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Serum Albumin Levels as an Independent Predictor of Hospital Mortality in COVID-19 Pneumonia

Gülçehre Oğuztürk[1], Ekrem Cengiz Seyhan[1*], Mehmet Atilla Uysal[1], Elif Yelda Niksarlıoğlu[1], Nurdan Şimşek Veske[1], Emine Şahin[1]

[1]Department of Chest Diseases, Yedikule Training and Research Hospital for Chest Diseases and Thoracic Surgery, Health Science University, İstanbul, Türkiye

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[*]***Corresponding Author***
Ekrem Cengiz Seyhan
Department of Chest Diseases
Yedikule Training and Research Hospital for Chest Diseases and Thoracic Surgery
Health Science University, İstanbul, Türkiye
Phone: +90 5052654417
E-mail: drekremcs@yahoo.com

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Authors' ORCIDs
Gülçehre Oğuztürk
https://orcid.org/0000-0001-9531-4448
Ekrem Cengiz Seyhan
https://orcid.org/0000-0001-6639-2797
Mehmet Atilla Uysal
https://orcid.org/0000-0002-0430-498X
Elif Yelda Niksaroğlu
https://orcid.org/0000-0002-6119-6540
Nurdan Şimşek Veske
https://orcid.org/0000-0001-6817-3416
Emine Şahin
https://orcid.org/0000-0002-2114-9213

Abstract: COVID-19 is associated with systemic inflammation, contributing to disease progression and mortality. This study evaluates the prognostic significance of inflammatory markers, particularly serum albumin, in predicting hospital mortality in COVID-19 pneumonia patients. A retrospective cohort study included 200 patients hospitalized with COVID-19 pneumonia. The relationship between inflammatory markers (CRP, procalcitonin, ferritin, NLR, PLR, LMR, and albumin), disease severity, and hospital mortality was analyzed using multivariate logistic regression. The mean age was 56.7 ± 16 years, with an in-hospital mortality rate of 16.5%. Univariate analysis identified albumin, CRP, PSI, CT-SS, and NLR as potential predictors of mortality. Multivariate analysis confirmed that low albumin levels ($p<0.001$), PSI ($p<0.001$), and CT-SS ($p<0.001$) were independent prognostic factors. Serum albumin is a cost-effective and widely available biomarker independently predicting hospital mortality in COVID-19 pneumonia. Its routine measurement may assist in early risk stratification. ©2025 NTMS.

Keywords: Albumin; Inflammatory Markers; Hospital Mortality; COVID-19 Pneumonia.

1. Introduction

Coronavirus disease 2019 (COVID-19) is an inflammatory illness by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that manifests as a variety of symptoms ranging from none to severe pneumonia [1]. The inflammatory reply induced by SARS-CoV-2 viral replication and cellular death can collect macrophages and monocytes, resulting in the exrication of chemokines and cytokines [2]. These cytokines and chemokines subsequently attract and activate immune cells, resulting in cytokine storms [2]. Cytokine storms cause severe damages to multiple organs. Therefore, circulating inflammatory markers that might depict inflammation and immunological state are possible predictors of COVID-19 patient prognosis [2].

A growing body of data suggests that inflammatory respond play an essential role in the course of COVID-19 [3-5]. Several studies have stated that biomarkers in COVID-19 patients are linked with multiple organ insufficiency and severe systemic disease.

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Inflammatory markers such as C-reactive protein (CRP), serum ferritin, erythrocyte sedimentation rate (ESR), procalcitonin (PCT), and interleukin-6 (IL-6) have been related to an increased chance of progressive severe COVID-19 [6]. However, the prognostic role of serum albumin, an established negative acute-phase reactant, has not been sufficiently emphasized.

COVID-19 mortality rates in hospitalized patients have been reported to vary between 4% and 28% [7-10]. In order to quicken the results of COVID 19 patients in the hospital, parameters to predict mortality that can be applied easily and quickly are needed. In this context, we aimed to analyze the relationship between inflammatory markers and the clinical and radiological severity of the disease in patients with COVID-19 pneumonia and to investigate the influence of these markers (especially of serum albumin) on hospital mortality.

2. Material and Methods

2.1. Study Population

A retrospective cohort study was performed on patients with COVID-19 pneumonia hospitalized in our hospital between April 2020 and October 2020. Before or during the hospitalization, all patients had their SARS-CoV-2 nucleic acid real-time polymerase chain reaction (RT-PCR) results verified positively using samples taken from oropharyngeal swabs or sputum and had abnormal CT findings diagnosed as viral pneumonia. Cases with malignancy, chronic renal disease, liver disease, human immunodeficiency virus infection, tuberculosis, and fungal infection, a history of receiving steroids, chemotherapy, or radiotherapy were excluded. The investigate was carried out under the Declaration of Helsinki (1989) of the World Medical Association, and this study was approved by the Ethics Committee (28.1.2020/ E3200- 509). Written informed consent was acquired from the patients who participated in this study.

