Original Article

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Prognostic Significance of Lymphocyte Percentage and IL-6 Level in Patients Undergoing Radiotherapy for Advanced Lung Cancer

Radyoterapi Yapılan İleri Akciğer Kanseri Hastalarında Lenfosit Oranı ve IL-6 Düzeyinin Prognostik Önemi

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ABSTRACT

Objective: Although most patients with locally advanced lung cancer show a moderate response to chemoradiotherapy, the results are not satisfactory. In lung cancer, lymphocyte percentages and interleukin-6 (IL-6) cytokine levels have been reported to be significantly correlated with survival rates. In this study, we investigated the effects of lymphocyte percentages and IL-6 levels on overall survival and progression-free survival.

Methods: One hundred forty-two patients diagnosed with lung cancer and treated with radiotherapy were included in the study. Patients were examined according to gender, age, clinical stage, Eastern Cooperative Oncology Group performance status, pathology and pre-radiotherapy lymphocyte percentages and IL-6 cytokine levels. The results were also analyzed according to radiotherapy dose, treatment sites and response rates.

Results: When comparing patients with lymphocyte percentage >15% to those with lymphocyte percentage ≤15%, median overall survival was 18 months and 7 months, progression-free survival was 17 and 5 months, respectively, and median overall survival and progression-free survival were significantly higher in those with lymphocyte percentage >15% (p=0.007 and p=0.006). When comparing patients with IL-6 ≤7 pg/mL to those with >7 pg/mL, median overall survival was 14 and 7 months, progression-free survival was 9 and 4 months, and median overall survival and

ÖZ

Amaç: İlerlemiş akciğer kanseri hastalarının çoğunda, kemoradyoterapiyle orta düzeyde bir cevap alınsa da sonuçlar yüz güldürücü değildir. Akciğer kanserinde, lenfosit yüzdeleri ve interlökin-6 (IL-6) sitokin düzeylerinin yaşam oranları ile anlamlı düzeyde korelasyon gösterdiği bildirilmiştir. Bu çalışmada, lenfosit yüzdeleri ve IL-6 düzeylerinin genel sağkalım ve progresyonsuz sağkalım üzerine etkisini araştırdık.

Yöntemler: Çalışmaya akciğer kanseri tanısı almış ve radyoterapi görmüş 142 hasta dahil edildi. Hastalar cinsiyet, yaş, klinik evre, Eastern Cooperative Oncology Group performans durumu, patoloji ve radyoterapi öncesi lenfosit yüzdeleri ve IL-6 sitokin seviyelerine göre incelendi. Sonuçlar ayrıca radyoterapi dozu, tedavi bölgeleri ve yanıt oranlarına göre analiz edildi.

Bulgular: Lenfosit yüzdesi >%15 olan hastalar lenfosit yüzdesi ≤%15 olan hastalarla karşılaştırıldığında, medyan genel sağ kalım sırasıyla 18 ay ve 7 ay, progresyonsuz sağ kalım sırasıyla 17 ve 5 ay olarak bulundu ve medyan genel sağ kalım ve progresyonsuz sağ kalım lenfosit yüzdesi >%15 olanlarda anlamlı şekilde daha yüksekti (p=0,007 ve p=0,006). IL-6 ≤7 pg/mL olan hastalar >7 pg/mL olan hastalarla karşılaştırıldığında, medyan genel sağ kalım 14 ve 7 ay, progresyonsuz sağ kalım 9 ve 4 ay idi ve medyan genel sağ kalım ve progresyonsuz sağ kalım IL-6 ≤7 pg/mL olan hastalarda anlamlı derecede daha yüksekti (p=0,011 ve p=0,01).

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ABSTRACT

progression-free survival was significantly higher in patients with IL-6 ≤7 pg/mL (p=0.011 and p=0.01).

Conclusion: In advanced lung cancer patients, lymphocyte counts and IL-6 levels before radiotherapy are important prognostic biomarkers, and these tests can be used in patient follow-up and to develop different treatment strategies.

