Prognostic Effects of Red Blood Cell Transfusion in Lung Cancer Patients Receiving Chemotherapy

Olcay Aycicek (olcayaycicek@yahoo.com)
Karadeniz Technical University Faculty of Medicine: Karadeniz Teknik Universitesi Tip Fakultesi https://orcid.org/0000-0002-0697-5680

Ahmet Oguzhan Kucuk
Karadeniz Technical University Faculty of Medicine: Karadeniz Teknik Universitesi Tip Fakultesi

Mehtap P. Kucuk
Karadeniz Technical University Faculty of Medicine: Karadeniz Teknik Universitesi Tip Fakultesi

Merve Ozdogan Algın
Karadeniz Technical University Faculty of Medicine: Karadeniz Teknik Universitesi Tip Fakultesi

Aysegul Pehlivanlar
Karadeniz Technical University Faculty of Medicine: Karadeniz Teknik Universitesi Tip Fakultesi

Funda Oztuna
Karadeniz Technical University Faculty of Medicine: Karadeniz Teknik Universitesi Tip Fakultesi

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Abstract

Introduction: The effects of blood transfusion on the prognosis in lung cancer patients are not yet clearly known, but it is frequently applied in clinical practice.

Aim: The aim of this study is to evaluate the relationship between blood transfusion frequency and disease prognosis in lung cancer patients receiving chemotherapy.

Results: A total of 405 patients were included in the study. Blood transfusion was performed in 96 (23.7%) of the patients. While the progression rate was 67.4% in the infected group, this rate was 47% in the non-infected group *(p<0.001)*, similarly, the median number of progressions was statistically significantly higher in the infected group *(p=0.001)*. While the rate of infection development was 68.8% in the transfused group, this rate was statistically significantly lower at 35.3% in the non-transfused group *(p<0.001).* It was determined that 21 (38.2%) of the patients who resulted in exitus were transfused with 3.1 ± 3.0 units to the mean, and an average of 2.81 ± 2.24 units of blood was transfused to 75 (21.4%) of the 350 (86.4%) surviving patients. While there is a statistically significant difference in terms of whether or not blood transfusion is performed in survived and non-survived patients *(p=0.011),* no significant difference was found in the average blood transfusion amounts per person *(p= 0.640).*

Conclusion: It was determined that red blood cell transfusions due to anemia during the disease in lung cancer patients who were treated with chemotherapy, adversely affected survival and disease progression.

Introduction

Lung cancer is a cancer type with a high incidence of cancer-related mortality and morbidity. During the follow-up of lung cancer patients, blood transfusion is often needed for reasons such as cancer-induced anemia, blood loss during surgery, or bone marrow suppression caused by chemoradiation (1, 2). Although Red Blood Cell (RBC) transfusion is a common practice in cancer patients, its effects on patient outcomes and possible complications are still not clearly explained, and there are considerable variations among physicians and institutions. The hypothesis that blood transfusions in various types of cancer may be harmful due to the possible immunosuppression effect has been investigated. This makes us think that in addition to the damage caused by cancer to the body, it may also lead to transfusion-related mortality and morbidity. In addition, transfusion-related infectious conditions and transfusion-related febrile/non-febrile reactions can be included among other conditions that cause concern in these patients. NCCN guidelines guides recommendations on the management of chemotherapy-induced anemia in lung cancer patients (3).

Although it has been studied in a large number of cancer types, few studies have followed the effects of red blood cell (RBC) transfusion throughout the disease course on patient outcomes in lung cancer. The aim of our study, specifically designed out of this curiosity, is to evaluate the relationship between blood transfusion frequency and disease prognosis in lung cancer patients receiving chemotherapy and to review our clinical practices.

Materials- Methods

1- Patients

Patients diagnosed with Small Cell Lung Cancer (SCLC) and Non-Small Cell Lung Cancer (NSCLC) and given chemotherapy between 01/01/2014-31/12/2018 in the Department of Chest Diseases of our Faculty of Medicine were included in the study. Patient data were collected retrospectively using file records and hospital automation system (clinical course, blood bank data, consultation records, etc.). Staging of the patients was performed according to the results of fluorine-18-fluorodeoxy glucose positron emission tomography/computed tomography, computed tomography, and brain magnetic resonance imaging. All patients who received adjuvant and neoadjuvant chemotherapy were included in the study.