2.2. Demographic Data

Demographic information (age, gender, body mass index [BMI], current smoking status, medical history, and drug use), clinical features, chest computed tomography (CT) scan findings, laboratory results, treatment methods, hospitalization times, and results (discharge, intensive care referral, and death) were obtained from the electronic medical record system.

2.3. Clinical Severity Assessment

Pneumonia severity index (PSI) was used to define the clinical severity of the patients. Patients were assigned to risk classes I–V based on their calculated PSI score. Patients in risk classes I to III were considered to have "non-severe pneumonia," whereas those in risk classes IV or V were supposed to have "severe pneumonia."[11].

2.4. Chest CT Severity Score (CT-SS) Assessment

The disease was categorized according to the Chest CT involvement of patients with COVID-19 pneumonia. (https://radiologyassistant. nl/chest/lk-JG-1.) The percentage of involvement of each of the five lobes with involvement was calculated. (<5% involvement: 1 point; 5-25% involvement: 2 points, 26-49% involvement: 3 points, 50-75% involvement: 4 points, > 75% involvement: 5 points).

2.5. Laboratory Testing

The hematological analysis was performed with a Mindray BC-6800 hemogram device (Beckman Coulter, Fullerton, California). Albumin, RDW, ferritin, PCT, and CRP were measured using commercially available kits based on routine methods with an automated analyzer (Hitachi cobras 6000-cobuse 601, Hitachi Ltd, Tokyo, Japan). Fibrinogen was estimated using Stago STA Compact Max. In the study group, blood gases were obtained from the radial artery (ABL 800 FLEX, Radiometer, Bronshoj, Denmark).

2.6. Statistical Analysis

The data acquired in the study were analyzed statistically using R software version 3.5.1/2018-7-01 (Bell Laboratories, Lucent Technologies, New Jersey, USA). Continuous variables with a normal distribution are expressed as mean±standard deviation (SD). Continuous variables with a non-normal distribution are summarized as median (interquartile range [IQR]). The Student's t-tests were used to compare mean values, while as Mann-Whitney U test was used to compare the non- normal distributed continuous variables. The Chi-square and Fisher's exact tests were used to compare frequency distributions. Receiver operating characteristic (ROC) analysis was used to develop a cut-off value for inflammatory marker levels for distinguishing severe COVID-19 pneumonia patients from non-severe COVID-19 pneumonia patients. The same research and comparisons were also performed to classify the COVID-19 pneumonia patients as mortal or non-mortal. Binary logistic regression analysis was used to find independent predictors for mortality and severe in COVID-19 pneumonia patients**.** For this analysis, variables with a significance level less than $p<0.10$ in univariate analysis were considered as candidate variables for multiple analysis (Model 1). Variables with $p<0.05$ in Model 1 were included in the multiple model (Model 2). A statistically significant value of $p<0.05$ was used.

3. Results

3.1. Demographic, Clinical, Laboratory and Radiological Characteristics

A total of 200 patients (mean age, 56.7 ± 16 years; range, 20–86 years) with COVID-19 pneumonia were included in the study. The mean duration of symptoms before hospital admission was 8±3 days. More than half of the patients (40%) had at least one comorbidity. When the clinical severity of the patients was evaluated, the patients were categorized into the non-severe group (134 cases) and severe (66 cases) groups.

The levels of CRP, fibrinogen, ferritin, and PCT increased in 189 (94%), 141 (70%), 60 (30%), and 14 (7%) patients on admission, respectively. On the other hand, the levels of albumin decreased by 62 (31%). The predominant CT characteristics consisted of ground-glass opacity (82%), bilateral sides involved (71%), peripheral distribution (65%), and lower lung predominant (68%). The median CT-SS was 5.5 (3-11). The demographic, radiological, and clinical characteristics of the patients are demonstrated in Table 1.

3.2. Receiver Operating Curve (ROC) Analyses

The optimal cut-off levels in the estimation of severe COVID-19 pneumonia were 3.60 g/L, 108 mg/L, 0.08 ng/mL, 457 mg/dL, 325ng/mL, 12 %, 3.51, 2.44 and 265 for albumin, CRP, PCT, fibrinogen, ferritin, RDW, NLR, LMR, and PLR, respectively. ROC analysis revealed that RDW, NLR, albumin, and ferritin were the most effective markers in estimating the severity of COVID-19 pneumonia (Table 2). However, these markers were not significantly different from each other (*albumin vs. PCT, p=0.068; albumin vs. ferritin, p=0.551, albumin vs. NLR, p=0.348)* (Figure 1).