Keywords: IL-6 in cancer, lymphocyte in cancer, inflammation in cancer, radiation in hematotoxicity

ÖZ

Sonuç: İlerlemiş akciğer kanseri hastalarında, radyoterapi öncesi lenfosit sayımı ve IL-6 düzeyleri önemli prognostik biyobelirteçlerdir ve bu testler hasta takibinde ve farklı tedavi stratejileri geliştirmek için kullanılabilir.

Anahtar Kelimeler: Kanserde IL-6, kanserde lenfosit, kanserde inflamasyon, hematotoksisitede radyasyon

Introduction

Lung cancer (LC) is divided into two main histopathologic groups: small cell LC (SCLC) and non-SCLC (NSCLC). SCLC is a malign neuroendocrine neoplasm that constitutes 15-20% of all LCs. NSCLC occurs in 80-85% of cases. NSCLC has different histopathologic subtypes such as squamous cell, adeno and large cell carncer. Adenocancer and squamous cell cancer are the most common subtypes of NSCLC and exhibit different genetic pathways, control mechanisms and prognostic features. These differences have important clinical implications in terms of disease pathogenesis, treatment response and patient prognosis (1).

In addition, clinical studies in NSCLC have revealed that adenocarcinoma and squamous cell carcinoma respond differently to chemotherapy, agents targeting kinase mutations, and immune checkpoint inhibitors (2). Accordingly, these two histopathological subtypes of LC are considered to be different diseases at the molecular, pathological and clinical levels (3). Despite all advances in diagnosis and therapies of LC, overall survival (OS) rates are still not not enough yet (4,5).

Prognostic factors affecting survival are known to be factors such as histopathology, tumor stage and markers, poor performance, weight loss in a short time, increasing acute phase reactans, such as interleukin-6 (IL-6), ferritin, C-reactive protein (CRP) and D-dimer levels (6,7).

Surgery in the early stage and radiotherapy (RT) in inoperative patients are important accepted treatments in LC. Although a moderate response is obtained with chemotherapy, RT or chemoradiotherapy with or without immunotherapy (IT) in most patients with LC, the results are not satisfactory (8).

Lymphocytes and neutrophils play important roles in inflammation in tumors (6,9,10). The distruption of normal ratio between neutrophils and lymphocytes causes imbalance between apoptotic and cytotoxic effects, and may contribute to development of hypoxia in tumor and metastases (11).

Since RT has a cytotoxic effect especially on hematopoietic cells, the number of lymphocytes decreases very early because they are more sensitive to radiation. Once lymphopenia develops, it may take a long time to recover (12). In addition, there is information in the literature that radiation increases immunity at certain doses (13). It has been shown that immunity can be increased and survival rates can be improved with low-volume, high-dose, few-fractionated RT, as in stereotactic radiosurgery (14).

To increase the effect of treatments, targeted treatments and IT are increasingly preferred in addition to chemotherapy. Various methods such as increasing lymphocyte rates have been tried in IT in order to increase the effectiveness of treatment in LC and improve survival rates (15).

In various cancers, high pre-treatment "neutrophil-to-lymphocyte ratio" (NLR) determined with peripheral blood tests has been reported to be an independent, inexpensive, and easily applicable prognostic biomarker associated with poor survival, especially in breast and gastrointestinal cancers (16-18). In addition, the prognostic impact of NLR on LC has been shown in many studies.

In LC, inflammatory markers such as CRP, "platelet-to-lymphocyte ratio", NLR and "lymphocyte-to-monocyte ratio" has been shown to significantly associate with prognosis (19-21).

"Absolute lymphocyte counts" (ALC) below <500 cells/mL are reported to negatively affect cancer treatment responses (22). Although new immunological and histological biomarkers such as "epidermal growth factor receptor" and "intercellular adhesion molecule-1" have been identified, the measurement of these markers is costly and often time-consuming (23).

There is still no reliable prognostic factor that can be easily determined and is closely related to clinical outcomes determined by meta-analyses in patients with LC. In this study, we aimed to investigate the effects of factors such as pre-RT lymphocyte percentages and IL-6 levels on prognosis of advanced LC patients.

Methods

Study Design and Participants

This study was an observational retrospective cohort study and 142 patients who were diagnosed with LC and received RT between 2020 and 2024 were included in the study. Patients were examined according to gender, age, clinical stage, Eastern Cooperative Oncology Group (ECOG) performance status, pathology and pre-RT lymphocyte percentages, and levels of IL-6 cytokine and other inflammatory markers such as D-dimer.