The following parameters were defined as the exclusion criteria. Patients with known hematological malignancies other than lung cancer, age<18 years, patients with a second primary malignancy, patients who were treated with the diagnosis of anemia before the diagnosis of lung cancer, patients who were diagnosed with lung cancer in our clinic but did not continue their treatment in our

clinic, data integrity due to missing data Patients thought to be impaired were excluded from the study. Patient data were followed up until the patient were exitus or for a maximum of 24 months.

The primary outcome of the study was survival at 24 months, and the secondary outcome was the total number of progressions.

2- Data Collection

Demographic characteristics, comorbid diseases, cancer type and stage, how long he/she was followed with this diagnosis, Hb value before starting chemotherapy, whether red blood cell (RBC) transfusion was performed during the follow-up period, if so at which Hb value blood transfusion was applied, during the total follow-up period how many units of RBC or other blood product replacements they received, how many chemotherapy cycles they received in total, which chemotherapy drugs they received, whether there was a delay in treatment due to treatment-related anemia, the most common transfusion indications and complications (frequency of allergic reaction, febrile reaction, infection and thromboembolic complications) whether they received additional radiotherapy, whether they received GMC-SF for anemia, blood types, survival times, how many cancer progressions under treatment happened, and if there was distant metastasis, metastasis sites were reported.

The definition of anemia was made according to the definition of the World Health Organization (WHO) and Turkish Society of Hematology, and the lower limit of Hemoglobin (Hb) was 13 g/dL in men over 15 years of age, 12 g/dL in women over 15 years of age and nonpregnant, and in pregnant women it was taken as below 11 g/dL.

In our clinic, patients on a chemotherapy plan are hospitalized the day before, and blood parameters including hemoglobin are studied, and all patients are evaluated in detail before each cycle in terms of clinical and radiological suitability for chemotherapy, even if it is time for chemotherapy. In patients with active infection, the treatment regimen is delayed until after antibiotics. Likewise, the chemotherapy regimens of the patients whose blood transfusion decision is taken are also carried out in the post-transfusion period.

3- Ethical approval

The study was performed in accordance with the Declaration of Helsinki and was reviewed by the Karadeniz Technical University Faculty of Medicine Ethics Committee and was accepted with the ethics committee approval (Protocol no: 2019/263, Date: 08.11.2019)

4- Statistical Analysis

In the analysis of data; the conformity of the data to the normal distribution was examined using the Shapiro Wilk and Kolmogorow Smirnov tests. Kruskall-Wallis, Mann-Whitney U, student-t and chi-square tests were used for comparisons between groups. General linear models, Wilcowon and Friedman tests were used in serialized data. Data were given as percentage, mean (std deviation), and median (minimum-maximum). Chi-square test was used to compare the qualitative data. Categorical data were presented as frequency and percentage.

Findings

A total of 405 patients were included in the study. Of these patients, 380 (93.8%) were male and 25 (6.2%) were female. The median age was 63 (IQR: 57 – 70) years. 250 (61.7%) of the patients had at least one comorbidity. The most common comorbidities were cardiac disease (n: 149-36.8%) and respiratory disease (n: 87-21.5%) excluding lung cancer. It was observed that the survey of 55 (13.6%) of the patients included in the study was shorter than 24 months.

Anemia was present in 184 (45.4%) of the patients (male patients with a hemoglobin value below 13 g/dL and female patients with a hemoglobin value below 12 g/dL were considered anemic according to the definition of anemia by the World Health Organization). It was observed that 96 (23.7%) of all study patients received blood transfusion. Demographic and clinical information of the patients included in the study and transfused patients are given in

The mean Hb values of the transfused patients were 8.76±0.78, regardless of gender. It was determined that each patient received an average of 2.87±2.42 transfusions (Table 2). When the patients' Hb values requiring transfusion were analyzed, they were

respectively 8.76±0.78, 8.51±1.19, 8.56±0.90 g/dL in the 1st, 2nd, and 3rd transfusions. Since the number of patients requiring further transfusion was very small, they were not included in the evaluation.