The optimal cut-off levels in the estimation of mortal COVID-19 pneumonia were 3.40 g/L, 119 mg/L, 0.08 ng/mL, 400 mg/dL, 330 ng/mL, 13.50 %, 4.10, 2.70 and 328 for albumin, CRP, PCT, fibrinogen, ferritin, RDW, NLR, LMR, and PLR, respectively. ROC analysis revealed that CRP, NLR, albumin, and PCT were the most effective markers in classifying COVID-19 pneumonia as mortal or non-mortal than the other markers (Table 2). However, these markers were not significantly different from each other (*albumin vs. PCT, p=0.211; albumin vs. CRP, p=0.079, albumin vs. NLR, p=0.783)* (Figure 2).

3.3. Outcomes

The mean follow-up duration was 7 (5-11) days. Of the patients, 33 (16.5 %) had died (29 in intensive care and 4 in the service department), 39 (19%) had been referred from the intensive care unit, and 158 (79%) had been discharged from the hospital. Factors that were found to affect the clinical severity on the univariate analysis (*p<0.1*) (PCT, ferritin, fibrinogen, albumin, RDW and CRP levels, CT-SS, NLR, smoking status, and lymphocyte count) were used in a binary regression analysis for multivariate analysis of the factors that may affect the clinical severity (Table 3). The analysis showed that NLR (*p=0.003*), and albumin (*p=0.002*) were both independent factors (Table 4).

Factors that were found to affect the hospital mortality on the univariate analysis (*p< 0.1*) (PCT, PSI, ferritin, albumin and CRP levels, CT-SS, NLR, age, and lymphocyte count) were used in a binary Logistic regression analysis for multivariate analysis of the factors that may affect the hospital mortality (Table 5). The analysis showed that albumin levels (*p<0.001*), PSI (*p<0.001*), and CT-SS (*p<0.001*) were both independent prognostic factors (Table 6).

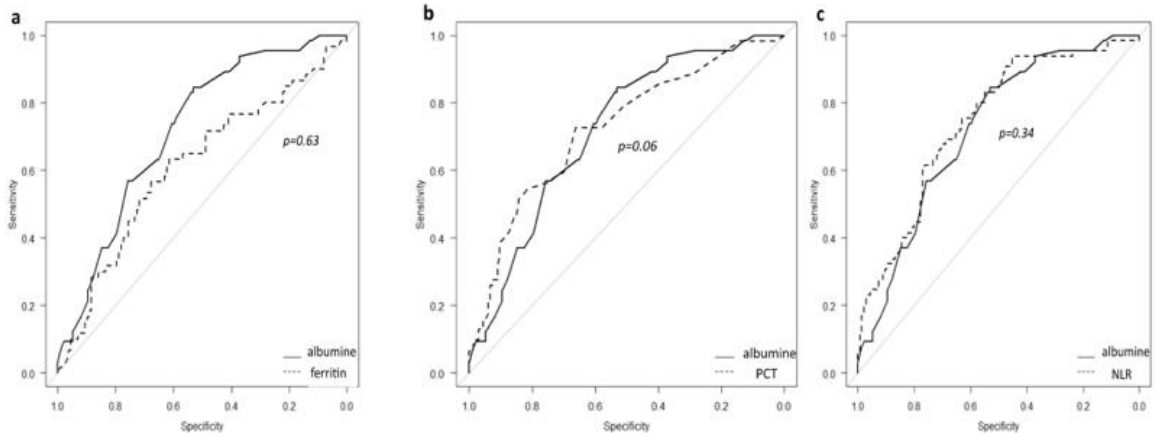

Figure 1: Comparison of ROC analysis of albumin, PCT, ferritin and NLR in the ROC curves of the biomarkers in clinical severity of COVID-19 pneumonia; (AUC values are not different from each other significantly; AUC; 0.70, 0.72, 0.67 and 0.72, respectively); (albumin vs. PCT, p=0.068; albumin vs. ferritin, p=0.551, albumin vs. NLR, p=0.348).

Table 1: Demographic, clinical and radiologic characteristics of the study population (n=200).

Variables	Value
Age, years [a]	56.77±16
Gender, (male)n(%)	113(56)
Comorbidities, n(%)	80(40)
Diabetes mellitus	19(10)
Cardiovascular Disease	21(22)
Cerebrovascular Disease	9(5)
Chronic pulmonary Disease	22(11)
Others	9(10)
BMI(kg/m^2)[a]	28.45±5.12
Active smoking	87(43)
PSI risk class	
I/II/III/IV/V, n	36/48/51/47/18
CT features; n,(%)	
GGO	164(82)
Consolidation	108(54)
Nodular opacities	30(15)
Inverted halo sign	41(21)
Pleural effusions	8(4)
Bilateral involved	142(71)
Peripheral distribution	130(65)
CT-SS[b]	5.50(3-11)

[a]Results given as mean±SD; [b]Results given as median(Interquartile rage(IQR)); n, number of cases; Others; sleep apnea Syndrome (3), asthma (4), hypothyroidy (2), BMI: Body Mass Index, PSI: Pneumonia Severity Index, GGO: Ground Glass Opacity, (CT-SS): Chest CT Severity Score.

