RESEARCH

THE EFFECT OF SURGICAL TREATMENT ON SURVIVAL IN GERIATRIC PATIENTS WITH STAGE I SMALL-CELL LUNG CANCER

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2020.183
2020; 23(4): 455-462

Gülay İlkhan DAŞDEMİR[1]
Hakan ÇELİKHISAR[2]
Aslı KILAVUZ[3]

CORRESPONDANCE

[3]Aslı KILAVUZ

Ege University Faculty of Medicine, Division of Geriatric Medicine, Department of Internal Medicine, Izmir, Turkey

Phone: +905323536570
e-mail: asli.kilavuz@gmail.com

Received: Sep 30, 2020
Accepted: Nov 24, 2020

[1] Tire Public Hospital, Chest Diseases Clinic, Izmir, Turkey

[2] Izmir Metropolitan Municipality Hospital, Chest Diseases Clinic, Izmir, Turkey

[3] Ege University Faculty of Medicine, Division of Geriatric Medicine, Department of Internal Medicine, Izmir, Turkey

Abstract

Introduction: The aim of our study is to investigate the effects of early stage surgical treatment on the survival of the geriatric patient group in small cell lung cancer.

Materials and Method: Patients over 65 years of age with a diagnosis of stage I small cell lung cancer were included. The patients included in the study were divided into three groups. 1. The surgical group 2. Non-surgical group 3. Untreated group. Overall survival and lung cancer-specific survival were evaluated among these 3 groups.

Results: A total of 1248 patients were included in the study. 28.9% of the patients did not receive any treatments, 47.2% of the patients received non-surgical treatment and 23.9% of the patients received surgical treatment. The 5-year overall survival rates of the untreated group, non-surgical group and surgical group were 7%, 10% and 32%, respectively ($p < 0.0001$). According to the results of multivariable analysis, surgical treatment was an important factor in increasing overall survival when compared to the non-surgical treatment.

Conclusion: In patients aged 65-84 with stage I small-cell lung cancer, surgical treatment increased overall survival at a statistically significant level.

Keywords: Geriatrics; Small Cell Lung Cancer; General Surgery; Survival

INTRODUCTION

Today, lung cancer is the most commonly observed type of cancer in the world (1), responsible for 12.8% of all cases. Lung cancer is also ranked first in cancer-related deaths, accounting for 17.8% of all cases (2). When 5-year survival rates are analyzed, the percentage is around 15% for all lung cancer patients (3). A further 15% of lung cancer patients are diagnosed with small-cell lung cancer (SCLC). At the time of diagnosis, the disease is generally at an extensive stage and, among untreated patients, the average survival time is limited to mere months (4). The prognostic significance of some parameters of SCLC patients were checked prior to treatment and analyzed with retrospective studies. It was shown that one of the most significant markers of survival is the stage of the tumor (5). Sex, age, and weight loss are also factors that affect prognoses (6). As humans' average lifespan has increased, so has the average age of patients diagnosed with SCLC. A study supporting this view found that the percentage of SCLC patients over the age of 70 increased from 23% to 44% over a period of 35 years, and that almost half of the limited-stage SCLC patients were diagnosed once past the age of 70 (7). Radiotherapy and chemotherapy are regarded as the basic treatments for patients with SCLC. Lately, however, several retrospective studies have shown that, in limited numbers of patients with SCLC who have undergone surgery, the overall survival duration increased and the 5-year survival rate was around 50% (8). Additionally, National Comprehensive Cancer Network (NCCN) guidelines state that surgical treatment should primarily be considered for Stage I (T1–2, N0) SCLC patients (9). However, in clinical practice, it is believed that younger patients may be more suitable candidates for surgical treatment, due to co-morbidities, post-operative complications, and patient performance (10).

