

Surgical outcomes of lung cancer patients with dementia

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Abstract

Dementia is a common medical disorder and many surgical procedures carry a higher risk of complications in dementia patients. The aim of this retrospective study is to evaluate the operative results and prognosis of lung cancer patients with dementia. In this study, 9 consecutive patients with dementia who were diagnosed with lung cancer and underwent an anatomic lung resection between January 2016 and January 2021 were assessed retrospectively. The data included age, gender, duration of treatment for dementia, comorbid diseases, body mass index, symptoms, smoking status, respiratory function test results, localization of the tumor, methods used for preoperative tissue diagnosis, histopathological cell type, American Society of Anesthesiologists physical status classification scores, type of surgical resection, pathological stage, postoperative complications, postoperative tracheostomy, postoperative intensive care, length of the clinic and overall hospital stay, mortality rate, total cost, and length of patient follow-up. All patients in this study had several serious comorbid diseases and high body mass index. Delirium and cognitive function impairment were found in 2/3 of the patients in the postoperative period. All patients developed postoperative respiration-associated complications and extended periods of hospital stay. The mean total hospital cost of the patients was 2.5 times the normal. Finally, the mortality rate was 45%. The lung cancer surgery on dementia patients should be carefully considered because of poor surgical outcomes including increased severe and multiple postoperative complications such as pulmonary complications and delirium, long hospitalization time, and high mortality rates.

Keywords: lung cancer, dementia, surgery, delirium, mortality

1. Introduction

Defined as the progressive deterioration of cognitive functions or brain functions in general, dementia is a major public health concern. Affected patients experience cognitive dysfunction in multiple domains, behavior disturbances, psychiatric manifestations, memory, executive function, and attention loss, and as a result of these they suffer serious social inadaptability, dependence on others, and even confinement to bed (1). The common causes of dementia include neurodegenerative and vascular disorders and the group most at risk is the elderly. Due to the increase in average lifetime across the world, there has been an apparent increase in the number of patients diagnosed with dementia in the last few decades (1-3).

Lung cancer is the most common cause of cancer-related deaths worldwide and only 15-25% of these cases are operable at the time of diagnosis. Among the known treatment modalities of lung cancer, the most effective method is surgery and all patients should be assessed thoroughly for their chances of surgery (4). Since modern diagnostic devices such as computerized tomography and positron emission tomography

have become widespread and therefore access to them has become easier recently, the number of lung cancer cases that are diagnosed at an early stage has increased in our country.

Many major surgical procedures are known to cause cognitive disorders and to carry a higher risk of complications, particularly in older dementia patients (3). There are many factors that may provoke dementia during and after the operation such as hypoxia, hypo/hypercapnia, hypovolemia, and hypotension-perfusion disorder as well as surgical trauma, extended surgical time, and anesthetic agents used. Although inflammatory cascade and immune response are often blamed, molecular mechanisms underlying this condition are unknown for the most part. The above-mentioned factors are thought to trigger the neuropathogenesis of dementia, leading to serious cognitive disorders and delirium in the postoperative period (2, 5). In this situation and since most of the patients with dementia are elderly people with complicated medical comorbidities, surgical procedures in these patients involve increased morbidity and mortality (6, 7). There is a need, therefore, for comprehensive studies to better understand the potential

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relationship between surgery and dementia and to find solutions to preventable problems.

The aim of this retrospective study is to evaluate the surgical outcomes of anatomical lung resection surgery in

patients diagnosed with lung cancer patients with dementia. We hypothesized dementia to be independently associated with increased mortality, postoperative complications, length of stay (LOS), and hospitalization costs. The visual abstract of the study is presented in Fig. 1.