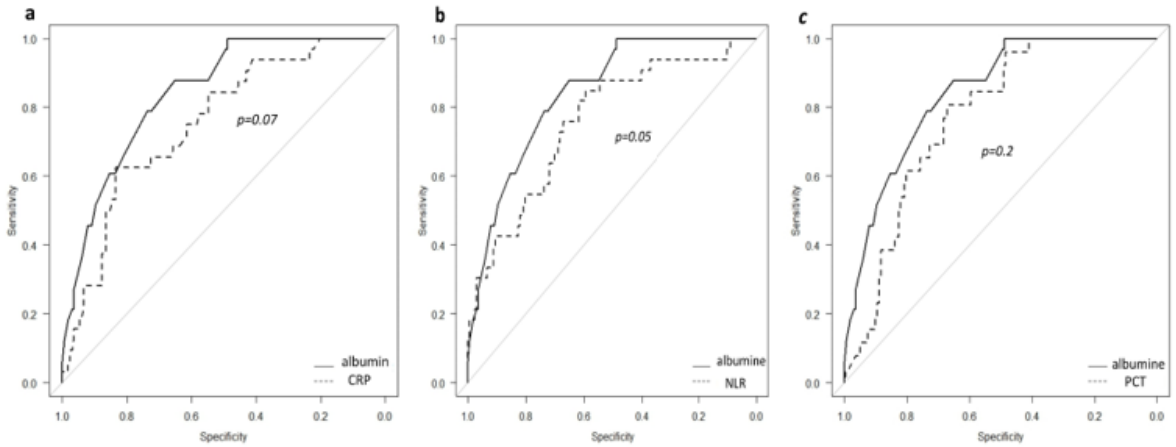

Figure 2: Comparison of ROC analysis of albumin, CRP, PCT and NLR in the ROC curves of the biomarkers in the estimation of mortal COVID-19 pneumonia; (AUC values are not different from each other significantly; AUC; 0.84, 0.75, 0.80 and 0.75, respectively); (albumin vs. PCT, p=0.211; albumin vs. CRP, p=0.079, albumin vs. NLR, p=0.783).

Table 2: Diagnostic performance of the inflammatory markers in estimating severe vs. non-severe, and mortal vs. non-mortal COVID-19 pneumonia patients.

Groups	**Variables (The best cut-off levels)**	**Sensitivity/Specificity (%)**	**AUC Area** (95% CI)
Severe vs. non-severe patients	Albumin; 2.60 g/L	53/84	0.70 (0.61-0.79)
	CRP; 108 mg/L	45/78	0.67 (0.63-0.75)
	Ferritin; 325 ng/mL	80/42	0.62 (0.50-0.70)
	Fibrinogen; 457 mg/dL	55/66	0.61 (0.52-0.71)
	LMR; 2.44	55/73	0.63 (0.55-0.72)
	NLR; 3.51	45/83	0.72 (0.67-0.81)
	PLR; 265	78/38	0.53 (0.55-0.72)
	PCT; 008 ng/mL	66/72	0.72 (0.64-0.80)
	RDW; 12%	63/61	0.59 (0.45-0.69)
Mortal vs. non-mortal patients	Albumin; 2.42 g/L	65/87	0.84 (0.77-0.92)
	CRP; 119 mg/L	83/62	0.75 (0.66-0.84)
	Ferritin; 330 ng/mL	62/85	0.64 (0.54-0.74)
	Fibrinogen; 400 mg/dL	32/82	0.61 (0.50-0.73)
	LMR; 2.72	43/78	0.61 (0.49-0.72)
	NLR; 4.13	59/84	0.75 (0.66-0.85)
	PLR; 328	82/36	0.59 (0.47-0.71)
	PCT; 008 ng/mL	62/90	0.80 (0.73-0.90)
	RDW; 13.51%	56/63	0.60 (0.50-0.71)

AUC; area under ROC curve; CI; Confidence Interval, PCT; procalcitonin, CRP; C-reactive protein, RDW; Red Blood cell distribution Width, NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio; LMR, lymphocyte monocyte ratio

Table 3: Univariate analysis of variables in patients with COVID-19 pneumonia between the severe and non-severe group.

	Non- severe patients (n=134)	**Severe patients (n=66)**	**Significance**
Gender (Male), n, (%)	71 (53)	42 (63)	*0.128*
BMI (kg/m2) [a]	28.82±5.40	27.50±5.81	*0.140*
Chest CT Severity Score [b]	5 (3-9)	6.6 (3-13.50)	***0.049***
Laboratory variables			
Lymphocyte count, [b]	1360 (980-1820)	1100 (710-1435)	***<0.001***
RDW (%) [a]	13.42 ± 1.71	14 ± 2.72	***0.001***
CRP (mg/L) [b]	39 (14.30-78)	74 (10.91-133)	***0.005***
NLR [b]	2.8 (1.92-5)	5.4 (3.71-12)	***<0.001***
PLR [b]	188 (110-304)	200 (131-399)	*0.323*
LMR [b]	2.7 (1.51-3.55)	2 (1.12-2.72)	*0.130*
Albumine, (g/L) [a]	3.02 ±0.53	2. 22 ±0.42	***<0.001***
PCT, (ng/mL) [b]	0.05 (0.03-0.11)	0.15 (0.06-0.30)	***<0.001***
Fibrinogen, (mg/dL) [b]	438 (379-566)	504 (414-613)	***0.017***
Ferritin,(ng/mL) [b]	192 (87-403)	318 (139-703)	***0.013***