Chronological age is often a poor predictor of treatment response and toxicity. An ECOG or Karnofsky Performance Status assessment, which are frequently used in patients to be treated with cancer, may also be insufficient (11). When planning cancer treatments in geriatric patients, their level of functionality and physiological capacity should be well evaluated before any other measures are undertaken. The International Society of Geriatric Oncology and the NCCN recommend a comprehensive geriatric assessment for patients over 65 years of age (12).

Nonetheless, in several studies, it is suggested that age is not a contraindication for surgery, so carefully selected Stage I SCLC patients aged 80 or above may benefit from surgical resection (13).

MATERIALS AND METHOD

Our study has a retrospective design. Patients over the age of 65 who were diagnosed with Stage I SCLC between January 1996 and December 2014 were analyzed using the data obtained from the records of two hospitals. A total of 1248 patients were included in the study. Stage I was defined clinically or pathologically in accordance with the American Joint Committee on Cancer (AJCC) Staging systems. Additionally, patients without sufficient survival data (whose survival duration in months is unknown, or whose survival duration is absent or not calculated) and patients whose pulmonary surgery details are not clear were excluded from the study. Patients whose pathological staging and surgery data are not present were also excluded. For each case, the patient's demographic data, the year and age at time of diagnosis, sex, location of the tumor, pathology, AJCC staging details, treatments (surgery, chemotherapy, or radiation), surgical procedures performed for reasons other than cancer, vital status, cause of death, and survival duration were recorded.

Ethical approval was obtained from the local ethics committee (approval number: 54022451-050.05.04-1786).

Statistical Analysis

In this study, SCLC patients were classified into surgical, non-surgical, and untreated groups. The clinicopathological characteristics among the three groups were analyzed with Pearson's Chi-squared test. The log-rank test and Kaplan-Meier analysis were used to estimate the patients' overall survival and lung cancer-specific survival (LCSS). Multivariate Cox models were realized to determine the predictors of survival. All statistical analyses were performed with IBM SPSS 22. The p-values are bilateral, and $p < 0.05$ was regarded as significant.

RESULTS

In total, 1248 patients were deemed to fulfil the study criteria and were assessed. The characteristics of the patients enrolled are provided in Table 1. Among all patients, 51.7% were male and 48.3% were female. The primary tumor location was most commonly the upper lobe (52.1%), followed by the lower lobe (32.1%), lingula (9.6%), and the middle lobe (6.2%) ($p < 0.0001$).

Distribution of patients based on the treatment administered was as follows: 365 patients were untreated (29.3% of total), 582 patients received non-surgical treatment (46.6%), and 301 patients received surgical treatment (24.1%) ($p < 0.001$). The percentage of untreated patients for patients ages 65–69 was 2.1%, 5.2% for patients aged 70–74, 11.9% for patients aged 75–79, 31.7% for patients aged 80–84, and 49.1% for patients older than 85 years.

Concerning the reasons for not performing surgery on 947 Stage I SCLC patients who received non-surgical treatment, we observed that, for 781 patients (82%), surgery was not recommended; in 65 patients (7%), there were surgical contraindications; a further 18 patients (2%) refused the operation; and 83 patients (9%) were not operated on for unknown reasons.

In general, the overall survival duration and the LCSS duration of patients receiving surgical treatment were observed to be longer. In terms of overall survival, the group receiving non-surgical treatment was second, following the surgical group. The median survival in the surgical group was 26 months (95% confidence interval [CI] 18.4–31.6 months), in the non-surgical group it was 14 months (95% CI 11.6–14.4 months), and in the untreated group, the duration was 6 months (95% CI 4.6–7.4 months). The 5-year survival percentages of the surgical group, non-surgical group, and untreated group were 34%, 13%, and 6%, respectively ($p < 0.0001$). The 5-year LCSS percentages of the surgical group, non-surgical group, and untreated group were 62%, 36%, and 21%, respectively ($p < 0.0001$). The multivariate Cox analysis of factors affecting the outcomes among the study population are presented in Table 2.