Table 1
Baseline Demographic and Clinical Characteristics

	Transfused Patients	Total
	N:96 (23.7%)	N:405 (100%)
Sex		
Female	5 (5.2%)	25 (6.2%)
Male	91 (94.8%)	380 (93.8%)
Age (Mean±SD)	63.51±8.768	63.73±9.016
Female	57.40±15.662	64.67±9.309
Male	63.85±8.250	63.67±9.045
Comorbidities		
Cardiac	42 (43.8%)	149 (36.8%)
Respiratory	20 (20.8%)	87 (21.5%)
Neurological	6 (6.3%)	18 (4.4%)
Other	28 (29.2%)	91 (22.5%)
Type of cancer		
Squamous	32 (33.3%)	144 (35.6%)
Adeno	31 (32.3%)	141 (34.8%)
Adenosquamous	1 (1.0%)	3 (0.7%)
Small Cell	23 (24.0%)	63 (15.6%)
Large Cell	0 (0.0%)	13 (3.2%)
Carcinoid	0 (0.0%)	1 (0.2%)
Anaplastic	0 (0.0%)	1 (0.2%)
Mesothelioma	0 (0.0%)	3 (0.7%)
Untyped	9 (9.4%)	36 (8.9%)
Cancer Stage		
Stage I	4 (4.2%)	18 (4.4%)
Stage II	10 (10.4%)	65 (16.0%)
Stage III	36 (37.5%)	170 (42.0%)
Stage IV	46 (47.9%)	152 (37.5%)
Chemotherapeutics		
Cisplatin	81 (84.4%)	353 (87.2%)
Carboplatinum	37 (38.5%)	127 (31.4%)
Gemcitabine	47 (49.0%)	157 (38.8%)
Vincristine	11 (11.5%)	23 (5.7%)
Vinorelbine	29 (30.2%)	137 (33.8%)

	Transfused Patients	Total
Paclitaxel	0 0.0	5 (1.2%)
Docetaxel	44 (45.8%)	173 (42.7%)
Etoposide	25 (26.0%)	80 (19.8%)
Cyclophosphamide	11 (11.5%)	23 (5.7%)
Topotecan	12 (12.5%)	32 (7.9%)
Pemetrexed	9 (9.4%)	39 (9.6%)
Doxorubicin	10 (10.4%)	21 (5.2%)
Radiotherapy	60 (62.5%)	225 (55.6%)
Progressive Disease	67 (69.8%)	226 (55.8%)
Exitus	21 (21.9%)	55 (13.6%)
Survey (Month)	19.52±15.012	19.40±15.561

Table 2
Characteristics of Transfused Patients by Gender

	Anemic Patients	Hemoglobin Value Before First Transfusion (g/dl)	Number of Patients Transfused	Number of Transfusions
	no, %*	Mean±SD		
Female	5 (20%)	8.36 ± 0.47	5	2.6 ±1.81
Male	179 (47.1%)	8.78 ± 0.79	91	2.89±2.45
Total	184 (45.2%)	8.76 ± 0.78	96	2.87±2.42

*Represents the ratios in female, male and total patient groups.

The blood group of 266 (65.7%) of 405 patients included in the study was known. Of these 266 patients, 93 (35%) were blood transfused, in emergency conditions without knowing their blood type 3 patients were transfused with 0 Rh blood transfusion. Transfusion-related complications were not observed in any of these patients.

There was no statistically significant difference in the number of blood transfusions according to blood groups. During the follow-up period, 175 (43.2%) of all patients and 118 (44.4%) of 266 patients with known blood type were found to have a severe infection requiring antibiotic use. However, there was no statistically significant difference between blood groups in terms of infection development (Table 3). There was no significant correlation between the number of transfusions with age (r=-0.043, *p=0.680*) and infection rate (r=-0.037, *p=0.454*).