SURGICAL OUTCOMES OF LUNG CANCER PATIENTS WITH DEMENTIA

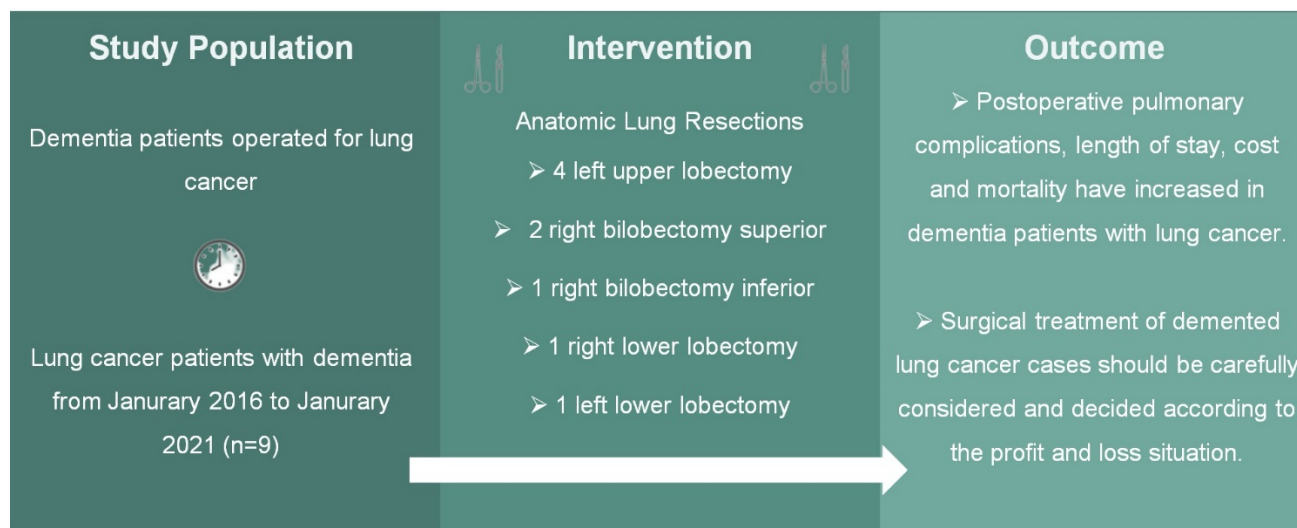


Fig. 1. Visual abstract of the study

2. Materials and methods

2.1. Patients and the study protocol

In this study, 9 consecutive Caucasian patients with dementia who were diagnosed with lung cancer and underwent an anatomic lung resection at our department between January 2016 and January 2021 were assessed retrospectively. Patients diagnosed with dementia by the neurology department and operated on for lung cancer were included in the study. Those who had a history of any psychiatric disease alongside dementia were excluded from the study.

The data evaluated included age, gender, duration of treatment for dementia, comorbid diseases, body mass index (BMI), symptoms, smoking status, respiratory function test results, localization of the tumour, methods used for preoperative tissue diagnosis, histopathological cell type, American Society of Anesthesiologists (ASA) physical status classification scores, type of surgical resection, pathological stage, postoperative complications, postoperative tracheostomy, postoperative intensive care, length of the clinic and overall hospital stay, mortality rate, total cost, and length of patient follow-up.

2.2. Statistical Analysis

The data obtained were analyzed statistically using the SPSS software. In descriptive analyses, the continuous variables were given as median (IQR: 25-75%) and categorical variables as percentages and counts.

2.3. Ethics Approval/Informed consent

This study was conducted ethically in accordance with the World Medical Association Declaration of Helsinki as revised in 1964. For studies with human subjects include the following: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2013.

Written informed consent was obtained from the patient or the next of kin for publication.

2.4. Limitations of the Research

The research has several limitations. First of all, since the study was retrospective, data were obtained from discharge summaries and medical records. Secondly, the sample size in the study is small. This may be due to difficulties in diagnosis of this type of patient group due to their existing psychosocial conditions. Third, the study period covers a long period of time.

3. Results

Out of 515 patients who were diagnosed with lung cancer and underwent an anatomic lung resection between January 2016 and January 2021, 9 (1.7%) patients who were also diagnosed with dementia were included in this study. Of these patients, 6 (66.6%) were male and 3 (33.3%) female with ages ranging between 63 and 88 years (median: 73, IQR: 66-75.5).

