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Research Letter to Editor

The usefulness of the Geriatric-8 screening tool and basic laboratory parameters in older patients with non-small cell lung cancer

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1. Introduction

Lung cancer, the third most common cancer, is the leading cause of cancer-related mortality and is frequently a disease of older patients [1]. As a result of the under-representation of older patients with lung cancer in clinical trials, there is a lack of scientific knowledge on how to select this patient group for different anticancer strategies [2]. It is critical to recommend appropriate treatment after evaluating frailty, life expectancy, and treatment-related potential toxicities for older patients with lung cancer. Comprehensive geriatric assessment (CGA) is the gold standard for multidimensional evaluation that determines medical, psychological, functional status, nutrition, cognition, social activity, support, and polypharmacy; however, this process is time-consuming [3]. Therefore, a two-step approach, beginning with a screening tool to select older patients with cancer who will benefit from CGA, has been proposed by the International Society of Geriatric Oncology (SIOG) [4]. The Geriatric-8 (G8) score, created for oncologists as a quick and useful screening tool for assessing the frailty of older patients [5], was found to have a high sensitivity in predicting abnormalities in the CGA and was also associated with survival and treatment-related complications [6]. Although G8 scores have been shown to be associated with overall survival (OS) after curative radiotherapy in older patients with cancer, the predictive value of G8 varies between various tumor types [7]. Regarding older patients with lung cancer, the diagnostic sensitivity of G8 is identified as reliable (89.8%) [8], and impaired G8 has been found to be an independent prognostic factor for OS in patients treated with chemotherapy or chemoradiotherapy (CRT) [9].

The prognostic significance of basic laboratory parameters such as hemoglobin, albumin, neutrophil-lymphocyte ratio (NLR), and thrombocyte-lymphocyte ratio (TLR), have been demonstrated in non-small cell lung cancer (NSCLC) [10]. In addition, the Glasgow prognostic score, which is a combination of albumin and C-reactive protein (CRP), has also been shown to be a predictive factor for OS and progression-free survival (PFS) in older patients with NSCLC treated with curative CRT [11]. A combination of G8 scores and basic laboratory parameters may cover the essential aspects of both nutritional and clinical characteristics, and provide a better prediction of survival in older patients with NSCLC than the G8 alone. Nevertheless, there is a paucity of studies examining the G8 screening tool and basic laboratory parameters together in older patients with NSCLC. The purpose of this study was to evaluate the role of G8 scores along with basic laboratory parameters in predicting PFS and OS of older patients with NSCLC undergoing radiotherapy.

2. Methods

After obtaining institutional ethical board approval (Number 2021–851), a retrospective analysis was performed on 61 patients with NSCLC aged ≥70 years who were treated with curative CRT or palliative radiotherapy to the thorax between January 2018 and November 2021. Patients with no histopathologic diagnosis, treated with immunotherapy agents, stereotactic radiotherapy, postoperative radiotherapy, and re-

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irradiation to previous radiation fields were excluded. The treatment strategy was determined based on the patient's age, Eastern Cooperative Oncology Group performance status (ECOG PS), and status of organ function, regardless of the G8 score. External-beam radiotherapy with a total dose of 30 to 40 Gy for palliative and 60 to 66 Gy for curative intent was administered using a 6–10 MeV linear accelerator. The concurrent chemotherapy regimen was weekly carboplatin and paclitaxel in the CRT group.

All patients underwent G8 screening by physicians before the beginning of treatment. The G8 score contains eight components: patient age (>85, 80–85, <80 years), and seven components from the original Mini Nutritional Assessment (MNA) [appetite, weight loss, mobility, neuropsychological problems, body mass index (BMI), medication, and self-rated health status]. For identifying frailty, a normal G8 cut-off value of fourteen has generally been considered appropriate. Patient characteristics such as age, sex, histology, ECOG PS, and stage were also collected. In addition, laboratory parameters related to systemic inflammatory response (SIR) such as complete blood count, albumin, and lactate dehydrogenase (LDH) were registered before treatment. Serum albumin levels <3.5 mg/dL were classified as hypoalbuminemia. LDH values over 250 U/L were considered high LDH. The neutrophil count divided by the lymphocyte count was defined as the NLR. The thrombocyte count divided by the lymphocyte count was defined as the TLR. Patients with NLR ≥5 and TLR ≥150 were evaluated to have SIR.