Table 3
Evaluation of Transfused Patients by Blood Groups

	A Rh⁻ N= 23	A Rh⁺ N= 109	B Rh⁻ N= 4	B Rh⁺ N= 28	0 Rh⁻ N= 12	0 Rh⁺ N= 78	AB Rh⁻ N= 3	AB Rh⁺ N= 9	*P*
Transfusion-no. (%)	6 *(26.1)*	43 *(39.4)*	0 *(0)*	10 *(35.7)*	3 *(25)*	28 *(35.9)*	1*(33.3)*	2 *(22.2)*	*0.645*
Infectionneededantibiotherapytreatment-no. (%)	10 *(43.5)*	44*(40.4)*	2 *(50)*	12 *(42.9)*	7 *(58.3)*	37 *(47.4)*	1 *(33.3)*	5 *(55.6)*	*0.916*

The cancer type distribution of the patients is given in Table 4. The most common type of cancer detected was squamous cell lung cancer with 144 (22.2%) patients. No statistically significant difference was found in the number of blood transfusions according to cancer types *(p=0.156)* (Table 4).

Table 4

Evaluation of Transfusion Needs by Cancer Types

	Untyped n= 36	Squamous n= 144	Adeno n= 141	Large Cellular n= 13	AS n= 3	Carcinoid n= 1	Small Cell n= 63	Anaplastic n=1	Mesothelioma n= 3	*P*
T no (%)	9 *(25)*	32 *(22.2)*	31*(22)*	0 *(0)*	1 *(33.3)*	0 *(0)*	23 *(36.5)*	0 *(0)*	0 *(0)*	*0.156*

	Stage 1 n= 18	Stage 2 n= 65	Stage 3 n= 170	Stage 4 n= 152	*P*
Transfusion no. (%)	4 *(22.2)*	10 *(15.4)*	36 *(21.2)*	46 *(30.3)*	*0.081*
Transfusion Count-unıt,mean ± sd	2.5 ± 1.73	1.78 ± 0.83	2.92 ± 2.05	3.13 ± 2.9	*0.490*

T: Transfusion, AS: Adenosquamous

When the 405 patients included in the study were grouped according to stages, the highest number of patients was in the Stage 3 group with 170 (42%). This was followed by the Stage 4 group with 152 (37.5%) patients. There was no statistically significant difference between the number of patients who were transfused according to the stages *(p= 0.081).* There was no statistically significant difference in the mean blood transfusion amounts between the stages *(p=0.490).*

Treatment delay due to anemia was observed in 18 (4.4%) of the patients. While 4 (22.2) of these 18 patients died, the mortality rate in the group without treatment delay due to anemia (387-95.4%) was 13.2% with 51 patients *(p=0.286).* There was no statistically significant difference in the progression rates in both groups *(p=0.825)* (Table 5).

Table 5
The Relationship Between Anemia and Delayed Treatment

	Delayed of Therapy Due to Anemia		
	Yes	**No**	P
	n=18	n=387	
Exitus-no. (%)	4 *(22.2)*	51 *(13.2)*	*0.286*
Progresyon-no. (%)	11 *(61.1)*	215 *(55.6)*	*0.825*

Table 6
The Relationship Between Transfusion and Infection Development and Disease Progression

	Infeciton Needed to Atb Treatment		
	Yes	**No**	P
	n=175	n=230	
Progresyon-no. (%)	118 *(67.4)*	108 *(47)*	<0.001
Progresyon count-median (IQR)	1 *(1-2)*	0 *(1-2)*	0.001
Transfusion need-no. (%)	66 *(37.7)*	30 *(13)*	<0.001
Transfusion count-unıt, median (IQR)	2 *(1-4)*	2 *(1-3.25)*	*0.372*
	Transfusion		
	Yes	**No**	P
	n=96	n=309	
Infeciton need to atb treatment-no. (%)	66 *(68.8)*	109 *(35.3)*	< 0.001
Pneumoia-no. (%)	22 *(22.9)*	91 *(29.5)*	*0.206*
Upper respiratory tract infection-no. (%)	5 *(5.2)*	22 *(7.1)*	*0.668*
Progresyon-no. (%)	67 *(69.8)*	159 *(51.5)*	0.002
Progresyon count-median (IQR)	1 (1-2)	1 (0-2)	0.001
* Percentages may not total 100 because of rounding. Some patients have more than one infection			

Infection requiring antibiotics was detected in 175 (43.2%) of the patients. The progression rate was 67.4% in the infected group, while this rate was 47% in the non-infected group *(p< 0.001)*, similarly, the median number of progressions was statistically significantly higher in the infected group *(p=0.001)*. While the rate of infection development was 68.8% in the transfused group, this rate was statistically significantly lower at 35.3% in the non-transfused group. *(p<0.001).* A statistically significant positive weak correlation was found between the administration of transfusion to the patients and the development of infection (r= 0.287, *p<0.001*).