In multivariate analyses, surgical treatment was associated with longer overall survival duration (Hazard Ratio [HR] 0.506; 95% CI 0.391–0.655[$p < 0.0001$]) and LCSS duration (HR 0.449; 95% CI 0.309–0.653 [$p < 0.0001$]), as compared to the non-surgical treatments, as shown in Table 3. The adjusted HRs for the effect of surgery, non-surgical treatment, and no treatment on overall survival and LCSS in each age sub-group are provided in Table 3.

Similar results were observed in the patient group aged 80–84. The median survival in the surgical group was 23 months (95% CI 17.2–28.8 months); in the non-surgical group, it was 12 months (95% CI 11.4–14.6 months); and in the untreated group, this duration was 6 months (95% CI 4.2–7.8 months). The 5-year survival percentages of the surgical group, non-surgical group, and untreated group were 32%, 11%, and 5%, respectively ($p < 0.0001$). Lung cancer-specific survival percentages of the surgical group, non-surgical group, and untreated group were 55%, 27%, and 31%, respectively ($p < 0.0001$). In multivariate analyses, when compared to non-surgical treatment, surgical treatment remained an independent significant predictor of improved overall survival (HR 0.539; 95% CI 0.391–0.763 [$p < 0.0001$]) and LCSS (HR 0.449; 95% CI 0.281–0.729 [$p = 0.001$]).

In the patient group aged over 85, the median survival in the surgical group was 19 months (95%

Table 1. Characteristics of patients

Characteristics	Total n (%)		Untreated n (%)		Non-surgical n (%)		Surgical n (%)		p
Sex									0.198
Female	603	(48.3)	188	(51.5)	262	(45.1)	153	(50.8)	
Male	645	(51.7)	177	(48.5)	320	(54.9)	148	(49.2)	
Age									<0.0001
65-69	135	(10.8)	8	(2.1)	57	(9.8)	157	(52.1)	
70-74	188	(15.1)	19	(5.2)	72	(12.3)	72	(23.9)	
75-79	347	(27.8)	43	(11.9)	107	(18.4)	34	(11.3)	
80-84	414	(33.2)	116	(31.7)	146	(25.2)	21	(7.1)	
≥85	164	(13.1)	179	(49.1)	200	(34.3)	17	(5.6	
Tumour location									<0.0001
Upper lobe	650	(52.1)	149	(40.1)	312	(53.6)	178	(59.1)	
Lower lobe	401	(32.1)	116	(31.7)	187	(32.1)	98	(32.5)	
Middle lobe	77	(6.2)	63	(17.2)	48	(8.2)	22	(7.3)	
Lingula	120	(9.6)	37	(10.1)	35	(6.1)	3	(1.1)	
Grade									<0.0001
Grade I-II	217	(11.8)	41	(11.2)	7	(1.2)	178	(59.1)	
Grade III	421	(33.7)	98	(26.8)	228	(39.2)	87	(28.9)	
Grade IV	583	(46.7)	217	(59.4)	337	(57.9)	28	(9.3)	
Unknown	27	(2.2)	9	(2.4)	10	(1.7)	8	(2.7)	
Patients receiving adjuvant therapy	-		-		-		137	(45.5)	>0.05
Patients receiving no adjuvant therapy	-		-		-		164	(54.5)	>0.05

CI 16.0–22.0 months); in the non-surgical group, it was 13 months (95% CI 8.4–17.6 months); and in the untreated group, this duration was 6 months (95% CI 3.4–8.6 months). The 5-year overall survival percentages of the surgical group, non-surgical group, and untreated group were 18%, 14%, and 4%, respectively (p = 0.002). The 5-year LCSS percentages of the surgical group, non-surgical group, and untreated group were 55%, 40%, and 20%, respectively (p = 0.012). In multivariate analyses, surgical treatment was associated with higher overall survival (HR 0.913; 95% CI 0.511–1.649; [p = 0.771]) and LCSS rates (HR 0.661; 95% CI 0.271–1.617; [p = 0,361]), compared to the non-surgical group.