Descriptive statistics were performed to present baseline characteristics. The distribution of the participants' G8 scores and the accuracy of predicting PFS were examined using receiver operating characteristic (ROC) curve analysis and by determining a cut-off value using Youden's Index. A G8 score of ≤14 was used as the cut-off value because the cut-off value was calculated as 14.5 (area under the ROC curve (AUC) 0.69, 95% confidence interval (CI) 0.56–0.82) using Youden's Index. Survival curves were constructed using the Kaplan-Meier method, and the differences between the survival curves were examined using the log-rank test. Univariate Cox proportional hazards regressions were applied to estimate the individual hazard ratio (HR) for the PFS and OS. Significant variables in the univariate analyses ($p < 0.05$) were then used in the multivariate analysis. Spearman's correlation coefficient was used to assess correlations between the G8 score and laboratory parameters. *P*-values <0.05 were considered statistically significant. All statistical analyses were performed using the IBM SPSS Statistics version 24.0 software (Armonk, NY: IBM Corp. 2016).

Table 1
Patient and clinical characteristics at baseline.

Characteristic	$N = 61$
Age (years)	
70–80	55 (90.2%)
≥80	6 (9.8%)
Sex	
Female	5 (8.2%)
Male	56 (91.8%)
NSCLC histology	
Squamous	44 (72.1%)
Adenocarcinoma	17 (27.9%)
Stage	
Stage III	42 (68.9%)
Stage IV	19 (31.1%)
ECOG-PS	
0–1	46 (75.4%)
2–3	15 (24.6%)
G8 score	
≤ 14	32 (52.5%)
> 14	29 (47.5%)
Albumin level	
<3.5 mg/dL	19 (31.1%)
≥3.5 mg/dL	42 (68.9%)
LDH level	
≤250 U/L	48 (78.7%)
>250 U/L	13 (21.3%)
NLR level	
<5	39 (63.9%)
≥5	22 (36.1%)
TLR level	
<150	26 (42.6%)
≥150	35 (57.4%)

NSCLC non-small cell lung cancer, ECOG-PS Eastern Cooperative Oncology Group performance status, LDH lactate dehydrogenase, NLR neutrophil-lymphocyte ratio, TLR thrombocyte-lymphocyte ratio.

3. Results

Patient characteristics are summarized in Table 1. The median age was 72 (range, 70–89) years and most of the patients were male (91.8%). CRT was performed on 70.5% of the patients, and 29.5% of the patients received palliative radiotherapy to the thorax. The median follow-up period of patients was 12.3 (range, 1.7–46.1) months.

The median PFS was 14.2 months. As illustrated in Fig. 1a, the two-year PFS rate for normal and impaired G8 groups was 61.9% vs. 0.06%, respectively ($p = 0.001$). Univariate analysis demonstrated lower PFS for patients with palliative irradiation ($p = 0.001$), stage IV ($p = 0.001$), ECOG PS 2–3 ($p = 0.001$), impaired G8 scores ($p = 0.001$), lower albumin levels ($p = 0.001$), higher LDH levels ($p = 0.02$), higher NLR levels ($p = 0.02$), and higher TLR levels ($p = 0.01$). In multivariate analysis, G8 scores ($p = 0.004$) and treatment type ($p = 0.01$) remained significant prognostic variables for PFS.

