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Original Article */ Özgün Makale*

A comparison of the intensive care unit outcomes of pneumonectomy and lobectomy patients with lung cancer

Akciğer kanseri nedeni ile pnömonektomi veya lobektomi uygulanan hastalarda yoğun bakım sonuçlarının karşılaştırılması

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ABSTRACT

Background: This study aims to compare intensive care unit (ICU) outcomes of patients with lung cancer who developed acute respiratory failure after pneumonectomy or lobectomy.

Methods: This retrospective observational cohort study included 57 lung cancer patients admitted to ICU who developed acute respiratory failure after pneumonectomy or lobectomy. Patients were divided as pneumonectomy (group 1; 19 males, 1 females; median age 65 years) and lobectomy (group 2; 36 males, 1 females; median age 62 years) groups. Pulmonary function test, invasive or noninvasive mechanical ventilation results, duration of ICU stay, and ICU mortality and long-term mortality were recorded. The groups were compared according to the recorded data.

Results: In group 1 and group 2, median preoperative forced expiratory volume in one second values were 1.58 L (predicted 61%) and 1.82 L (predicted 63%), respectively (p=0.82). Rates of patients with acute respiratory failure due to postoperative sepsis were similar in group 1 (65%) and group 2 (52.6%) (p=0.37). Group 1 and group 2 had similar median duration of ICU stay (9 and 8 days, respectively; p=0.76), ICU mortality (30.0% and 18.6%, respectively; p=0.34), and long term survival (n=6, 11 months; n=21, 5 months, respectively; p=0.79).

Conclusion: Lung cancer patients who were performed pneumonectomy or lobectomy might require ICU stay due to postoperative sepsis. Our study suggests that ICU mortality and long-term survival are not affected by the type of lung resection in these patients.

Keywords: Acute respiratory failure; intensive care unit; lobectomy; lung cancer; pneumonectomy.

ÖZ

Amaç: Bu çalışmada pnömonektomi veya lobektomi sonrası akut solunum yetmezliği gelişen akciğer kanserli hastaların yoğun bakım ünitesi (YBÜ) sonuçları karşılaştırıldı.

Çalışma planı: Bu geriye dönük gözlemsel kohort çalışmaya pnömonektomi veya lobektomi sonrası akut solunum yetmezliği gelişip YBÜ'ye kabul edilen 57 akciğer kanseri hastası dahil edildi. Hastalar pnömonektomi (grup 1; 19 erkek, 1 kadın; ortanca yaş 65 yıl) ve lobektomi (grup 2; 36 erkek, 1 kadın; ortanca yaş 62 yıl) gruplarına ayrıldı. Solunum fonksiyon testi, invaziv veya noninvaziv mekanik ventilasyon sonuçları, YBÜ'de kalış süresi, YBÜ mortalitesi ve uzun dönem mortalite kaydedildi. Gruplar kaydedilen verilere göre karşılaştırıldı.

Bulgular: Grup 1 ve grup 2'de ameliyat öncesi ortanca birinci saniye zorlu ekspirasyon volümü değerleri sırasıyla 1.58 L (beklenen %61) ve 1.82 L (beklenen %63) idi (p=0.82). Ameliyat sonrası sepsise bağlı akut solunum yetmezliği olan hasta oranı grup 1 (%65) ve grup 2'de (%52.6) benzer idi (p=0.37). Grup 1 ve grup 2'nin ortanca YBÜ kalış süresi (sırasıyla 9 ve 8 gün, p=0.76), YBÜ mortalitesi (sırasıyla %30.0 ve %18.6, p=0.34) ve uzun dönem sağkalımları benzerdi (sırasıyla n=6, 11 ay; n=21, 5 ay, p=0.79).

Sonuç: Pnömonektomi veya lobektomi uygulanan akciğer kanseri hastalarının ameliyat sonrası sepsis nedeniyle YBÜ'de kalması gerekebilir. Çalışmamız bu hastalarda YBÜ mortalitesinin ve uzun dönem sağkalımın akciğer rezeksiyonu türünden etkilenmediğine işaret etmektedir.

Anahtar sözcükler: Akut solunum yetmezliği; yoğun bakım ünitesi; lobektomi; akciğer kanseri; pnömonektomi.