[a] Results given as Mean± SD. [b]Results given as median (Interquartile rage(IQR));, PCT; procalcitonin, CRP; C-reactive protein, RDW; Red blood cell distribution width, NLR, neutrophil–lymphocyte ratio; PLR, platelet-lymphocyte ratio; LMR, lymphocyte monocyte ratio; BMI: Body mass index, n; number of cases, The bold footnotes show the statistical meaning.

Table 4: Binary logistic regression analysis of variables between the severe and non-severe patients.

C	Model 1		Model 2	
	OR(95%CI)	**Significance**	**OR(95%CI)**	**Significance**
Chest CT Severity Score [b]	1.106(1.012-1.208)	**0.026**	1.030(0.973-1.089)	0.310
Laboratory variables				
Lymphocyte count, [b]	1.000(0.999-1.001)	0.590		
RDW (%) [a]	1.212 (0.950-1.546)	0.122		
CRP (mg/L) [b]	0.998 (0.991-1.006)	0.675		
NLR [b]	1.076 (1.000-1.158)	**0.050**	1.091(1.030-1.155)	**0.003**
Albumin, (g/L) [a]	0.907(0.827-0.995)	**0.040**	0.894(0.833-0.60)	**0.002**
PCT, (ng/mL) [b]	2.815(0.906-8.752)	0.074		
Fibrinogen, (mg/dL) [b]	1.001 (0.999-1.004)	0.278		
Ferritin,(ng/mL) [b]	0.999(0.998-1.000)	0.119		

[a] Results given as Mean± SD. [b] Results given as median (Interquartile rage(IQR)), OR, odds ratio; CI; Confidence Interval, PCT; procalcitonin, CRP; C-reactive protein, RDW; Red blood cell distribution width, NLR, neutrophil–lymphocyte ratio; Hb; hemoglobin, The bold footnotes show the statistical meaning.

Table 5: Univariate analysis of variables between survived and non-survived in COVID-19 pneumonia patients.

	Non-survivors (n=33)	**Survivors (n=167)**	**Significance**
Age (years) [a]	66.21±13	54.80±15	***<0.001***
Gender (Male), n, (%)	22 (66)	91 (54)	*0.250*
Comorbidities; n, (%)	19(60)	35 (64)	*0.129*
BMI (kg/m2) [a]	26.42±5.52	28.85±5.71	*0.146*
PSI [a]	115±33	69±14	***<0.001***
Chest CT Severity Score [b]	15 (10-20)	5 (3-8)	***<0.001***
Laboratory variables			
Lymphocyte count, [b]	1000 (412-1335)	1310 (970-1810)	***<0.001***
RDW	14.42 ± 1.83	13.82 ± 2.20	*0.290*
CRP (mg/L) [b]	126 (57-171)	39 (14-92)	***<0.001***
NLR [b]	6.81 (4.52-16.53)	3.33(2.11-5.70)	***<0.001***
PLR[b]	188 (120-364)	169 (113-269)	*0.173*
LMR [b]	1.97 (1.07-3.40)	2.43 (1.51-3.64)	*0.440*
Albumin, (g/L) [a]	2.41±0.44	3.61 ±0.42	***<0.001***
PCT, (ng/mL) [b]	0.21 (0.09-0.37)	0.06 (0.03-0.12)	***<0.001***
Fibrinogen, (mg/dL) [b]	481 (419-611)	451 (369-599)	*0.135*
Ferritin,(ng/mL) [b]	509 (304-786)	192 (82-411)	***0.017***

[a]Results given as Mean± SD, [b] Results given as median (Interquartile rage(IQR)), PSI; Pneumonia severity index, PCT; procalcitonin CRP; C-reactive protein, RDW; Red blood cell distribution width, NLR, neutrophil–lymphocyte ratio; PLR, platelet-lymphocyte ratio; LMR, lymphocyte monocyte ratio; BMI: Body mass index, CT-SS; Chest CT Severity Score, n; number of cases, The bold footnotes show the statistical meaning.

Table 6: Binary logistic regression analysis of variables between the survived and non-survived patients.