The median OS was 18.5 months. As illustrated in Fig. 1b, the two-year OS rate for normal and impaired G8 groups was 82.8% vs. 0%, respectively ($p = 0.001$). In univariate analysis, the factors that predicted significantly poorer OS were palliative irradiation ($p = 0.001$), stage IV ($p = 0.001$), ECOG PS 2–3 ($p = 0.001$), impaired G8 scores ($p = 0.001$), lower albumin levels ($p = 0.001$), higher LDH levels ($p = 0.004$), higher NLR levels ($p = 0.001$), and higher TLR levels ($p = 0.005$). According to multivariate analysis, G8 scores ($p = 0.008$), albumin levels ($p = 0.004$), and treatment type ($p = 0.02$) remained significant prognostic variables for OS.

There was a positive correlation between G8 scores and albumin levels ($r = 0.499$, $p < 0.01$), and G8 scores were negatively associated with LDH ($r = -0.415$, $p < 0.01$), NLR ($r = -0.442$, $p < 0.01$), and TLR levels ($r = -0.441$, $p < 0.01$).

4. Discussion

In geriatric oncology practice, to avoid under-treatment and over-treatment, we need to predict patients who can respond to treatment and those who can tolerate treatment with geriatric assessments. Many geriatric screening tools are used for this purpose. Previous studies reported that the G8 screening tool was a useful predictive tool for survival in older patients with lung cancer [9,12]. Similarly, G8 was evaluated and found to be a statistically significant prognostic tool for OS in the present study. Moreover, we revealed that the G8 score was an independent prognostic factor for PFS. Although our analysis did not include acute and late toxicity, there are many studies in the literature

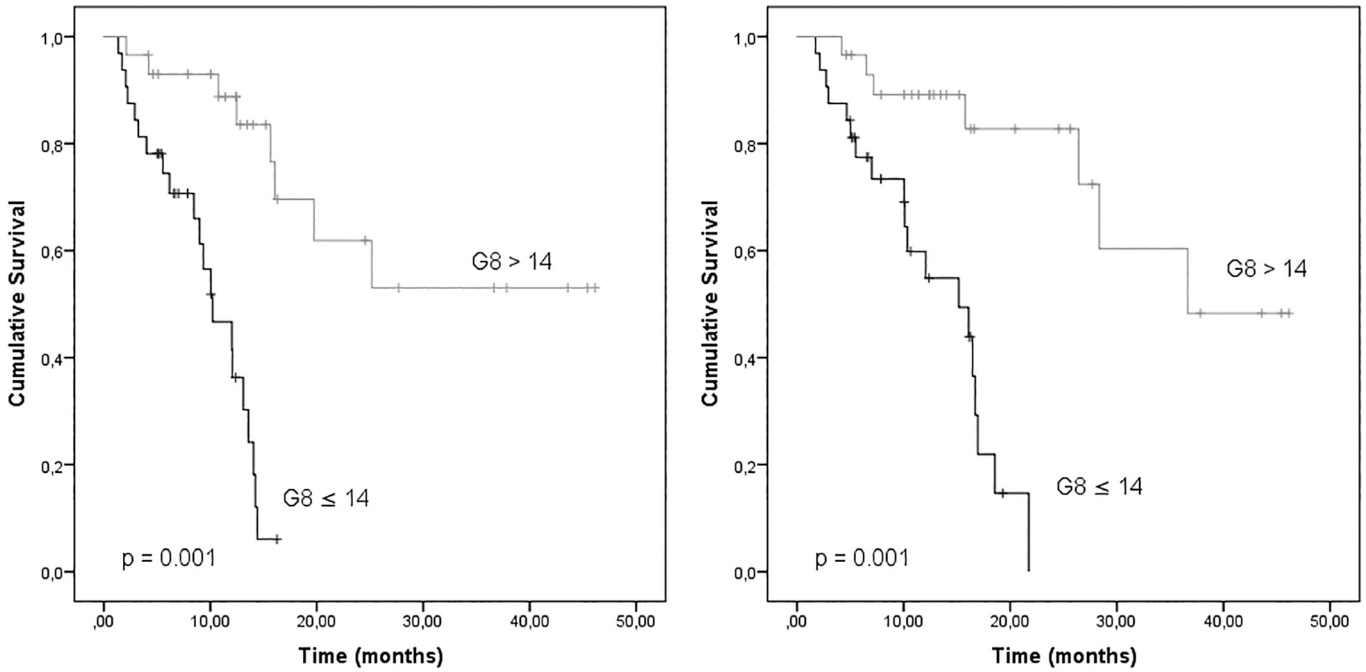


Fig. 1. a. Progression-free survival in the G8 score ≤ 14 and >14 groups. P values were calculated using the log-rank test with stratification according to the G8 score.
b. Overall survival in the G8 score ≤ 14 and > 14 groups. *P* values were calculated using the log-rank test with stratification according to the G8 score.