While the rates of infection development were found to be statistically different in the transfused and non-transfused groups, this statistical significance was not detected in pneumonia and upper respiratory tract infections (*p=0.206*, p=0.668, respectively).

While progression was observed in 67 (69.8%) of transfused patients this rate was 51.5% in non-transfused patients *(p= 0.002).* As well as the progression rates, there was a statistically significant difference in the number of progressions between the groups that received and did not receive transfusion *(p=0.001)* (Table5).

By transfusing the patient (r=-0.027, *p=0.587)* and the amount of transfusion (r= 0.106, *p= 0.306*) no statistically significant difference was found between the length of hospital stay. There was no statistically significant correlation between the transfusion and the total length of hospital stay. Similarly, there was no statistically significant correlation between the amount of transfusion and the total length of hospital stay.

Neutropenia developed in 78 (81.3%) of 96 transfused patients and 149 (48.2%) of non-transfused patients *(p<0.001).* In connection with this, GM-CSF treatment was also higher in the transfused group *(p<0.001).*

GM-CSF was administered to 49 (12.1%) of 405 patients included in the study. While the rate of infection development was 77.6% in the GM-CSF-administered group, this rate was statistically significantly lower with 38.5% in the non-administered group (p<0.001). However, there was no difference between the two groups in terms of the development of pneumonia or upper respiratory tract infection. (p=0.787, p=0.865, respectively).

It was observed that 55 (13.6%) of the 405 patients included in the study died within a 24-month period. Majority of the patients with exitus (30-54.5%) consisted of Stage IV patients and there was a significant difference between them and the other stages (p=0.042). It was determined that 21 (38.2%) of the patients who resulted in exitus were transfused with 3.1 ± 3.0 units to the mean, and an average of 2.81 ± 2.24 units of blood was transfused to 75 (21.4%) of the 350 (86.4%) surviving patients. While there is a statistically significant difference in terms of whether or not blood transfusion is performed in surviving and non-survived patients *(p=0.011)*, no significant difference was found in the average blood transfusion amounts of per person *(p= 0.640)*

No significant correlation was found between the amount of transfusion and mortality with Univariate logistic regression analysis (*p=0.665*, B=1.043 (CI 95% 0.861-1.263)

Discussion

Anemia is a common condition in the treatment process of cancer patients. The aim of this study is to detect lung cancer cases who received red blood cell transfusion due to anemia and to evaluate the results of transfusion-related patients.

Tumor-associated anemia may occur in lung cancer patients may occur due to tumoral factors and tumor treatment-related factors. Chemotherapy-induced anemia (CIA) often develops in patients with cancer who are treated with myelosuppressive chemotherapy (4, 5, 6). On the other hand, it has been shown that when diagnosed with cancer, patients already have a significant risk of anemia, almost five times that of healthy people.

In our study, the data of 405 patients were scanned and 184 of these patients were detected as anemia (45.4%), 96 (23.7%) of all patients were with transfused red blood cells (RBC). According to the latest current guidelines, RBC transfusion should not be performed according to a certain “threshold value” or “trigger point”. The NCCN panel view draws attention to 3 important points; 1. Observation and periodic reassessment should be performed in asymptomatic patients without serious comorbidities. 2. Transfusion may be considered in patients receiving high-risk intensive chemotherapy and radiotherapy if there is a progressive decrease in Hb level, or in asymptomatic patients with comorbidities (cardiac disease, chronic pulmonary disease, cerebral vascular disease). 3. Transfusion should be applied in symptomatic patients (such as tachycardia, tachypnea, chest pain, exercise dyspnea, syncope). The onset, severity, and duration of anemia, as well as other factors affecting tissue oxygen delivery, are related to the clinical manifestations of anemia. Adaptation to the process in chronic anemias depends on heightened cardiac output, increased coronary flow, altered blood viscosity, oxygen consumption and extraction. The decision to correct anemia mainly depends on the individual characteristics of the patients, the severity of the anemia, the severity of comorbidities, and the clinical judgment of the physician (3).