Results were also analyzed according to RT dose, treatment sites and response rates.

Inclusion Criteria

Patients aged 18 years and over, diagnosed with LC and received RT and/or chemotherapy were included.

Exclusion Criteria

Patients with serious infection, those treated in the intensive care unit, and those who received IT were excluded from the study.

Ethical Approval

Ethical approval was obtained from the University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital Ethics Committee (decision no: 149, date: 07.05.2025). Informed consents were obtained from patients.

Statistical Analysis

Statistical analyses of this study were performed with R software with version 4.2.0. Variables were analyzed for normality using Kolmogorov-Smirnov and Shapiro-Wilk tests together with Q-Q plots and histograms. Median and mean ± standard deviation values were used for continuous variables. Categorical variables were expressed as frequency (percentage). Mann-Whitney U and Kruskal-Wallis tests were applied for independent continuous variables. Wilcoxon signed-rank test was used for dependent variables. Spearman correlation test was used to analyze the relationships between continuous variables. Log-rank with Kaplan-Meier analysis were performed for "OS" and "progression-free survival" (PFS). Factors affecting the risk of recurrence were analyzed with univariate Cox regression analysis. Variables found to be significant in univariate Cox analysis were re-evaluated with multivariate Cox regression analysis. Model fit odds ratio was evaluated using Akaike information criterion and fit values. $P<0.05$ was defined as significant.

Results

Patient Characteristics

One hundred forty two patients were included in this study. Patients' median age was 59 years (18-89). The rate of stage IV disease was 76.05% (n=108). Performance scoring of ECOG was greater than 2 in 122 patients (85.91%). Characteristics of the patients are shown in Table 1.

Laboratory Tests

Pre-RT median lymphocyte percentage was 12% and median level of inflammatory cytokine IL-6 was 12 pg/mL (Table 2).

Response Rates and Survival by Lymphocyte Percentages and IL-6 Cytokine Levels

In 61 patients (42.25%) with lymphocyte percentage >15%, the median RT response rate was 70%, (0-100%). In 81 patients (57.04%) with lymphocyte percentage ≤15%, the median RT response rate was 40%, (0-100%).

In patients with lymphocyte percentage >15%, median OS was 18 months (1-60 months). In patients with lymphocyte percentage ≤15%, median OS was 7 months (1-36 months). In patients with lymphocyte percentage >15%, median PFS was 17 months and in those with lymphocyte percentage ≤15%, median PFS was 5 months (1-31 months).

In 114 patients (80.28%) with IL-6 level >7, the median RT response rate was 40% (0-100%). In 28 patients (19.71%) with IL-6 level ≤7, the median RT response rate was 80% (0-100%).

In patients with IL-6 level ≤7, median OS was 14 months, and in 114 patients with IL-6 level >7, median OS was 7 months with a minimum of 3 and 0 and a maximum of 60 and 60 months. In patients with IL-6 level ≤7, median PFS was 9 months, and in 114 patients with IL-6 level >7, median PFS was 4 months with a minimum of 1 and 0 and a maximum of 60 and 60 months.

Survival According to RT Characteristics and Response Rates

The median daily RT fraction number and dose were 12 and 250 centigray, respectively. Stage IV disease rate was 76.05% in this study,

Table 1. Characteristics of the patients

Parameters	Number of patients	%
Age		
18-50	33	23.23
51-65	70	49.29
66-74	29	20.42
75-89	10	7.04
Stage		
1-2	8	5.63
3	27	19.01
4	108	76.05
ECOG performance status		
1	6	4.22
2	14	9.85
3	17	11.97
4	105	73.94
Comorbidity		
CAD	15	10.56
CAD+COPD	6	4.22
None	121	85.21
Patoloji		
NSCLC	115	80.98
SCLC	27	19.02
Metastasis area		
Bone	64	45.07
Brain	32	22.53
Liver	9	6.33

ECOG: Eastern Cooperative Oncology Group, CAD: Coronary artery disease, COPD: Chronic obstructive pulmonary disease, NSCLC: Non-small cell lung cancer, SCLC: Small cell lung cancer

The median RT response was 50%. Complete response was achieved in 22 (15.49%) patients.