	Model 1		Model 2	
	OR(95%CI)	**Significance**	**OR(95%CI)**	**Significance**
Age (years) [a]	**0.897(0.810-0.994)**	**0.039**	0.958(0.899-1.022)	0.192
PSI [a]	**1.102(1.040-1.168)**	**0.001**	**1.077(1.036-1.119)**	**<0.001**
Chest CT Severity Score [b]	1.380(1.176-1.618)	**<0.001**	**1.304(1.166-1.459)**	**<0.001**
Laboratory variables				
Lymphocyte count, [b]	0.999(0.997-1001)	0.181		
CRP (mg/L) [b]	0.998 (0.986-1.010)	0.727		
NLR [b]	1.014 (0.924-1.112)	0.774		
Albumin, (g/L) [a]	0.703 (0.552-0.895)	**0.004**	**0.689(0.568-0.835)**	**<0.001**
PCT, (ng/mL) [b]	0.906(0.645-1.273)	0.568		
Ferritin,(ng/mL) [b]	0.990(0.947-1.002)	0.538		

a Results given as Mean± SD. b Results given as median (Interquartile rage(IQR)), OR, odds ratio; CI; Confidence Interval, PCT; procalcitonin, CRP; C-reactive protein, NLR; neutrophil–lymphocyte ratio, The bold footnotes show the statistical meaning.

It was determined that the side effects developed after vaccination lasted 4.0 ± 2.6 days on average.

The relationship between the local side effects and the participants' demographic data are given in Table 3. Accordingly, local pain was significantly higher in young participants who had no chronic disease, had a previous COVID-19 history, had never smoked and were students in the health field. The local redness was significantly higher in participants with a history of COVID-19 (P<0.05). While abscess and bleeding more than normal were found to be related to age (respectively P=0.002 and P=0.001), local pain was found to be related to gender (P<0.001).

The systemic side effects and the participants' demographic data are presented in Table 4. Systemic side effects such as arthralgia, increased blood pressure, weakness, and fatigue were found to be significantly more common in younger participants (P<0.05). When systemic side effects were compared according to gender, it was found that many side effects, such as fatigue, headache, myalgia, and high blood pressure, were significantly more common in women. Regarding the participants' occupations, systemic side effects such as fatigue and joint pain were significantly more common in nurses and midwives, who were primarily female.

When systemic side effects were evaluated according to whether there was a chronic disease, many systemic side effects, such as joint pain and muscle pain, were more common in those without chronic disease. At the same time, only high blood pressure was found to be significantly more common in those with chronic disease. While alcohol consumption did not cause any side effect differences (P>0.05), fatigue, headache, and joint pain were significantly higher in nonsmokers. Shaking was associated with gender, ocupation and presence of chronic disease, loss of taste was associated with presence of chronic disease, and runny nose was associated with gender and ocupation (P<0.05 for all).

In terms of a previous history of COVID-19, only myalgia and fever were significantly more common among systemic side effects in people without previous COVID-19. In terms of known allergy history, many side effects, such as weakness, fatigue, and headache, were more common in those without a history of allergy. In contrast, taste loss, lymph node swelling and postvaccine allergy development were significantly higher in individuals with an allergic constitution (P<0.05).

4. Discussion

Inflammatory responses play a key role in viral clearance and in determining the clinical course of COVID-19 pneumonia. An exaggerated response, such as a cytokine storm, contributes to disease severity and increased mortality in the absence of timely intervention. In our study, low serum albumin levels-a negative acute phase reactant-were significantly associated with in-hospital mortality in patients with COVID-19.

A meta-analysis of 16 retrospective studies showed that inflammatory markers such as PCT, CRP, IL-6, and ESR are significantly associated with COVID-19 severity [13]. In another study, ROC curve analysis was used to determine optimal cut-off values for NLR, PLR, and LMR, with NLR showing the highest prognostic accuracy for distinguishing mild and severe cases (optimal threshold: 3.3) [14]. These findings support the role of an exaggerated inflammatory response in severe disease progression. In line with previous research, our

study found that patients with severe COVID-19 had lower albumin levels and higher CRP, PCT, ferritin, and fibrinogen levels. ROC analysis in our cohort also identified optimal thresholds for albumin, PCT, NLR, and ferritin, which showed the highest sensitivity, specificity, and AUC for predicting clinical severity. These results suggest that monitoring inflammatory markers may serve as an early warning tool to prevent progression to severe COVID-19.

In-hospital mortality rates among patients with COVID-19 pneumonia vary across regions, ranging from 8% to 21% [7-10]. A meta-analysis of 56 studies including 8,719 patients found that WBC, CRP, PCT, ESR, and IL-6 levels were significantly higher in patients with mild disease and in those who died during follow-up, compared to survivors [15]. Previous studies have identified advanced age, comorbidities (e.g., diabetes, hypertension, chronic lung and cardiovascular diseases, cancer), severe disease, respiratory failure, elevated D-dimer and CRP levels, lymphopenia, and secondary infections as predictors of mortality [4,7-10,16]. Consistent with the literature, our univariate analysis showed that multiple inflammatory markers were associated with mortality. However, multivariate analysis revealed that only low albumin levels were independently predictive of death. Based on our findings, low serum albumin may serve as a critical warning marker, and patients with hypoalbuminemia should be monitored more closely during hospitalization for COVID-19 pneumonia.