In newly diagnosed cancer patients; Kenar et al. evaluated that metastatic disease, deficiencies such as iron, B12 and folate, gastrointestinal cancer, and a history of previous tumor surgery are possible risk factors (7). Direct infiltration of the bone marrow by cancer cells, reduction of RBC production by causing iron sequestration of cancer cells and shortening its life, chronic blood loss from tumoral areas, deterioration in oral intake and deterioration in the coagulation system can be evaluated as the causes of anemia seen in patients with cancer. All these reasons are mechanisms that increase proportionally with cancer weight (8, 9, 10).

The main purpose of RBC transfusion is to increase the oxygen carrying capacity to provide tissue oxygenation. In 2016, the American Association of Blood Banks made several recommendations suggesting that the threshold values of 7 g/dL Hb in hospitalized and hemodynamically stable patients, and 8 g/dL Hb levels in patients with orthopedic, cardiac surgery or known cardiovascular disease require transfusions (11). However, this recommendation did not include cancer patients. NCCN panelists state that a single value cannot be determined for all patients in the transfusion decision, and this decision should be made according to the individual risk/benefit ratios for the patient. In our study, the patients with an average value of 8.76 ± 0.78 Hb received transfusions based on not only the clinical assessment but also the finding that cardiac disease (36.8%) was the most common comorbidity.

In several reports, the mean Hb level was 9 g/dL, 9.5 g/dL, 9.7 g/dL before starting iron supplementation, transfusion or ESA use in cancer patients (12, 13, 14). Rather than a specific absolute value, studies have identified anemia symptoms as an important clinical indicator in the decision to transfusion, in contrast to non-cancer anemia states (15). In general, fatigue is not a major indication for transfusion other than cancer. In our study, 55 (13.6%) of 405 patients diagnosed with lung cancer died within a 24-month period. It is determined that while 38.2% of these patients (median 3.1 ± 3.0 units) were transfused, 21.4% (mean 2.81 ± 2.24 units) of 350 surviving patients were blood transfused *(p=0.011)*. It was observed that 24-month mortality increased with blood transfusion. However, there was not a dose-dependent association between the amount of blood transfusions and survival outcomes of patients with lung cancer. There are few studies examining transfusion outcomes during routine chemotherapy in lung cancer patients. In a meta-analysis including 12,175 patients with lung cancer and 23 studies, it is found that blood transfusions were associated with decreased survival. However, only 1 of these studies evaluated transfusions during chemotherapy and perioperative transfusion results were evaluated in other patients (16). In the study of Sakin et al., similar to our results in this study, red blood cell transfusion was significantly associated with earlier progression and shorter survival. This study is important because it is the first study that evaluates transfusion outcomes in metastatic NSCLC patients. In this study, 87 patients who received blood transfusion were included and patients with small cell lung cancer and non-metastatic were not included. (17). In our study, there were 96 patients in the transfusion group and the results of all patients who received chemotherapy with the diagnosis of lung cancer were evaluated. Aoe et al. reported that regardless of the need for transfusion, survival was significantly shorter in 298 patients with anemia (median survival time (MST): 7.5 months) compared to 313 patients without anemia (MST: 11.8 months, P<0.0001) (18). As found in our study, there may be several possible reasons for more frequent blood transfusions in non-surviving patients; one of these can be explained as the fact that many chemotherapy agents cause myelosuppression and lead to anemia, and severe cancer patients are exposed to a longer and high-dose chemotherapy burden. In addition, the initial stages of non-survival patients in our study were more advanced and this may increase the need for blood transfusions in accordance with the anemia hypotheses. Another reason is the higher incidence of infectious complications, as determined in our study with frequent blood transfusions. In our study, the rate of infection requiring antibiotic use was 68.8% in the transfused group, while this rate was 35.3% in the non-transfused group. *(p<0.001).* In addition, the primary disease progression rate was found to be significantly higher in the infected group (67.4%) and this may have contributed to the increased mortality rates in the high group with transfusion frequency. The incidence of sepsis due to bacterial infections, which is one of the undesirable transfusion-related complications, is reported as less than 10 per year (19, 20). In a randomized controlled trial with 31 RCTs and 12587 patients, restrictive transfusion strategy was suggested and for nosocomial infections, there was a significant higher risk of infection among patients receiving fresher RBCs (21). On the other hand, recognition of the immunosuppression caused by frequent transfusions for cancer patients has raised concerns that blood transfusions may increase the risk of cancer recurrence, particularly after curative surgery (22). Over the past four decades, it has been estimated that blood transfusions cause cancer progression by reducing the immunity of patients. (23). Primer disease progression, which is an important prognostic indicator in lung cancer patients, was observed more frequently in patients who underwent transplantation in our study. Our results are important because they are one of the latest and rare data on transfusion in patients with lung cancer receiving chemotherapy. In fact, although the life-threatening risk is lower, the most common nonhemolytic transfusion reactions associated with RBC transfusion are expected. Hemolytic reactions, febrile reactions, lung damage, transfusion associated circulatory overload can be counted as other possible complications, but since our study was retrospective, these data could not be clearly reached in our patients.