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It is well known that non-small cell lung cancer (NSCLC) patients who had postoperative respiratory failure that required mechanical ventilation are associated with limited pulmonary functions and cardiovascular comorbidity.[1-4] In addition, the type of surgical procedure, especially an extensive lung resection (pneumonectomy), contributes independently to postoperative respiratory morbidity. Besides the extensive surgical procedure, the extension of the cancer affects the patient's outcome.[4] After both pneumonectomies and lobectomies, some patients required prolonged postoperative intubation because of an inability to spontaneously breathe in the early postoperative period or in the recovery room, which resulted in them being referred to the intensive care unit (ICU).[5]

To best of our knowledge, there has been no definitive study in the English literature that has evaluated the outcomes of pneumonectomies or lobectomies in the ICU, and only limited data exists concerning those patients' pulmonary functions, length of ICU stays, and long-term outcomes. In this study, we compared the ICU data and outcomes for acute respiratory failure (ARF) patients who underwent pneumonectomies and lobectomies along with their long-term survival rates.

PATIENTS AND METHODS

This retrospective observational cohort study was conducted between January 2008 and December 2011 in a tertiary chest and thoracic surgery education and research hospital. The intensive care management of the patients was done by the same pulmonary intensivists in a 22-bed level III respiratory ICU. The study was approved by the local ethics committee.

Fifty-seven consecutive lung cancer patients (55 males and 2 females) who had resections via either a pneumonectomy or lobectomy and who had been admitted to the ICU with ARF were included in this study. Group 1 consisted of patients who had a pneumonectomy while group 2 was composed of those who had a lobectomy. Additionally, the study was open only to patients with a histopathological diagnosis of NSCLC.

The preoperative evaluation included obtaining the patients' medical history, giving a physical examination, and performing routine blood tests, electrocardiography (ECG), a pulmonary function test (PFT), and a perfusion lung scan. In addition, spirometry (Zan GPI 3.00, nSpire Health, Longmont, Colorado, USA) was performed according to the European Respiratory Society (ERS) guidelines[6] to obtain the forced expiratory volume in one second (FEV_1), percentage of the predicted FEV_1 (%), forced vital capacity (FVC), percentage of predicted FVC (%), and FEV_1/FVC ratio. If the FEV_1 was more than 80% of the predicted norm or more than two liters, the patient was considered to be suitable for a pneumonectomy without any further evaluation,[7] and if the FEV_1 was more than 1.5 liters, the patient was considered suitable for a lobectomy without any further evaluation. Those patients with FEV_1 values of less than 80% of the predicted norm underwent additional tests such as a ventilation-perfusion scan with technetium-99m, after which calculations were made to understand the postoperative lung reserve of the patients. The predicted postoperative FEV_1 (ppoFEV_1) for the pneumonectomy candidates was calculated using the following formula: preoperative FEV_1 x rate of perfusion of remaining lung/perfusion of total ipsilateral lung. Furthermore, a quantitative radionuclide perfusion scan was performed to measure the relative function of each lung. The ppoFEV_1 for the lobectomy was calculated with a similar to the perfusion scan using the number of segments removed via the following formula: the preoperative FEV_1 x the number of segments which is remaining/the number of total segments.

The patients who underwent a lung resection were followed up in the recovery room for a period ranging from a few hours to 24 hours by an anesthesiologist after surgery. Those who were spontaneously breathing were either extubated in the operating room or in the recovery room after a few hours had passed. The stable patients were admitted to the surgical ward after being extubated in the recovery room. The patients who needed respiratory support via mechanical ventilation or who were clinically unstable (hemodynamically unstable, hypotensive, or hypoxemic [partial arterial oxygen pressure over fractionated inspired oxygen (PaO_2/FiO_2) of <200] or those with a systolic pressure <90 mmHg were admitted to the respiratory ICU. The ICU patients were cared for with both invasive and noninvasive mechanical ventilation (IMV and NIMV). The NIMV was applied when it was not contraindicated,[8] whereas the IMV was applied when the NIMV was not suitable or when it was contraindicated.[8]

The pressure assist-control mode was initially chosen for the IMV, and the inspiratory positive airway pressure (IPAP) was set to have a tidal volume of 250-300 mL for the pneumonectomies and 300-350 mL for the lobectomies. We also paid special attention to make sure that the plateau pressure was less than 35 cm H_2O and that the positive end-expiratory pressure (PEEP) was cautiously applied with less than 5 cm H_2O. In addition, the respiratory rate was set at 12-20 breaths/minute. All of the patients were weaned using our normal ICU protocol, which we adapted from the ERS protocol.[9] The patients' IPAP settings were then slowly raised from 5 cm H_2O to 25 cm H_2O using the ventilators in the NIMV mode. Furthermore, the sedation and agitation levels of the patients were determined according to the Richmond Agitation-Sedation Scale (RASS).[10]