The 301 patients in the surgical group were assessed for the analysis performed for the assessment of patients receiving adjuvant therapy. Among this group, 137 (45.5%) patients received post-operative adjuvant therapy, while 164 (54.5%) received only surgical treatment. The median overall survival duration of patients who only received surgical treatment was 18 months (95% CI 11.8–24.2 months), while it was 38 months for those patients receiving post-operative adjuvant therapy (95% CI 24.2–51.8 months). The 5-year overall survival rate in patients receiving post-operative adjuvant therapy was 36%; the rate was 32% in patients who only received surgical treatment (p = 0.031). The 5-year LCSS rate in patients receiving post-operative adjuvant therapy was 65%, and it was 55% in patients who only received surgical treatment (p = 0.036).

Table 2. Multivariate analysis of clinicopathological factors affecting outcomes in elderly and geriatric patients

Clinical parameters	Overall survival			Lung cancer-specific survival		
	HR	95% CI	p	HR	95% CI	p
Sex						
Female	0.920	0.726-0.929	0.004	0.913	0.754-1.105	0.404
Male						
Age (years)						
65-69	1.110	1.065-1.345	0.011	1.186	0.934-1.442	0.189
70-74	1.170	1.048-1.362	0.013	1.174	0.910-1.476	0.217
75-79	1.185	1.035-1.374	0.017	1.161	0.755-1.480	0.329
80-84	1.205	1.029-1.386	0.014	1.158	0.949-1.423	0.128
≥85	1.255	1.016-1.540	0.035	1.106	0.816-1.516	0.465
Tumour location						
Upper lobe	0.834	0.831-1.119	0.039	0.896	0.746-1.124	0.029
Lower lobe	0.959	0.899-1.301	0.612	1.031	0.829-1.271	0.802
Middle lobe	1.399	1.071-1.839	0.021	1.539	1.049-2.259	0.031
Lingula	1.159	0.925-1.486	0.216	1.399	1.019-1.939	0.041
Grade						
Grade I-II	1.676	0.878-2.986	0.379	1.394	0.624-3.216	0.479
Grade III	1.669	0.899-3.089	0.099	1.369	0.589-3.181	0.459
Grade IV	1.611	0.869-2.949	0.131	1.541	0.681-3.499	0.299
Unknown	1.689	0.919-3.099	0.089	1.341	0.591-3.051	0.489
Treatment			<0.0001			<0.0001
Untreated	0.631	0.541-0.736	<0.0001[x]	0.619	0.501-0.771	<0.0001[x]
Surgical	0.549	0.279-0.431	<0.0001[y]	0.469	0.361-0.619	<0.0001[y]
Non-surgical	0.351	0.461-0.669	<0.0001[z]	0.289	0.221-0.389	<0.0001[z]

x: p to compare the untreated group with the non-surgical group,
y: p to compare the non-surgical group with the surgical group,
z: p to compare untreated group with the surgical group.

DISCUSSION

Although lung cancer is more common in elderly patients than young patients, studies specific to the elderly are very few. In studies conducted to determine the optimal treatment of lung cancers, patients under the age of 65 were often included in the patient group (14). In the last 10–15 years, studies have begun among geriatric patient groups; however, in these studies, patients in their seventh decade constitute the majority of subjects, and the number of patients over age 80 remains small (15).

