %14,3'ü evre 2a, %9,5'i evre 1b ve %9,5'i evre 1a2 idi. Çok boyutlu ölçekleme analizinde tümör tipi ile sigara kullanımının ilişkisi saptanmış ancak aile öyküsü ile tümör tipi arasında ilişki kurulamamıştır (sırasıyla P=0.024, P=0.586).

Sonuç: Cerrahi rezeksiyon olarak morbidite ve mortalitesi yüksek olan pnömonektominin bile yaşlı hastalarda iyi bir preoperatif değerlendirme, evreleme, eşlik eden hastalıkların etkileri ve mortalite tayini ile başarılı bir şekilde uygulanabileceği bilinmelidir.

Anahtar kelimeler: Akciğer kanseri, Cerrahi, Pnömonektomi, Yaş

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Introduction

Lung cancer is the leading cause of cancer death worldwide and non-small cell lung cancer (NSCLC) accounts for more than 80% of all lung cancers [1]. Surgical treatment is the first-line treatment for early stage non-small cell lung cancer [2]. Increased life expectancy is associated with higher numbers of patients diagnosed with lung cancer and older patients [3]. Aging leads to physiological changes in cardiovascular and respiratory systems, resulting in increased rate of comorbidities, and older patients are more likely to develop life-threatening complications following surgical resection [4].

Future projections suggest that there will be more older people affected by NSCLC over the next years due to longer life expectancy and aging global population. It is not possible to determine the real biological age of a person and therefore, chronological age is used to define elderly. Different cut-offs for chronological age have been used in studies to define elderly including 65, 70 and 75 years of age. 70 years of age is the most accepted lower limit of senescence since most physiological changes occur after this age [5]. Studies on optimal treatment of NSCLC patients have mostly enrolled patients under 65 years of age [6]. Older patients with lung cancer are less likely to receive conventional cancer treatments compared to younger patients [7]. Toxicity, the presence of coexisting conditions associated with increased morbidity and mortality, difficulties in access to healthcare services and patient and physician preferences may present barriers to patients in getting maximal therapy. Age is not the sole criterion to decide whether a patient may or may not tolerate cancer treatment. Outcomes of lung cancer therapy in most elderly patients are generally comparable to those in younger patients [8,9]. Comorbid conditions, age-related physiological losses, chronic medication use, and smoking status of the patients should be considered when determining the therapeutic options. In brief, functional status and physiological capacity of the patient should be carefully evaluated in older patients with lung cancer while making treatment plans.

The aim of the current study was to review demographic, epidemiological and clinical characteristics of patients over the age of 70 diagnosed with NSCLC who underwent pneumonectomy at our clinic in a retrospective manner.

Materials and methods

The study involved a retrospective assessment of 21 patients diagnosed with NSCLC and underwent pneumonectomy between January 2010 and January 2020 at the clinics that we provided medical service. Epidemiological, demographic, clinical, laboratory, histopathological and treatment data were retrieved from the medical files of the patients and statistical analyses were performed on these data. Gender, age, presenting symptom, smoking status, family history, preoperative diagnostic method, anatomical location of the mass, lymph node involvement on preoperative PET-CT and maximum standardized uptake values (SUVmax) of the tumor, operated side and type of surgery, early postoperative complications, tumor size, results of postoperative histopathological examination and pathological staging of the patients were reviewed. Cardiology and internal medicine departments had evaluated all patients preoperatively.

Preresection pulmonary assessment included respiratory function tests, DLCO (diffusing capacity for carbon monoxide), the six-minute walk test, postoperative FEV1 measurement and cardiopulmonary exercise testing (vo2 max) for borderline values. The type of tumor, family history and smoking status were also examined using multidimensional scaling and correspondence analysis.

Statistical analysis

Recorded data were analyzed using the SPSS for Windows, version 23.0 software package. Descriptive statistics of studied numerical variables were reported using mean as a measure of central tendency and standard deviation as a measure of dispersion. Mann-Whitney U and Wilcoxon tests were used to compare study variables between groups. A *P*-value of less than 0.05 was considered statistically significant.

Results

All 21 patients were male, with a mean age of 72.5 years. The presenting symptom was dyspnea in 23.8% of the patients, cough in 28.6%, hemoptysis in 19%, chest pain in 14.3% and weight loss in 4.8% of the patients, and 9.5% of the cases were detected incidentally. Among patients, 66.7% were current smokers 4.8% never smoked and 28.6% had quit smoking. Family history was absent in 81% of the patients. Preoperative diagnosis was established with bronchoscopy in 71.4%, transthoracic biopsy in 19% and intraoperative frozen section procedure in 9.5% of the patients. When the respiratory reserve of the patients was evaluated, only one patient had a FEV1 value less than 2 L/min (1.89 L) who was subjected to further assessment by postoperative FEV1 measurement and 6-minute walk test. Upon pulmonary clearance for pneumonectomy, the patient underwent resection.