evaluating the relationship between G8 scores and toxicity. Middelburg et al. reported that there was no statistically significant relationship between G8 scores and grade 3 and higher late toxicity [7]. However, the study was underpowered for results about late toxicity due to the heterogeneous population and the considerable low incidence of late toxicity. By contrast, Cuccia et al. reported a correlation between G8 scores and late toxicity in older patients with early-stage NSCLC treated with hypofractionated stereotactic radiotherapy [13]. It can be concluded that G8 scores may contribute to treatment decisions in older patients with lung cancer. However, it should be kept in mind that the specificity of G8 is low and it can be combined with other geriatric screening tools [3,12].

Inflammation is the hallmark of every step of carcinogenesis in most cancers, including NSCLC. Additionally, inflammation is thought to play an important role in the development of frailty because many age-related conditions, such as dementia, depression, and sarcopenia, arise from inflammatory pathogenesis [14]. Albumin, LDH, NLR, and TLR, which are measures of systemic inflammation, are predictors of prognosis in NSCLC. However, studies evaluating the prognostic ability of systemic inflammation biomarkers in older patients with NSCLC are limited. According to the univariate analysis in our study, significantly worse PFS and OS were found in patients with lower albumin and higher LDH, NLR, and TLR. However, in multivariate analysis, only albumin levels remained a significant prognostic factor for OS.

The ECOG PS and Karnofsky performance status (KPS) are critical components in patient management because they influence treatment decisions. However, the performance status is a purely subjective assessment of a patient's physical activity and shows clear inter-observer variability [15]. Moreover, it was reported that geriatric assessments outperformed KPS in predicting severe toxicities in older patients receiving chemotherapy [16,17]. In the multivariate analysis in our study, impaired G8 scores and lower albumin levels were found to be independent prognostic factors for OS, whereas ECOG PS was not a statistically significant prognostic factor. As a result, G8 scores and laboratory parameters are as important as ECOG PS in prognosis evaluation. Moreover, we consider that G8 scores and basic laboratory parameters should be routinely assessed, as well as the ECOG PS, before making a treatment decision. In the future, a prospective study evaluating an "enhanced" version of the G8 (including laboratory parameters) against more commonly used assessments (such as the ECOG PS) may be considered to confirm these findings.

5. Conclusion

To the best of our knowledge, this is the first clinical study in older patients with NSCLC to combine the G8 screening tool with easily accessible, cheap, and easy-to-perform basic laboratory methods. Our study found that G8 scores were positively correlated with albumin and negatively correlated with LDH, NLR, and TLR in older patients with NSCLC. Moreover, we revealed that G8 scores and laboratory parameters were prognostic factors for PFS and OS. These findings suggest that the G8 screening tool and basic laboratory parameters can be used individually or in combination to predict prognosis and to prevent older patients with NSCLC from receiving inappropriate anti-cancer therapy.

Author Contributions

Study concepts and design: RA. Aksoy, V. Kaya.
Data acquisition: T. Koca.
Quality control of data and algorithms: A.F. Korcum.
Data analysis and interpretation: V. Kaya, A.F. Korcum.
Statistical analysis: R.A. Aksoy, V. Kaya.
Manuscript preparation: R.A. Aksoy.
Manuscript editing: V. Kaya.
Manuscript review: V. Kaya, A.F. Korcum.

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Ethical Approval

This study was approved by Akdeniz University Faculty of Medicine

Clinical Research Ethics Committee on 01.12.2021 (Decision number: 851).

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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