All of the patients' data was recorded retrospectively from an electronic database and written medical records, and information regarding age, gender, body mass index (BMI), comorbid diseases such as chronic obstructive pulmonary diseases (COPD)[11] diabetes mellitus (DM), arrhythmia [atrial fibrillation (AF) and supraventricular tachycardia), hypertension (HT), type of surgery (pneumonectomy or lobectomy), and the preoperative PFT results of both groups was obtained. Those patients who were 70 years old or older were deemed to be elderly.[12] Moreover, the C-reactive protein (CRP) levels, leukocyte counts, serum albumin levels, and blood biochemistry results (blood glucose and creatinine) were recorded when the patients were admitted to the hospital for the surgery and when they were admitted to the ICU. The IMV/NIMV demand and duration and arterial blood gas (ABG) values were also recorded. In addition, the ICU severity score was evaluated using the Acute Physiology and Chronic Health Evaluation II (APACHE II) after admission to the ICU.[13] Postoperative respiratory failure and ICU demand were defined as having hypoxemia (paO_2/FiO_2 <300) as well as either sepsis, severe sepsis, or septic shock.[14]

Statistical analysis

The two groups were compared using the Mann-Whitney U test for nonparametric continuous variables, Student's t-test for parametric continuous variables, and a chi-square test for dichotomous variables. The median and interquartile range (IQR) were used to describe the nonparametric continuous variables, and mean ± standard deviation (SD) was used for the parametric continuous variables. Furthermore, numerical values and percentages were used when applicable, and the Kaplan-Meier survival analysis was used to determine long-term survival. A *p* value of <0.05 was considered to be statistically significant.

RESULTS

The patient demographics along with their pre- and postoperative surgical and ICU outcomes are summarized in Table 1. The groups were similar with respect to age, BMI, gender distribution, and comorbid diseases. The preoperative PFT results were also similar, except for FEV_1/FVC. The majority of the patients had American Society of Anesthesia (ASA) scores ranging from 2-3, and approximately 80% of the patients in each group were successfully extubated within six hours postoperatively. The revision surgery rate was nearly four times higher in group 1, but this did not reach statistical significance. Sepsis was the major reason for respiratory failure and ICU demand in groups 1 and 2 (65% and 54%, respectively) and about 90% of the patients with ARF were intubated before being admitted to the respiratory ICU (Table 1).

Groups 1 and 2 had similar basic blood chemistry results (Table 2), but the serum albumin levels were significantly lower in group 1 (p=0.034). Moreover, the ABG analysis upon admission to the respiratory ICU were similar in both groups (Table 2). We also determined that approximately 90% of the patients in the two groups were initially ventilated with IMV but that after extubation, half of the patients underwent NIMV (Table 2). Furthermore, the patients in group 2 (41.4%) needed a higher rate of IMV (more than 14 days) than those in group 1 (22.2%) (Table 2). Although not statistically significant, the number of patients who required a blood transfusion during their stay in the ICU was four times higher in group 2 than in group 1 (21% vs. 5%, respectively). Furthermore, the length of time spent in the respiratory ICU was similar in both groups as was the mortality and long-term survival rate in months (Table 2).

Figure 1 shows the similar long-term survival rates of groups 1 and 2 (p=0.79). Twenty-seven patients were discharged from the respiratory ICU; the patients with pneumonectomies (n=6) median survival was 11 months (IQR, 3-25) and the patients with lobectomies (n=21) median survey was five months (IQR, 1-17). However, this difference was not statistically significant (Figure 1).

DISCUSSION

This study demonstrated that ICU outcomes and the long-term survival rates of patients who undergo either a pneumonectomy or lobectomy due to lung cancer did not differ significantly. However, we determined that the patients who were followed up in the ICU because of respiratory failure after a lung resection showed signs of pulmonary infections, higher inflammatory markers, and lower preoperative PFT results.

Two past studies with very large sample sizes found mortality rates of between 1.2 and

Table 1. Patient demographics and pre- and postoperative surgical intensive care unit outcomes of groups 1 and 2