The tumor types included squamous cell carcinoma (57.1%), adenocarcinoma (23.8%), adenosquamous carcinoma (14.3%) and large cell carcinoma (4.8%). Tumor site was the left hilum in 61.9% and right hilum in 14.3% of the patients, the upper left lobe in 14.3%, the upper right lobe in 4.8% and the left lower lobe in 4.8% of the patients. The mean tumor SUVmax value was 16.15 (5.9-42.92). Among all, 57.1% of the patients underwent left pneumonectomy, 19% had mediastinoscopy and left pneumonectomy, 14.3% had right pneumonectomy, 4.8% had mediastinoscopy and right pneumonectomy and 4.8% had left pneumonectomy and thoracic wall resection.

Early postoperative complications occurred in 5 (23.8%) patients. Three of these patients developed atrial fibrillation and two patients suffered hemorrhage. Emergency treatment was initiated in patients with atrial fibrillation upon consultation with the cardiology department, with no additional arrhythmia-related complications occurring until discharge. Among patients with bleeding, the volume of hemorrhagic fluid drained within 24 hours was 800 cc in one patient and 500 cc in the other. One patient was on anticoagulant therapy due to coronary artery disease and anticoagulant therapy was not discontinued in the preoperative period. Patients did not undergo repeat thoracotomy but were kept under close drainage monitoring. These patients were discharged within 15 days.

Postoperative tumor stages of the patients were stage 3a (47.6%), stage 2b (19%), stage 2a (14,3%), stage 1b (9.5%) and stage 1a2 (9.5%).

Multidimensional scaling analysis showed an association between the type of tumor and smoking (P=0.024) but no association was found between tumor type and family history (P=0.586) (Figure 1). The correspondence analysis was used to analyze the relation between smoking and cancer cell type and showed strong associations with squamous (P=0.024) and adenosquamous carcinoma (P=0.017) among patients who were smokers or those who quit smoking but no associations with adenocarcinoma or large cell carcinoma (P=0.274) (Figure 2).

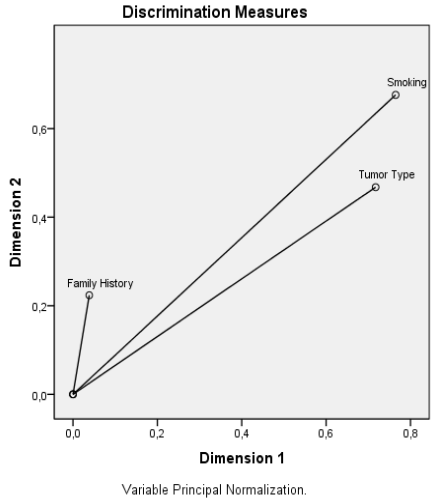

Figure 1: Association between the type of tumor, family history and smoking

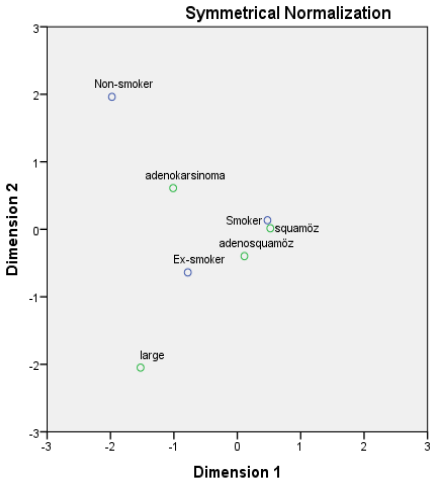

Figure 2: Association between the type of tumor and smoking

Discussion

As with patients from other age groups, surgical resection at an appropriate stage is the standard of care in patients over 70 years of age. When deciding on the suitability of a patient for surgical treatment, physical performance and comorbidities of the patient are considered rather than his/her age [10]. Consistently, the decision for surgical treatment in our patients was made based on their performance, comorbidities, and patient consent rather than their age. There is an increased likelihood of tumor resectability and an early detection of the tumor with advancing age. According to the Guideline on Preoperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgeries published by the American College of Cardiology, thoracic surgery is considered a high-risk surgery that poses cardiac risk. High-risk surgery includes major emergency surgery, particularly in the elderly; aortic and other major vascular surgery, peripheral vascular surgery, major intrathoracic surgery and anticipated prolonged procedures associated with large fluid shifts and/or blood loss. Intermediate-risk procedures include intraperitoneal, head, neck, orthopedic, urological, gynecological, and non-major thoracic surgery [11].