Today, for early stage SCLC, the standard treatment is concomitant radiochemotheraphy; for advanced stage SCLC, the standard of care for first-line systemic therapy is platinum-based systematic chemotherapy (16). Some recent studies have reported positive outcomes for the surgical treatment of early stage SCLC patients (17). Additionally, NCCN guidelines state that surgical treatment should be considered for Stage I (T1–2, N0) SCLC patients (18). However, the median age of the patients included in the retrospective studies on which these guidelines are based was 60–75 years (19,20). To the best of our knowledge, there are no studies in the literature that specifically assesses the survival-related outcomes of surgical treatment in SCLC

Table 3. Adjusted hazard ratios for the effect of surgery, non-surgical treatment and no treatment on overall survival and lung cancer-specific survival in each age sub-group

Sub-group	Overall survival			Lung cancer-specific survival		
	HR	95% CI	p	HR	95% CI	p
Age ≥65 years			<0.0001			<0.0001
Untreated	0.935	0.615-0.904	<0.0001[x]	0.801	0.342-0.494	<0.0001[x]
Surgical	0.395	0.214-0.684	<0.0001[y]	0.234	0.225-0.433	<0.0001[y]
Non-surgical	0.265	0.274-0.856	<0.0001[z]	0.196	0.141-0.304	<0.0001[z]
Age ≥70 years			<0.0001			<0.0001
Untreated	0.786	0.584-0.836	<0.0001[x]	0.702	0.389-0.671	<0.0001[x]
Surgical	0.436	0.314-0.565	<0.0001[y]	0.364	0.274-0.514	<0.0001[y]
Non-surgical	0.296	0.286-0.915	<0.0001[z]	0.214	0.166-0.296	<0.0001[z]
Age ≥75 years			<0.0001			<0.0001
Untreated	0.610	0.479-0.769	<0.0001[x]	0.601	0.429-0.821	<0.0001[x]
Surgical	0.498	0.389-0.649	<0.0001[y]	0.451	0.310-0.649	<0.0001[y]
Non-surgical	0.299	0.231-0.409	<0.0001[z]	0.271	0.181-0.399	<0.0001[z]
Age ≥80 years			<0.0001			<0.0001
Untreated	0.659	0.509-0.861	0.002[x]	0.721	0.499-1.019	0.071[x]
Surgical	0.539	0.391-0.759	<0.0001[y]	0.449	0.281-0.729	0.001[y]
Non-surgical	0.359	0.249-0.521	<0.0001[z]	0.319	0.189-0.539	<0.0001[z]
Age ≥85 years			0.001			0.003
Untreated	0.449	0.291-0.719	0.001[x]	0.401	0.211-0.789	0.008[x]
Surgical	0.909	0.499-1.649	0.759[y]	0.661	0.271-1.621	0.361[y]
Non-surgical	0.421	0.229-0.749	0.004[z]	0.259	0.111-0.641	0.003[z]

x: p to compare the untreated group with the non-surgical group,
y: p to compare the non-surgical group with the surgical group,
z: p to compare untreated group with the surgical group.

patients over the age of 75. Due to this situation, our study was particularly focused on patients over the age of 75, in hopes of clarifying the clinical value of surgery in the treatment of elderly and geriatric patients with SCLC. In clinical practice, considering the association of old age with increased comorbidity, reduced functionality, more post-operative complications, and relatively higher mortality, surgery is rarely performed on geriatric patients. However, contradictorily, some studies show that age is not an independent prognostic factor affecting survival and that the performance status and treatments appear to be valid prognostic factors (21,22). Satisfactory long-term results were obtained when surgical resection was applied to carefully selected Stage I SCLC patients over the age of 80 (23,24). In our study, the median overall survival duration of the surgical group was found to be significantly higher than the non-surgical group.

Using subgroup analyses, we found that there was a clinical benefit and survival contribution of surgery observed in patients aged 65–69, 70–74, 75–79, and even in the population aged 80–84, who have traditionally been assumed to derive fewer benefits from lung resection. In the group of patients aged 85 and above, patients receiving surgical or non-surgical treatment had longer overall and LCSS durations, when compared to the untreated patients. No significant differences were observed between the surgical and non-surgical treatment

groups. According to our study, surgery may be an acceptable element of multimodal treatment in patients aged 75–84. Additionally, when the role of post-operative adjuvant therapy was compared with only surgical treatment in geriatric patients, it was observed that post-operative adjuvant therapy contributed to their survival.