The time passed since the patients had been diagnosed with dementia ranged from 2 to 10 years (median: 5, IQR: 3.5-6.5).

The comorbid diseases of the patients had were hypertension in 8 (88.8%), coronary artery disease in 3 (33.3%), diabetes mellitus in 3 (33.3%), cerebrovascular event in 2 (22.2%), chronic obstructive pulmonary disease in 2 (22.2%), bronchial asthma in 1 (11.1%), bladder carcinoma in 1 (11.1%), and hepatitis-C in 1 (11.1%). The patients' BMI ranged between 26 and 43 (median: 30, IQR: 29-33.5). The symptoms found at the time of admittance were coughing in 5 (55.5%), pain in the chest in 2 (22.2%), and haemoptysis in 2 (22.2%). None of the patients were active smokers but 5 (55.5%) had a history of smoking cessation. A respiratory function test was performed in 7 (77.7%) patients. The FEV1 values were between 67% and 99% (median: 86, IQR: 68-97).

All patients had thoracic computerized tomography and positron emission tomography (PET) scans; the tumours were localized at the left upper lobe in 4 (44.4%), at the right upper-middle lobe in 2 (22.2%), at the right middle-lower lobe in 1 (11.1%), at the right lower lobe in 1 (11.1%), and at the left lower lobe in 1 (11.1%). For preoperative tissue diagnosis, a transthoracic fine needle aspiration biopsy was performed in 8 (88.8%) patients and flexible bronchoscopy in 4 (44.4%). Histopathological examination of the tissue samples revealed that 5 (55.5%) patients had squamous-cell carcinoma and 4 (44.4%) adenocarcinoma. The ASA score of the patients was median 2 (IQR: 2-3).

The surgical resections included left upper lobectomy in 4

(44.4%), right bilobectomy superior in 2 (22.2%), right bilobectomy inferior in 1 (11.1%), right lower lobectomy in 1 (11.1%), and left lower lobectomy in 1 (11.1%). In these operations, posterolateral thoracotomy was used in 5 (55.5%) patients and video-assisted thoracoscopic surgery (VATS) in 4 (44.4%). Additionally, mediastinal lymph node dissection was performed in all patients.

The pathological stages were T2aN0M0 (Stage IB) in 4 (44.4%), T3N0M0 (Stage IIB) in 3 (33.3%), T1bN1M0 (Stage IIB) in 1 (11.1%) and T4N0M0 (Stage IIIA) in 1 (11.1%). The postoperative complications included pneumonia in 8 (88.8%), atelectasia in 7 (77.7%), delirium and impaired cognitive functions in 6 (66.6%), pleural effusion in 3 (33.3%), prolonged air leakage in 1 (11.1%), haemothorax in 1 (11.1%), surgical site infection in 1 (11.1%) and atrial fibrillation in 1 (11.1%). Postoperative tracheostomy was performed in 4 (44.4%) patients. The lengths of stay in the intensive care, clinic and the total hospital stay were 6-23 days (median: 15, IQR: 7.5-17), 4-17 days (median: 5, IQR: 5-7.5), and 11-40 days (median: 21, IQR: 12.5-24), respectively. The cost per patient was median \$4300 (IQR: 3850-4600). Mortality occurred in 4 (44.4%) patients, 3 males and 1 female. The follow-up periods of the living patients ranged between 8 and 45 months (median: 21, IQR: 9.5-38.5). All of the above-mentioned results of the patients are shown in Table 1 and Table 2.