One of our interests in our study was whether there was a delay in treatment in patients due to anemia. The chemotherapy of a small number of our patients (18 patients 4.4%) was delayed until after replacement or anemia treatment was arranged due to

anemia, but this did not cause any difference in disease progression or mortality.

A. Tiotiu et al. rated the frequency of chemotherapy-induced anemia (CIA) in lung cancer and emphasized the impact on patients' quality of life. They stated that maintaining a normal Hb level is important in improving the quality of life of these patients and recommended reducing the number of blood transfusions and initiating treatment with ESA (Erythropoietin Stimulating Agents) in symptomatic patients. They recommended that it should be used at the lowest effective dose and sharing the results with patients to avoid from increased risk of thromboembolism, accelerated tumor progression, decreased survival, and major cardiovascular adverse reactions and blood transfusion (24). ESAs stimulate erythropoiesis in patients with low Hb levels, but their effects appear weeks later, and an Hb increase of 1 g/dL was observed in only 65% of patients (25). The current guideline recommends that ESAs should not be used in cancer patients who are not receiving myelosuppressive therapy. Except the patients requiring blood transfusion and those in palliative care, the NCCN panelists do not recommend routine ESA treatment to increase Hb levels (3). ESA was not applied to any of the patients in our study. In the data of our study, in parallel with the data of our country, the most common cancer type was determined as SCC (22.2%) and no difference was observed in the need for blood transfusion according to cancer types and stages.

The limitations of our study can be listed as follows; 1. Since our study was planned retrospectively, patients who received immunotherapy were not included. 2. The effects of radiotherapy applied to patients have not been examined. 3. While detecting infections requiring antibiotics, data loss may happen because the focus of infection in some patients cannot be fully learned from retrospective records. Only pneumonia and upper respiratory tract infection data were included. 4.The assessments of iron stores ore iron treatments were not recorded. 5. Complications associated with transfusion therapy were not recorded.

As a result of our study, it was determined that red blood cell transfusions due to anemia during the disease in lung cancer patients who underwent chemotherapy, adversely affected survival and disease progression. Although the exact mechanism is not known, it is thought that transfusion-related immunomodulatory effects are effective on this result. We intend that our study will contribute to the literature as one of the few studies in the literature in this isolated patient group.

Declarations

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No financial disclosure was declared by the authors.

Conflicts of interest/Competing interests:

No conflict of interest was declared by the authors

Availability of data and material:

Corresponding author is the responsible for all data and material. If data is necessary, data could be supplied from corresponding author.

Code availability:

Not applicable.

Authors' contributions:

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Olcay Aycicek, Mehtap P. Kucuk, A. Oguzhan Kucuk, Aysegul Pehlivanlar, Merve Ozdogan Algın and Funda Oztuna. The first draft of the manuscript was written by Olcay Aycicek and Mehtap P. Kucuk and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript."

Ethics approval:

Approval was granted by the Clinical Research Ethics Committee of Karadeniz Technical University (Protocol no: 2019/263, Date: 08.11.2019).

Consent to participate:

This study was performed in line with the principles of the Declaration of Helsinki. After ethcial approven all data were obtained from records of hospital. Ethics Committee has confirmed that no consent to participate form from patients is required.

Consent for publication:

After ethcial approven all data were obtained from records of hospital. This is an observational study. The Karadeniz Technical University Clinical Research Ethics Committee has confirmed that no consent for publication from patients is required.

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