This study had some restrictions. First, as this is a retrospective study, inherent selection bias was unavoidable. It is also possible that patients in the surgical group were healthier than the patients in the non-surgical and untreated groups. Another restriction was the lack of specific details regarding the performance status, chemotherapy and radiotherapy regimen, comorbidities, etc. in the patient records we consulted.

CONCLUSION

We have concluded that Stage I SCLC patients aged 65–84 benefit from surgical resection with a 5-year overall survival rate of 32% and a 5-year LCSS rate of 55%. Surgical resection treatment could be considered as a promising first-line treatment in suitable geriatric Stage I SCLC patients in the future.

REFERENCES

1. Low M, Ben-Or S. Thoracic surgery in early-stage small cell lung cancer. Thorac Surg Clin 2018;28(1):9-14. (PMID: 29150041).
2. Huang C-Y, Au K-K, Chen S-L, Wang S-C, Liao C-Y, Hsu H-H, Sung W-W, Wang Y-C. Unfavorable Mortality-To-Incidence Ratio of Lung Cancer Is Associated with Health Care Disparity. International Journal of Environmental Research and Public Health. 2018; 15(12):2889.
3. Garon EB, Hellmann MD, Rizvi NA, Carcereny E, Leighl NB, Ahn MJ, Eder JP, Balmanoukian AS, Aggarwal C, Horn L, Patnaik A, Gubens M, Ramalingam SS, Felip E, Goldman JW, Scalzo C, Jensen E, Kush DA, Hui R. Five-Year Overall Survival for Patients with Advanced Non‐Small-Cell Lung Cancer Treated with Pembrolizumab: Results From the Phase I KEYNOTE-001 Study. J Clin Oncol. 2019 Oct 1;37(28):2518-2527. doi: 10.1200/JCO.19.00934. Epub 2019 Jun 2. PMID: 31154919; PMCID: PMC6768611.
4. Du X, Tian D, Liu L, et al. Surgery in patients with small cell lung cancer: A period propensity score matching analysis of the Seer database, 2010-2015. Oncol Lett 2019;18(5):4865-81. (PMID: 31611997).
5. Shepherd FA, Ginsberg R, Patterson GA, et al. Is there ever a role for salvage operations in limited small-cell lung cancer? J Thorac Cardiovasc Surg 1991;101(2):196-200. (PMID: 1846927).
6. Matsumoto Y, Ohara S, Furukawa R, Usui K. The Prognosis of Small Cell Lung Cancer in Patients with Pulmonary Fibrosis. Anticancer Res. 2017 Oct;37(10):5791-5795. doi: 10.21873/anticanres.12021. PMID: 28982903.
7. Govindan R, Page N, Morgensztern D, et al. Changing epidemiology of small-cell lung cancer in the United States over the last 30 years: analysis of the surveillance, epidemiologic, and end results database. J Clin Oncol 2006;24(28):4539-44. (PMID: 17008692).
8. Wang Z, Pang L, Tang J, et al. Video-assisted thoracoscopic surgery versus muscle-sparing thoracotomy for non-small cell lung cancer: a systematic review and meta-analysis. BMC Surg 2019;19(1):144. (PMID: 31615490).
9. Zhong L, Suo J, Wang Y, et al. Prognosis of limited-stage small cell lung cancer with comprehensive treatment including radical resection. World J Surg Oncol 2020;18(1):27. (PMID: 32013993).
10. Tjong MC, Mak DY, Shahi J, Li GJ, Chen H, Louie AV. Current management and progress in radiotherapy for small cell lung cancer. Front Oncol 2020; 10:1146. (PMID: 32760673).
11. Repetto L, Fratino L, Audisio RA, et al. Comprehensive geriatric assessment adds information to Eastern Cooperative Oncology Group performance status in elderly cancer patients: An Italian Group for Geriatric Oncology Study. J Clin Oncol 2002;20(2):494-502. (PMID: 11786579).
12. Extermann M, Aapro M, Bernabei R, et al. Use of comprehensive geriatric assessment in older cancer patients: recommendations from the task force on CGA of the International Society of Geriatric Oncology (SIOG). Crit Rev Oncol Hematol 2005;55(3):241-52. (PMID: 16084735).
13. National Comprehensive Cancer Network (NCCN) guidelines. Non-small cell lung cancer. Version

2.2018. [Internet]. Avaliable from: http://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed: 20.06.2020.