Table 1. The demographics, clinical characteristics and surgical results of the patients

Patient No	Gender	Age	Signs and Symptoms	Smoking	BMI	Follow-up Period with Dementia Diagnosis	Spirometry	Preoperative Diagnosis	Comorbidity	ASA Classification	Pathological Type
1	M	88	Cough	-	29	10	-	TTNA	HT, Bladder Carcinoma	ASA 2	SCC
2	M	75	Pain in the chest	55 Pack/Year	32	7	FEV1:77	-	DM, CVA, Hepatitis-C	ASA 2	SCC
3	M	73	Hemoptysis	30 Pack/Year	35	4	FEV1:97	TTNA	HT, CVA	ASA 2	SCC
4	M	64	Cough	30 Pack/Year	30	3	FEV1:68	TTNA	HT, COPD	ASA 3	Adeno Ca
5	F	76	Cough	-	43	6	FEV1:99	TTNA	HT, CAD, DM, Bronchial Asthma	ASA 3	Adeno Ca
6	M	75	Hemoptysis	32 Pack/Year	26	5	FEV1:86	TTNA	HT, COPD	ASA 2	SCC
7	M	63	Cough	28 Pack/Year	29	2	FEV1:94	TTNA	HT, CAD	ASA 2	Adeno Ca
8	M	70	Pain in the chest	-	29	4	FEV1:67	TTNA	HT, DM	ASA 3	SCC
9	F	68	Cough	-	30	6	-	TTNA	HT, CAD	ASA 2	Adeno Ca

Adeno Ca: Adenocarcinoma, AF: Atrial Fibrillation, ASA: American Society of Anesthesiologists Physical Status Classification Scores, BMI: Body Mass Index, CAD: Coronary Artery Disease, COPD: Chronic obstructive pulmonary disease, CVA: Cerebrovascular accident, DM: Diabetes Mellitus, F: Female, FEV1: Forced expiratory volume in 1 second, FOB: Flexible Bronchoscopy, HT: Hypertension, M: Male, PAL: Prolonged Air Leakage, SCC: Squamous cell carcinoma, TTNA: Transthoracic needle aspiration

Table 2. The demographics, clinical characteristics and surgical results of the patients

Patient No	Pathological Stage	Place of Involvement	Resection Type	Postoperative Complications	Postoperative Tracheostomy Opening	Postoperative Intensive Care Hospitalization Day	Postoperative Service Hospitalization Day	Postoperative Hospitalization Day	Mortality	Follow-up day	Cost (Dollar\$)
1	T3N0M0 Stage 2B	Right lower lobe	Right lower lobectomy	Hemothorax, PAL	-	6	5	11	-	21	3800
2	T1N0M0 Stage 1A	Left upper lobe	Left upper lobectomy	Pneumonia, Atelectasis, Delirium and Cognitive Dysfunction	+	23	17	40	+		5100
3	T2N0M0 Stage 1B	Right upper and middle lobe	Right bilobectomy superior	Pneumonia, Atelectasis, Pleural Effusion	-	7	4	11	-	8	3700
4	T2N0M0 Stage 1B	Left upper lobe	Left upper lobectomy	Pneumonia, Atelectasis, AF, Delirium and Cognitive Dysfunction	-	12	5	17	+		4300
5	T4N0M0 Stage 3A	Right middle and lower lobe	Right bilobectomy inferior	Pneumonia, Atelectasis, Delirium and Cognitive Dysfunction	+	16	5	21	+		4800
6	T3N0M0 Stage 2B	Left upper lobe	Left upper lobectomy	Pneumonia, Atelectasis, Pleural Effusion, Delirium and Cognitive Dysfunction	+	16	5	21	-	11	4400
7	T2N0M0 Stage 1B	Right upper and middle lobe	Right bilobectomy superior	Pneumonia, Pleural Effusion, Wound Infection	-	18	8	26	-	32	4300
8	T3N0M0 Stage 2B	Left upper lobe	Left upper lobectomy	Pneumonia, Atelectasis, Delirium and Cognitive Dysfunction	+	15	7	22	+		4400
9	T2N0M0 Stage 1B	Left lower lobe	Left lower lobectomy	Pneumonia, Atelectasis, Delirium and Cognitive Dysfunction	-	8	6	14	-	45	3900