Following the guideline, all our patients were stratified as high-risk cases. It is known that the risk of developing lung cancer increases significantly in patients with a smoking history of more than 20 pack-years. In our study, there were 14 active smokers with a smoking history of 53 pack-years on average. The risk of lung cancer increases at least two-fold in individuals with a first-degree relative with lung cancer regardless of smoking [12]. In our study, 2 patients had a first-degree relative with lung cancer and 2 other patients had a first-degree relative with gastrointestinal malignancy.

When the chief complaints of lung cancer patients were examined, cough was found to be the primary complaint (59.3%). Other complaints included lethargy (46.4%), shortness of breath (42.5%), chest pain (35.1%) and hemoptysis (24.6%). In our study, cough was the initial symptom (28.6%), followed by shortness of breath (23.8%) and chest pain (14.3%). Symptomatology of our patients was similar to that reported in literature. The tumor location is the major determinant of the initial clinical symptom. Centrally located tumors are more likely to present with cough and hemoptysis. All of the tumors in our patients were centrally located. Bronchoscopy provides a diagnostic yield of up to 90% in central endobronchial lesions [12]. 71.4% of our patients were diagnosed with the aid of bronchoscopy. Among 4 patients diagnosed with transthoracic biopsy, the lesions could be accessed with fine needle biopsy due to the large size of the tumors (mean size of 8.6 cm) despite their central location.

In the 1980s, advanced age was considered a contraindication to thoracotomy and resection. However, more elderly patients have undergone surgery in the last 20 years due to advances in anesthesia and surgical techniques. Studies demonstrated that age alone is not a risk factor for surgical resection [13]. Two major concerns need to be considered when planning surgical treatment in older patients and these include firstly survival and secondly, postoperative morbidity and mortality [14,15]. While some studies advocated that advanced age is associated with the occurrence of postoperative complications, others did not find such an association [16,17]. On the other hand, an increased incidence of fatal complications was reported in older patients by some studies on mortality, but other studies did not support this observation [16,18,19]. In a 2011 study, Melek et al. [20] reported a morbidity rate of 32% in patients over 70 years of age and 30% in patients under 70 years of age, with no significant differences between the two groups. While both age groups developed pulmonary complications such as persistent air leak, restricted lung expansion and atelectasis, and arrhythmias in the early postoperative period, no significant difference was found between the groups in terms of comorbid conditions and postoperative morbidity. Pulmonary complications related to surgery including air leak, pneumonia,

pulmonary embolism, respiratory failure, bronchopleural fistula and bleeding following pulmonary resection have been commonly reported in literature, the most frequent complications were air leak and arrhythmia [21,22]. Among cardiac complications, rhythm disorders were reported at rates varying between 3.8% and 37% [23]. In a study from Turkey, the prevalence of cardiac complications was reported at 20% among older patients [24]. In our study, the prevalence of early postoperative complications was 23.8%, including cardiac arrhythmia in 3 (14.3%) patients and bleeding in 2 (9.5%) patients. Complications have been successfully managed with appropriate treatment strategies.

Studies have reported a resectability rate of 25% in patients over 75 years of age and 15.3% in patients under 55 years of age [25,26]. Moreover, the reported rate of surgery refusal was 30% in geriatric patients but 8% in younger patients [27]. Acceptable mortality and morbidity rates can be achieved in the geriatric patients with a good preoperative evaluation and assessment of comorbidities, as demonstrated by literature data. In a study by Aelony [28], the mortality rates were 1.2% among patients over the age of 75 undergoing early stage resection and 0.45% in younger patients. Tumor stages of our patients were stage 3a (47.6%), stage 2b (19%), stage 2a (14,3%), stage 1b (9.5%) and stage 1a2 (9.5%). Thus, stage 1 and 2 tumors were predominant in our study sample.

Limitations

The patients over 70 years of age were selected cautiously. The comorbidities they have were not considered in statistical analyses. This was the limitation of our study.

Conclusion

NSCLC is a major health problem that affects younger individuals as well as elderly population. Chronological age should not be the sole determinant when deciding on surgical treatment in older patients. It should be kept in mind that surgical resection and even pneumonectomy which is associated with high mortality and morbidity can be successfully performed in older cancer patients through a good preoperative workup, tumor staging, assessment of the risk of mortality and the effects of comorbid conditions.

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