Median OS in complete responders was 34 months, with no deaths during the study and an upper limit of 60 months [not available (NA), 95% confidence interval (CI): 34-NA]. OS was significantly longer in complete responders (p<0.001). It was 12 (95% CI: 6-14) and 5 months (95% CI: 1-3) in partial and stationary responders, respectively. Survival rate was 15% at the time of analysis (n=22) (Table 3).

Median PFS was 28 months (NA, 95% CI: 28 months-NA) in patients with complete response, 24 months (95% CI: 5-NA) in good responders, 4 months in partial responders (95% CI: 3-10), and 0 months in patients with stationary or progressive disease (95% CI: 0-3).

Statistical Analysis

Significant relationships were found between pre-RT lymphocyte percentage, OS and PFS (p=0.007 and p=0.006, respectively). Median OS was 18 months (95% CI: 9-36) in patients with lymphocyte percentage >15% and 7 months (95% CI: 6-14) in those with lymphocyte percentage ≤15%. Similarly, PFS was found to be longer in patients with lymphocyte percentage >15% with a median of 17 months (95% CI: 8-36) compared to those with lymphocyte percentage ≤ 15% (5 months, 95% CI: 3-10) (Figure 1).

Pre-RT IL-6 levels were also found to be an important prognostic indicator. Median OS was 14 (95% CI: 8-NA) in patients with IL-6 levels ≤7 pg/mL while it was 7 months (95% CI: 6-NA) in patients with IL-6 levels >7 pg/mL. Median PFS was 9 months in patients with IL-6 levels ≤7 pg/mL while it was 4 months (95% CI: 3-10) in patients with IL-6 levels >7 pg/mL (p=0.009) (Figure 2).

Table 2. Laboratory test parameters

Parameters	n=142
Hematocrit, %	
Median (min-max)	36.0 (12.2-49.3)
Lymphocyte, %	
Median (min-max)	12 (5-36)
Platelet, 10^3/µL	
Median (min-max)	274 (80-461)
CRP, mg/dL	
Medyan (min-max)	30 (1-214)
Ferritin, ng/mL	
Median (min-max)	392 (14-2,674)
IL-6, pg/mL	
Median (min-max)	12 (2-68)
D-dimer µg/mL	
Median (min-max)	1.1 (0.1-20)

IL-6: Interleukin-6, CRP: C-reactive protein

Univariate and Multivariate Survival Analyses

Univariate analyses were determined to be significant for OS and PFS including stage IV disease (p=0.005 and p=0.005, respectively), ECOG performance status (p<0.001 and p<0.001, respectively), lymphocyte percentage (p=0.007 and p=0.007, respectively), IL-6 (hazard ratio=2.15, 95% CI: 1.19-3.87, p=0.011), total RT dose (p<0.001 and p<0.001, respectively), and D-dimer levels (p<0.001 and p<0.001, respectively) (Table 4 and Table 5). Although D-dimer levels were found to be prognostically significant, they were not included in this study because the subject is very long.

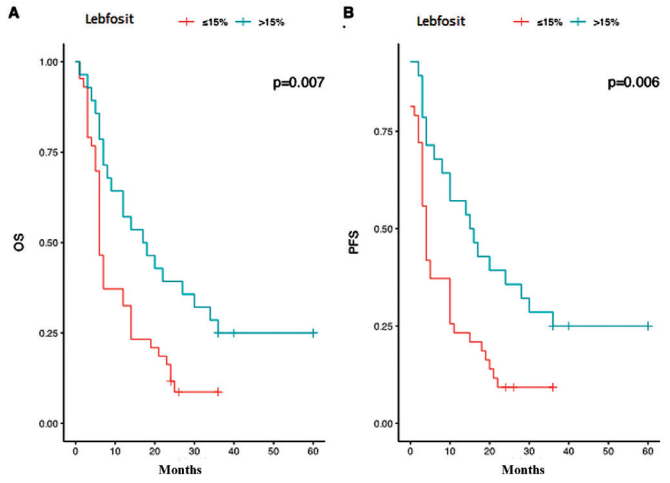

Figure 1. Kaplan-Meier curves for overall survival (OS) and progression-free survival (PFS)