Adeno Ca: Adenocarcinoma, AF: Atrial Fibrillation, ASA: American Society of Anesthesiologists Physical Status Classification Scores, BMI: Body Mass Index, CAD: Coronary Artery Disease, COPD: Chronic obstructive pulmonary disease, CVA: Cerebrovascular accident, DM: Diabetes Mellitus, F: Female, FEV1: Forced expiratory volume in 1 second, FOB: Flexible Bronchoscopy, HT: Hypertension, M: Male, PAL: Prolonged Air Leakage, SCC: Squamous cell carcinoma, TTNA: Transthoracic needle aspiration

4. Discussion

This study underlines six points: a) All patients had a number of serious comorbid diseases, particularly hypertension, coronary artery disease, and diabetes mellitus, and almost half of them had a high BMI. b) Delirium and cognitive function impairment were found in 2/3 of the patients in the postoperative period. c) All patients developed postoperative respiration-associated complications and close to half of them were subjected to tracheostomy. d) The patients had extended periods of intensive care, clinic, and overall hospital stays. e) The mean total hospital cost of the patients was 2.5 times the normal. f) The postoperative mortality rate was 45%.

Considering the developments in facilities today, this study showed that the postoperative outcomes obtained in patients with dementia who had thoracic surgery due to lung cancer were not satisfactory despite the improvements in preoperative

assessments, surgical techniques and practices, and postoperative care. Unlike other surgical risk factors, dementia is an independent and important risk factor that is associated with increased morbidity and mortality (6, 8). We observed that the major reason for this was the orientation and cooperation problems experienced by the patients due to postoperative delirium and impaired cognitive functions. These patients suffered fluctuations in mental status, attention problems, disorganized thinking, and changes in consciousness at varying degrees. As they developed a condition, which can be defined as complete introversion; it became very difficult for both their relatives and the healthcare staff to establish sound communication with them. During that period, the patients did not talk even to their companions, did not do what they were told, did not tell the medical staff about their complaints, and sometimes they even refused to drink water or

eat their food. There are publications in the literature stating that one of the major risk factors in developing postoperative delirium in the elderly is dementia (5-10). Some elective surgical procedures may trigger delirium for a longer duration, causing adverse postoperative outcomes including increased complications, length of stay, readmission rate, and overall long-term mortality in dementia patients who experience loss of cognitive functions (5, 7, 11-14).

Severe postoperative pain is common in both open and closed chest surgery. This pain causes patients to reduce their maximal voluntary ventilation, suppress coughing, and fail to use effective respiratory physiotherapy. Generally, the rate of developing pulmonary complications after chest surgery is 10-15%. Such complications increase morbidity and mortality to a large extent, impair quality of life and life expectancy, and increase hospital stays and costs. Various methods are used to prevent these complications including medical interventions such as effective analgesia, mucolytic agents, and antibiotherapy, as well as practices in which patients actively participate such as respiratory physiotherapy, postural drainage, deep breathing exercises spirometry use, and early mobilization. Obviously, patient consciousness and compliance are required to be able to implement these procedures in an effective way. Delirium and impaired cognitive functions observed in patients with dementia in the postoperative period diminish patient compliance to a minimum and make it difficult to fulfill the conditions required for a problem-free recovery following a thoracic surgery, such as active coughing, deep breathing, and effective mobilization. Adding to this, the negative effects of high ASA scores, higher rates of medical comorbidities and increased BMIs, and serious pulmonary complications such as primarily pleural effusion, atelectasia, and pneumonia were bound to occur in all of the patients in our study. Respiratory failure developed in 4 of these patients who were subjected to orotracheal intubation and then tracheostomy to reduce dead space volume and to enable a more effective respiration system aspiration. Another lesson to be drawn from these problems is that physicians dealing with such cases can achieve better outcomes if they know that such complications may occur and try to employ early diagnosis and treatment by giving more attention to their patients.