Variables	Group 1 (n=20)				Group 2 (n=37)				
	n	%	Median	Range	n	%	Median	Range	*p*
Age			65	61-71			62	59-68	0.38
Gender									
Female	1				1				0.65
Male	19				36				
Body mass index			25	23-27			24	21-25	0.39
Comorbidity factors									
Chronic obstructive pulmonary diseases	9	45			16	43.2			0.90
Diabetes mellitus	1	5			5	10.8			0.46
Hypertension	3	15			14	37.8			0.07
Cardiac arrhythmia	6	30			13	35.1			0.70
Preoperative pulmonary function tests									
FEV_1 (L)			1.58	1.38-1.90			1.82	1.54-2.27	0.26
FEV_1 (predicted %)			61	53-81			63	51-71	0.82
FVC (L)			2.26	1.87-2.78			2.31	1.81-2.85	0.73
FVC (predicted %)			63	51-79			61	55-74	0.87
FEV_1/FVC			74	67-79			87	71-90	0.009
Pre- and postoperative evaluations									
ASA 1	1	5			6	16.2			0.45
ASA 2	10	50			15	40.6			
ASA 3	9	45			16	43.2			
Postoperative extubation									
Postoperative early (<6 hours) extubation	15	75			30	81.1			0.73
Postoperative extubation failure	5	25			8	14.0			
Extubation day; median (IQR)			1	1-1			1	1-2	0.27
Operation for revision	4	20		2	5.4				0.08
Postoperative ICU day; median (IQR)			6	4-7			4	2-5	0.050
Postoperative IMV day; median (IQR)			2	0-4			2	1-6	0.29
Postoperative re-intubation reasons									
Respiratory failure	7	35			18	48.6			0.37
Sepsis	13	65			20	54.1			
Admission to respiratory ICU									
Intubation	18	90			30	81.1			0.39
NIMV	2	10			5	13.5			
High-flow oxygen	0	0			3	8.1			

FEV_1: Forced expiratory volume in one second; FVC: Forced volume capacity; ASA: American Society of Anesthesia; IQR: Interquartile range; ICU: Intensive care unit; IMV: Invasive mechanical ventilation, NIMV: Non-invasive mechanical ventilation.

4.2% for lobectomies and 3.2 and 11.6% for pneumonectomies.[15,16] In this study, although the overall lung resection mortality rate in our hospital was not included in the data, the mortality rates for lobectomies and pneumonectomies in the ICU were 18.9% and 30.0%, respectively. We previously found that postoperative respiratory failure was affected independently by the type of surgery and that the demand for mechanical ventilation was correlated with advanced disease and lower PFT scores.[17]

Several studies have shown that the postoperative complications associated with these procedures are primarily cardiac in nature and include myocardial infarction (MI), stroke, and severe arrhythmias.[18-20] In this study, we determined that a third of the patients had arrhythmias, despite having similar heart rates and HT, and that the arrhythmia rates were higher in group 2 than in group 1 (35% vs. 15%). This might be explained by the fact that the long-term survival of the majority of patients in group 2 (11 months) was twice as high as those in group 1 (5 months).

Perioperatively, age and comorbid diseases were important factors related to the morbidity and mortality of our patients with lung cancer. Recently

Table 2. Respiratory intensive care unit outcomes of groups 1 and 2

Variables	Group 1 (n=20)				Group 2 (n=37)				
	n	%	Median	Range	n	%	Median	Range	*p*
APACHE II score upon admission to the ICU			20	16-25			22	17-28	0.82
Biochemistry results in the ICU									
Blood glucose (mg/dL)			140	113-179			123	108-139	0.11
Serum albumin (mg/dL)			2.5	2.1-2.8			2.1	1.7-2.4	0.034
Serum creatinine			0.8	0.6-1.1			0.9	0.7-1.0	0.81
Leucocyte count (x10^3/mL)			13.9	11.2-18.2			13.4	10.0-15.9	0.50
C-reactive protein (mg/dL)			149	83-203			192	116-237	0.22
Arterial blood gas results upon admission to the ICU									
pH			7.44	7.39-7.50			7.44	7.37-7.50	0.58
$PaCO_2$ (mmHg)			46	7-5			41	37-55	0.81
PaO_2/FiO_2			127	74-231			133	93-180	0.82
Mechanical ventilation									
Noninvasive ventilation	9	45.0			13	35.1			0.47
Noninvasive ventilation (days)			3	2-5			3	2-6	0.70
Invasive ventilation	18	90			30	81.1			0.38
Invasive ventilation (median IQR in days)			5	3-10			7	3-17	0.26
Invasive ventilation longer than 14 days	4	22.2			12	41.4			0.18
Sepsis	13	65			20	54.1			0.42
Septic shock	10	50			13	35.1			0.28
Blood transfusion	1	5			8	21.6			0.10
Patients with thoracic tube	6	30			18	48.6			0.17
Length of ICU stay in (days)			9	6-13			8	5-22	0.76
Mortality	6	30.0			7	18.9			0.34
Median survival (months)			11	3-25			5	1-17	0.51

APACHE II: Acute Physiology and Chronic Health Evaluation; ICU: Intensive care unit; $PaCO_2$: Partial pressure of arterial carbondioxide; PaO_2/FiO_2: Partial pressure of arterial oxygen over fractionated pressure of inspired oxygen; IQR: Interquartile range.