14. Engelhardt KE, Coughlin JM, DeCamp MM, et al. Survival after adjuvant radiation therapy in localized small cell lung cancer treated with complete resection. J Thorac Cardiovasc Surg 2019;158(6):1665-77.e2. (PMID: 31627955).
15. Hutchins LF, Unger JM, Crowley JJ, Coltman CA, Albain KS. Underrepresentation of patients 65 years of age or older in cancer-treatment trials. N Engl J Med 1999;341(27):2061-7. (PMID: 10615079).
16. Duma N, Santana-Davila R, Molina JR. Non-Small Cell Lung Cancer: Epidemiology, Screening, Diagnosis, and Treatment. Mayo Clin Proc. 2019 Aug;94(8):1623-1640. doi: 10.1016/j.mayocp.2019.01.013. PMID: 31378236.
17. Blandin Knight S, Crosbie PA, Balata H, Chudziak J, Hussell T, Dive C. Progress and prospects of early detection in lung cancer. Open Biol. 2017 Sep;7(9):170070. doi: 10.1098/rsob.170070. PMID: 28878044; PMCID: PMC5627048.
18. Kalemkerian GP, Loo BW, Akerley W, Attia A, Bassetti M, Boumber Y, Decker R, Dobelbower MC, Dowlati A, Downey RJ, Florsheim C, Ganti AKP, Grecula JC, Gubens MA, Hann CL, Hayman JA, Heist RS, Koczywas M, Merritt RE, Mohindra N, Molina J, Moran CA, Morgensztern D, Pokharel S, Portnoy DC, Rhodes D, Rusthoven C, Sands J, Santana-Davila R, Williams CC, Hoffmann KG, Hughes M. NCCN Guidelines Insights: Small Cell Lung Cancer, Version 2.2018. J Natl Compr Canc Netw. 2018 Oct;16(10):1171-1182. doi: 10.6004/jnccn.2018.0079. PMID: 30323087.
19. Liu T, Chen Z, Dang J, Li G. The role of surgery in stage I to III small cell lung cancer: A systematic review and meta-analysis. PLoS One 2018;13(12):e0210001. (PMID: 30596754).
20. Wakeam E, Acuna SA, Leighl NB, et al. Surgery versus chemotherapy and radiotherapy for early and locally advanced small cell lung cancer: A propensity-matched analysis of survival. Lung Cancer 2017; 109:78-88. (PMID: 28577955).
21. Antonia SJ, Villegas A, Daniel D, et al. Durvalumab after chemoradiotherapy in stage iii non–small-cell lung cancer. N Engl J Med 2017; 377:1919-29. (PMID: 28885881).
22. Horn L, Mansfield AS, Szczęsna A, et al. First-line Atezolizumab plus chemotherapy in extensive-stage small-cell lung cancer. N Engl J Med 2018;379:2220-9. (PMID: 30280641).
23. Salazar MC, Rosen JE, Wang Z, et al. Association of delayed adjuvant chemotherapy with survival after lung cancer surgery. JAMA Oncol 2017;3(5):610-9. (PMID: 28056112).
24. Yang H, Xu J, Yao F, Liang S, Zhao H. Analysis of unexpected small cell lung cancer following surgery as the primary treatment. J Cancer Res Clin Oncol 2018;144(12):2441-7. (PMID: 30341687).