A) Comparison of OS for different pre-radiotherapy (pre-RT) lymphocyte percentages, B) Comparison of PFS for different pre-RT lymphocyte percentages

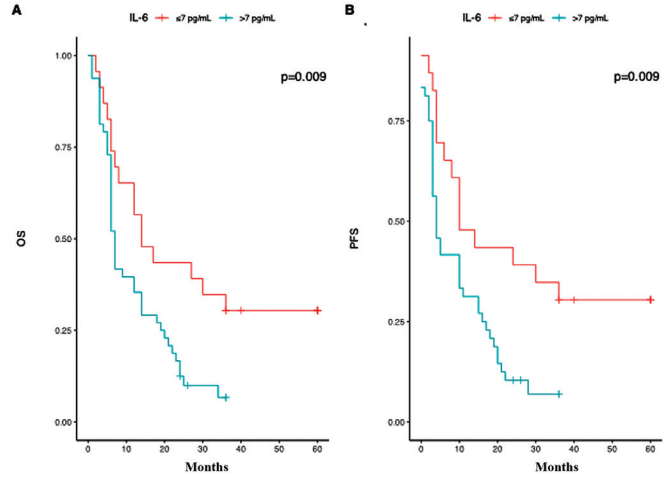

Figure 2. Kaplan-Meier curves for overall survival (OS) and progression-free survival (PFS)

A) Comparison of OS for different pre-radiotherapy (pre-RT) interleukin-6 (IL-6) levels, B) Comparison of PFS for different pre-RT IL-6 levels

In the analyses for survival, median OS and PFS were 7 and 5 months, respectively in patients with lymphocyte percentage ≤15%. In patients with lymphocyte percentage >15%, median OS and PFS were 18 and 14 months (p=0.007 and p=0.005, respectively).

OS and PFS in patients with lymphocyte percentage ≤6% were median 2 and 0 months, respectively, and were significantly lower than in patients with lymphocyte percentage >15% (p=0.001).

In patients with IL-6 level >7 pg/mL, median OS and PFS were 7 months and 4 months, respectively, and were significantly lower than in patients with IL-6 level ≤ 7pg/mL (median OS and PFS were 18 and 17 months, respectively) (p=0.011 and p=0.01, respectively).

Patient Follow-up and Response Assessment

Patients were followed up at 1-2 month intervals in the first year and at 3-5 month intervals in the second year. During follow-up, computed tomography (CT) or magnetic resonance imaging (MRI) was performed every 3 months and positron emission tomography (PET)/CT every 6 months.

Response rates of RT were determined by thoracic CT taken in the first 2 months after treatment, brain or liver MRI in patients with brain and liver metastases, and PET/CT taken 3-5 months later. Response rates of RT assessed using Response Evaluation Criteria in Solid Tumors (version 1.1) (IV, A) (24).

Table 3. RT characteristics, OS and PFS according to lymphocyte and IL-6 ratios

RT	Patient number (n) (%)	Median lenfosit (%)	Median IL-6 pg/mL	Median RT response (%)	Median OS (months)	Median PFS (months)
RT dose/day						
150-200	51 (35.91)	21	12	70	20	14
250 cGy	34 (23.94)	12	12	50	6	3
300 cGy	32 (22.53)	9	13	60	11	9
>400 cGy	25 (17.6)	7	16	50	5	2
RT site						
Lung	49 (34.5)	21	12	70	20	14
Bone	56 (39.43)	11	13	50	7	5
Brain	30 (21.12)	10	15	70	10	8
Bone and Brain	9 (6.33)	9	21	50	2	0
Liver	1 (0.7)	6	45	70	3	1
RT response (%)						
CR	22 (15.49)	26	3	100	60	28
PR						
70--90	14 (9.85)	21	7	70-90	17	14
25-60	79 (59.63)	12	12	25-60	7	5
S/P <25	27 (19.01)	7	45	10	3	0

OS: Overall survival, PFS: Progression-free survival, IL-6: Interleukin-6, RT: Radiotherapy, CR: Complete response, PR: Partial response, S/P <25: Stationary or progression, cGy: Centigray