Takamochi et al.[12] compared 409 elderly lung cancer patients (≥70 years) and 664 younger patients (<70 years) with regard to morbidity and mortality and found that the mortality and morbidity rates were higher for the elder patients.[12] In addition, Sekine et al.[21] determined that for postoperative patients diagnosed with NSCLC who underwent thoracic surgical procedures, pulmonary complications occurred more frequently in COPD patients than in non-COPD patients and that the major cause of non-cancer-related deaths in their COPD patient group was respiratory failure. In our study, approximately 50% of the patients in both groups had COPD.

Karakurt et al.[22] found that patients who undergo extended surgical procedures require prolonged mechanical ventilation, and they believed that this might have been the reason for the profound alterations in diaphragm functions and respiratory mechanics in their patients. They also determined that their patients who experienced weaning failure had higher blood glucose levels, lower PaO_2/FiO_2, and increased mortality. We did not measure diaphragm functions in our study, but the number of patients who had a prolonged weaning period of longer than 14 days was higher in group 2 (41%) than in group 1 (22%). After lung resection, the rate of ICU demand due to acute respiratory distress is 2.5% for lobectomies and 3.9% for pneumonectomies,[23,24] and Dulu et al.[23] indicated that earlier ICU admission may lead to favorable patient outcomes for those who undergo these procedures. In our study, the majority of patients had hypoxemia along with elevated inflammatory and infectious markers, and half were diagnosed with septic shock. The mortality rate was higher in those patients who had septic shock. In contrast, Dulu et al.[23] reported that ICU mortality occurred in the

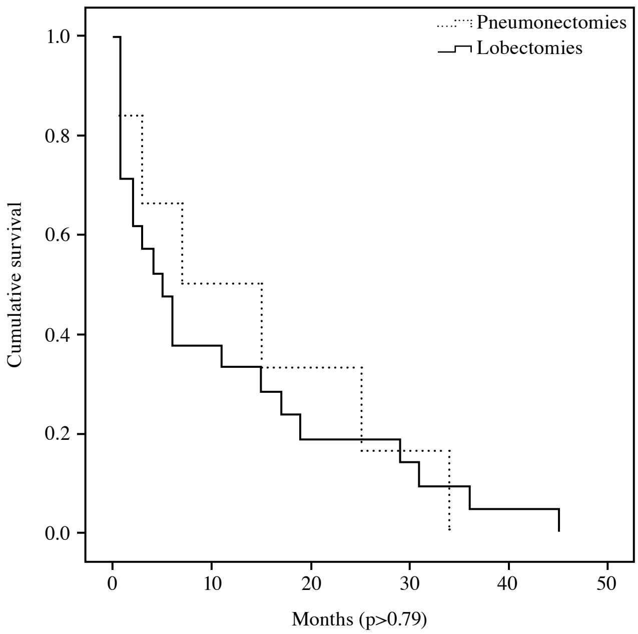

Figure 1. Comparison of the long-term survival after ICU discharge of the pneumonectomy (group 1) and lobectomy (group 2) patients.

majority of their patients who were admitted early to the ICU.

The main limitation of our study was that it was a retrospective, single-center cohort. In addition, because of the specific patient population, our results may not apply to all lung resection patients. Therefore, further randomized controlled studies must be conducted with a larger patient population. Furthermore, the inflammatory markers in this study were recorded upon admission to the ICU, and even though the majority of the patients in both groups were admitted to the ICU a couple of days after the surgery, we accepted that these values were still remarkable. Moreover, we did not record the pathogen of the sepsis/severe sepsis; however, the presence of sepsis and the mortality rates were statistically similar in both groups of patients in the ICU. Hence, a further detailed clarification of the pathogens may not have aided our results. Finally, the overall mortality rate in our hospital for lobectomies and pneumonectomies was not taken into account because our aim was to evaluate the ICU outcomes of the patients who had ARF.

The strength of our study was that all the patients in the ICU are followed around the clock during their hospital stays by pulmonary intensivists who were very familiar with the management of pulmonary complications, ventilator settings, and weaning procedures.

Conclusion

In a very specific patient population made up of lung cancer patients with borderline lung functions, presence of infection seems to be the most important reason for intensive care demand. Our findings showed that patients who underwent lung cancer resection via either lobectomies or pneumonectomies and had been admitted to the ICU because of ARF have similar ICU and long-term survival outcomes.

Declaration of conflicting interests

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