In this study, 5 patients were operated by way of open surgery using posterolateral thoracotomy incision and 4 patients by way of VATS. When compared to open surgery, VATS should actually cause less postoperative pain, thus improving patient comfort through active participation in respiratory physiotherapy, early mobilization, fast recovery, and return to social life. However, in our study, the entire postoperative complications showed equal distribution between the group that was administered VATS and the group that was administered open surgery.

We routinely employ in our clinic all means necessary to achieve effective postoperative analgesia in all patients, such

as peroperative intercostal blockage, patient-controlled analgesia, and epidural catheter placement. Therefore, we think that the more dominant cause of the complications occurring in these patients was delirium and cognitive function impairment rather than postoperative pain.

Complications relating to the respiratory system usually require the use of long-lasting medical treatment regimens. If these patients develop respiratory failure and need mechanical ventilator support, the difficulties in treating the causative or nosocomially occurring lung infections, functional status and cognitive function decline as well as malnutrition arising from the inability of the healthcare system to provide adequate nutritional support, and occurrence of muscle atrophies associated with the lack of mobilization for extended periods of time cause delays in extubation and rehabilitation of these patients and ultimately their return to normal life. In the study of Hu et al., 18,923 dementia patients were reviewed retrospectively and it was found that these patients had significantly higher overall postoperative complication rates, higher medical resources use and in-hospital expenditures as well as significantly higher 30-day postoperative mortality. The most common infective complications in their study were pneumonia and septicemia (3). Similarly, Kassahun found in their study high postoperative fatal complications and early death rates in patients with pre-existing dementia. In this study, the occurrence of surgical site infection, postoperative delirium, and pneumonia was found significantly higher in patients with pre-existing dementia compared to those without. They stated that this delirium was correlated with longer intensive care unit stays and longer overall hospital stays (6). In addition, Ali et al., found patients with dementia to experience greater postoperative respiratory and infectious complications (15). Unless serious complications develop in patients who are subjected to anatomic resection due to lung cancer, the average intensive care stay generally ranges between 1-2 days and clinic stay 5-7 days in our clinic. The total hospital costs of such patients are between 1400 and 1700 dollars. The postoperative delirium cognitive function impairment, and severe respiratory system complications observed in the patients in our study resulted in prolongation of intensive care unit stay, clinic stay, and total length of hospitalization, and a considerable increase in total hospital costs.

Our clinic predominantly admits lung cancer patients and our mortality rate ranges between 1.5 and 3%. However, mortality occurred in close to half of the patients in this study, which is not an acceptable rate in surgical treatment of lung cancer.

The limitations of this study include its retrospective nature, the inclusion of data from a single site, and a small number of patients. We believe that the results obtained from this study can gain more meaning after further multicenter prospective studies including a greater number of patients have

been conducted.

Considering the fast demographic, sociological, and economic changes and advancements in technology worldwide, it is highly probable that the diagnoses of operable lung cancer will be made more often in patients with dementia in the coming years. Before deciding on an operation for these patients, multifactorial poor surgical outcomes including increased severe and multiple postoperative complications such as pulmonary complications and delirium, long hospitalization time, and high mortality rates should be considered regardless of advanced surgical technique-experience and preoperative/postoperative care and the patients should be carefully assessed in the preoperative period. Treatment options should be thoroughly reviewed and potential benefit-harm assessment should be made when deciding on surgery in these patients who have shorter life expectancy than those without dementia. Additionally, to prevent any medicolegal problems that may arise later, patient relatives should be provided with sufficient information and included in the decision-making process for an operation.

Ethical Statement

This study protocol was reviewed and approved by the Karadeniz Technical University Faculty of Medicine Scientific Research Ethics Committee and approval number 2021/385.

Conflict of interest

The authors have no conflicts of interest to declare.

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Authors' contributions

Concept: S.K., O.T., A.A., Design: S.K., O.T., A.A., Data Collection or Processing: S.K., O.T., A.A., Analysis or Interpretation: O.T., A.T., C.T., Literature Search: S.K., O.T., A.A., Writing: S.K., O.T., A.A., A.T., C.T.

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