Table 4. Univariate and multivariate analyses for OS

	Univariate		Multivariate	
Parameters	**HR (95% CI)**	**p-value**	**HR (95% CI)**	**p-value**
Stage I-II-III-IV	2.67 (1.35-5.29)	**0.005**	0.50 (0.16-1.59)	0.242
ECOG ≤2/>2	3.06 (1.58-5.91)	**<0.001**	2.71 (0.95-7.72)	0.062
Lymphocyte >15%/≤15%	0.47 (0.27-0.81)	**0.007**	0.84 (0.37-1.87)	0.667
Lymphocyte >15%/≤6%	0.52 (0.21-0.73)	**0.001**	0.48 (0.13-0.97)	**0.01**
IL-6 ≤7 pg/mL/>7 pg/mL	2.15 (1.19-3.87)	**0.011**	1.07 (0.45-2.56)	0.884
Total RT dose, ≥40-60/<40 Gy	0.96 (0.95-0.98)	**<0.001**	0.97 (0.95-1.00)	**0.026**
CT usedNo used	0.50 (0.29-0.86)	**0.013**	0.55 (0.30-1.01)	**0.055**
Pre-RT D-dimer <0.5/≥0.5 µg/mL	3.62 (1.88-7.00)	**<0.001**	3.42 (1.44-8.14)	**0.005**

OS: Overall survival, HR: Hazard ratio, CI: Confidence interval, ECOG: Eastern Cooperative Oncology Group, IL-6: Interleukin-6, RT: Radiotherapy, CT: Chemotherapy, Gy: Gray

Table 5. Univariate and multivariate analyses for PFS

	Univariate		Multivariate	
Parameters	**HR (95% CI)**	**p-value**	**HR (95% CI)**	**p-value**
Stage I-II-III-IV	2.67 (1.35-5.29)	**0.005**	0.50 (0.16-1.59)	0.242
ECOG ≤2/>2	3.06 (1.58-5.91)	**<0.001**	2.71 (0.95-7.72)	0.062
Lymphocyte >15%/≤15%	0.47 (0.27-0.81)	**0.007**	0.84 (0.37-1.87)	0.824
Lymphocyte >15%/≤6%	0.54 (0.20-0.75)	**0.001**	0.45 (0.12-0.99)	**0.01**
IL-6 ≤7 pg/mL/>7 pg/mL	2.15 (1.19-3.87)	**0.011**	1.07 (0.45-2.56)	0.974
Total RT dose ≥40-60/<40 Gy	0.96 (0.95-0.98)	**<0.001**	0.97 (0.95-1.00)	**0.026**
CT used/No used	0.50 (0.29-0.86)	**0.013**	0.55 (0.30-1.01)	0.055
Pre-RT D-dimer <0.5/≥0.5 µg/mL	3.62 (1.88-7.00)	**<0.001**	3.42 (1.44-8.14)	**0.005**

PFS: Progression-free survival, HR: Hazard ratio, CI: Confidence interval, ECOG: Eastern Cooperative Oncology Group, IL-6: Interleukin-6, RT: Radiotherapy, CT: Chemotherapy, Gy: Gray

Survival Rates

Five-year OS was 25% in patients with lymphocyte percentage >15% and 12.5% in patients with ≤15%.

Five-year OS was 30% in patients with IL-6 levels ≤7 pg/mL and 8% in patients with >7 pg/mL. Median PFS was significantly longer in patients with complete response (p<0.001) (Figure 1).

RT-related Toxicity

RT-related toxicity was determined using the Common Terminology Criteria for Adverse Events, (version 6.0) (25). Grade 2 hematological and other toxicities were seen in 84 (59.15%) patients. Worse hematologic toxicity (grade 3) was seen in 14 (9.85%) patients.

Discussion

LC remains an important cause of cancer-related death worldwide, despite advances in diagnostic and therapeutic methods (26).

Systemic inflammation plays a major role in the rapid progression of many cancers by increasing tumor angiogenesis, cancer cell proliferation, tumor metastasis, and also by affecting tumor response to systemic therapy (27).