CRP is a systemic nonspecific pro-inflammatory marker of the acute phase response that can be used to detect inflammation, infection, and tissue damage. In most studies, the CRP level was recognized as having a positive association with the severity of COVID-19 [13, 17-19]. It has been reported in these studies that it can be used as an early predictive inflammation marker for severe COVID-19. Our research found CRP to be one of the factors indicating disease severity in patients with COVID-19 pneumonia.

The neutrophil-to-lymphocyte ratio (NLR) is an inflammatory marker associated with mortality in various diseases [20,21]. In COVID-19, elevated NLR may reflect dysregulated cytokine production, increased pathogenic neutrophils, and lymphocyte apoptosis. [21] NLR has been identified as an independent risk factor for severe disease in COVID-19 patients [22-24]. Several studies have shown that high NLR levels correlate with clinical progression, with one reporting a threshold of 3.3 for predicting severity [13]. In our study, an NLR cut-off of 3.5 showed high sensitivity, specificity, and AUC in identifying severe disease. Multivariate analysis confirmed NLR as an independent predictor of clinical severity, suggesting its potential as a reliable prognostic marker in COVID-19 pneumonia.

Procalcitonin (PCT) is a commonly used inflammatory marker in clinical practice. Several studies have shown that PCT levels are significantly higher in patients with severe COVID-19 [6,25]. A meta-analysis of 16 retrospective studies reported a positive association between elevated PCT and disease severity, with a fivefold increased risk of severe infection. [25, 26] In our study, although PCT levels were higher in severe cases and non-survivors, multivariate analysis showed no independent association with severity or mortality. This may be due to the use of initial PCT values at admission and the fact that mortality in COVID-19 is more closely linked to cytokine storm than to bacterial co-infection.

Serum ferritin, an acute-phase reactant used to diagnose iron deficiency anemia, can also be elevated in viral infections. Studies on COVID-19 have shown mixed results regarding its association with disease severity and mortality [27-29]. Wu et al. found elevated ferritin linked to ARDS, but not survival [28]. Zhou et al. reported a correlation between high ferritin and mortality in univariate analysis, but no multivariate analysis was performed [29]. In our study, univariate analysis showed higher ferritin levels in severe and non-survivor groups compared to non-severe patients, but no significant correlation was found between ferritin levels and hospital mortality or clinical severity in multivariate analysis.

Inflammatory mediators reduce albumin production during severe disease to prioritize the synthesis of other acute phase reactants. In addition, these mediators increment vascular permeability, allowing albumin to flee into the extravascular space, eventually resulting in low serum albumin levels [30]. In severe COVID-19, significantly decreased albumin levels are likely due to extensive systemic inflammation [31, 32]. Several previous studies have shown that low albumin levels are associated with disease severity and hospital mortality in patients with COVID-19 pneumonia [16, 31-33]. Hypoalbuminemia was an independent predictor of mortality in COVID-19 pneumonia patients, according to a retrospective cohort study of 299 patients [16]. The risk of death was increased at least 6-fold independently in COVID-19; if serum albumin level was <3.5 g/L at presentation according to this retrospective study. According to the results of our ROC analysis to predict in-hospital mortality, albumin levels reached 0.84 AUC and we found that albumin levels below 3.5 g/L had a predictive probability ratio of 5.61. Some studies identified PCT and ferritin as significant predictors, but in our multivariate model, albumin remained the sole independent biomarker. In addition, in support of other studies, we determined that low albumin levels were strongly associated with disease severity and were the only inflammatory marker that independently affected hospital mortality in multivariate analysis. Our findings reinforce the role of albumin as a reliable, cost-effective, and easily accessible biomarker for mortality risk in COVID-19 pneumonia. Unlike other inflammatory markers, albumin is routinely measured in clinical practice, making it practical for early risk stratification.

5. Conclusion

In conclusion, measurement of inflammatory markers, especially CRP, PCT, NLR, and albumin levels, might assist clinicians in monitoring and assessing the severity of COVID-19. Serum albumin is a strong, independent predictor of hospital mortality in COVID-19 pneumonia. Given its accessibility, it should be integrated into routine risk assessment models for COVID-19 patients.

Limitations of the Study

There are several drawbacks to this study. First, the tiny patient cohort in this study may have altered the statistical significance of the results. Second, we did not investigate the relationship between inflammatory indicators and viral loads. Furthermore, in this study, the inflammatory marker levels were reviewed on admission only. Perhaps the final inflammatory marker values, or changes in inflammatory marker values, are also indicators of disease severity.

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The content of the publication is entirely the authors' responsibility, and the authors examined and edited it as necessary. Each author states that the submitted article, either in full or in part, has not been previously published or is not being assessed for publication as an original article in either printed form or as digital media.