Lymphocytes are essential components of the immune response, and low ALC is associated with poor prognosis and an immunosuppressive state in patients of cancer (28). The prognostic significance of lymphocyte percentages and levels of cytokines such as IL-6 in patients undergoing RT for advanced LC has become an area of increasing interest (1).

This study is consistent with previous studies suggesting that lymphocytes play an important role in antitumor immunity, contributing to improved treatment responses and prolonged survival. Lymphopenia, which usually occurs as a result of radiation-induced cytotoxic effects, has been reported to negatively affect survival outcomes by impairing immune surveillance against tumor cells (29,30). These findings suggest that assessing pretreatment lymphocyte percentages may be a valuable tool for clinicians in determining personalized treatment strategies and improving patient outcomes.

Our findings showed that patients with higher pre-RT lymphocyte percentages (>15%) exhibited significantly longer OS and PFS compared to those with lower percentages (≤15% and ≤6%). Notably, patients with lymphocyte percentages above this threshold had a median OS of 18 months and survived significantly longer than patients with lymphocyte percentages ≤15% and ≤6% (7 and 2 months). This correlation is consistent with previous studies that identified lymphocyte counts as prognostic biomarkers in various malignancies and emphasized their role in immune response and tumor microenvironment dynamics (29).

ILs are not only important inflammatory cytokines that play a role in tumor formation, but are also being evaluated as a potential target for tumor treatment. Studies on this subject have shown that IL-6 is increased in various types of cancer, including breast (31), colorectal (32), and LC (33). It has also been determined that it has proliferation and metastasis-promoting effects on cancer cells.

IL-6 is a well-known proinflammatory cytokine that plays a role in tumor progression, immune suppression, and treatment resistance. Elevated IL-6 levels have been associated with increased tumor burden, systemic inflammation, and poor prognosis in various malignancies, including LC (34). In our study, IL-6 level was also identified as an important prognostic factor. Patients with pre-RT IL-6 levels ≤7 pg/mL survived significantly longer than those with higher IL-6 levels (>7 pg/mL), with a median OS of 14 months.

Correlation analyses between patient characteristics and D-dimer levels before and after RT provided important information regarding the inflammatory and coagulatory pathways involved in disease progression in advanced LC. Significant correlations were observed between D-dimer levels and inflammatory markers such as IL-6 highlighting the negative role of systemic inflammation in cancer prognosis (35). High CRP level has also been associated with systemic inflammation and may serve as a prognostic indicator for poorer survival rates in various cancers, including LC (36).

Our univariate and multivariate analyses confirmed that low IL-6 levels, advanced disease stage (IV), poor ECOG

performance status (>2), and high D-dimer levels in LC were also significant negative prognostic factors, while higher lymphocyte percentages, RT dose and patient CT were associated with improved survival outcomes. These results highlight the complex interaction between systemic inflammation, immune response, and therapeutic efficacy in LC. Our study was carrıed out on the analysis of lymphocyte percentage and immune-inflammatory markers in advanced LC patients receiving RT.

Study limitations

This study's limitations are its retrospective nature and its relatively small sample size. Future prospective studies with randomised larger cohorts and molecular characterization of tumors may provide more detailed information about the immunological mechanisms underlying the observed associations.

Conclusion

This study suggests that pre-RT lymphocyte percentage and IL-6 level are important prognostic biomarkers in advanced LC patients undergoing RT. Monitoring these parameters may aid in risk stratification and treatment optimization. Furthermore, strategies aimed at regulating systemic inflammation and preserving lymphocyte counts may offer potential therapeutic benefits in improving survival outcomes in LC patients.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital Ethics Committee (decision no: 149, date: 07.05.2025).

Informed Consent: Informed consents were obtained from patients.

Footnotes

Authorship Contributions

Surgical and Medical Practices: K.Ç., H.S.K., Concept: K.Ç., H.S.K., Design: K.Ç., H.S.K., Data Collection or Processing: T.D.U., T.H.U., Analysis or Interpretation: K.Ç., H.S.K., Literature Search: K.Ç., T.D.U., T.H.U., H.S.K., Writing: K.Ç., H.S.K.

Conflict of Interest: No conflict of interest was declared by the authors.

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