Conflict of Interests

The authors declare that there is no conflict of interest and this study was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

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Ethical Approval

The study was approved by Health Science University, Yedikule Training And Research Hospital For Chest Diseases And Thoracic Surgery, Ethics Committee 1 with approval number (28.1.2020/ E3200- 509)

Data sharing statement

The data presented in this study are available on request from the corresponding author.

Consent to participate

Consent was obtained from the patients participating in the study.

Informed Statement

Informed consent was obtained from all subjects involved in the study.

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In the Early Period (first 1 month) of the Covid 19-SARS-CoV-2 Pandemic, the Guidance of Computerized Tomography in Patient Diagnosis and Its Correlation With PCR Test in Emergency Services

Ayca Calbay[1*], Gülşen Çığşar[2], Zamir Kemal Ertürk[3], Atıf Bayramoğlu[4]

[1]Department of Emergency Medicine, Training and Research Hospital, Atatürk University, Erzurum, Türkiye
[2]Department of Emergency Medicine, Ministry of Health Etlik City Hospital, Ankara, Türkiye
[3]The Scientific and Technical Research Council of Türkiye, Ankara, Türkiye
[4]Department of Emergency Medicine, Faculty/ of Medicine, Alaaddin Keykubat University, Antalya, Türkiye

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****Corresponding Author***
Ayça Calbay
Department of Emergency Medicine
Training and Research Hospital
Atatürk University, Erzurum, Türkiye
Phone: +90 5334496104
E-mail: drycshn@gmail.com

Doi: 10.56766/ntms.1599912

Authors' ORCIDs
Ayca Calbay
https://orcid.org/0000-0002-7031-2689
Gülşen Çığşar
https://orcid.org/0000-0001-8377-5239
Zamir Kemal Ertürk
https://orcid.org/0000-0001-6837-2028
Atıf Bayramoğlu
https://orcid.org/0000-0003-3053-1956

Abstract: The first identification in our country for the COVID-19 disease was in March. Quick and valuable diagnostic methods for this disease are critical in the management of covid and non-covid patients. With this study, we arranged to investigate the compatibility of the utilized of computed thorax tomography as a scanning and diagnostic tool with PCR tests in the primary period (first 1 month) of the Covid 19 pandemic. Patients over the age of 18 whose chest CT scans were taken from feasible and positive Covid 19 cases who admitted to Ankara Etimesgut Şehit Sait Ertürk Hospital Emergency Department in the primary period of the Covid 19 pandemic (first 1 month) were included in the study. The study started on 15.05.2021 and finished on 30.05.2021 and a retrospective analysis was made. Statistical analysis of the study was performed with SPSS Version 20.0 program. The study was managed with a total of 393 patients. Of these, 259 were male and 134 were female. Between the radiological detections, the results with the highest sensitivity were GGO, atelectasis, presence of nodules, fibrosis, nodule formation and interlobular thickening. Thickness of interlobules and pleural effusion were had the high rise PPV. There are radiological detections that can be used in the identification of Covid 19: Thickness of interlobules and pleural effusion.©2025 NTMS.

Keywords: Covid 19; PCR; Torax CT; Ground Glass Opacity; Thickness of Interlobules.

1. Introduction

The first coronavirus disease case in Turkey occurred for the first time in our country in March and it was in connection with the Wuhan outbreak that began on December 31, 2019. As of March 11, 2020, the WHO had declared the viral infection a world pandemic and that became the turning point on the healthcare systems all over the globe. For the management of the patients with and without COVID-19, effective and rapid diagnostic techniques are of extreme importance.

According to the guidelines for diagnosis and treatment of COVID-19, the 'gold standard' for diagnosis is RT-PCR tests. However, RT-PCR is susceptible to false negative outcomes in certain instances. In addition, these tests were not cheap and there was often a delay in receiving test results in the first phase of the epidemic. These difficulties triggered the investigation of additional diagnostic methods such as chest CT scan as it was thought to help in differential diagnosis. For

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instance, systematic review and meta-analysis by Kim et al. demonstrated that chest CT had sensitivity of 94% (95% CI: 91%-96%) but only 37% (95% CI: 26%-50%) for specificity.

Not only are there cases of symptomatic disease, there are also many asymptomatic people who exhibit high transmission potential during the pandemic. Therefore, a screening methods such as chest CT should be used to complement RT-PCR tests to control the spread of the virus. Early detection through chest CT in individuals traced to confirmed COVID cases may identify a higher number of infections than RT-PCR.

The common symptoms of COVID-19 are fever as well as cough and shortness of breath. Patients may also experience diarrhea, muscle pain, and headaches. Laboratory markers such as lymphopenia, increased CRP, increased D-dimer and procalcitonin all good biomarkers for prognosis. Chest CT is the most useful technique for diagnosis of disease, with identified findings such as multiple plaque-like opacities, interstitial changes in the lungs, and bilateral ground-glass opacities. All these findings have a definite peripheral and subpleural distribution. Moreover, a chest CT could be very useful for monitoring a patient's progress of treatment. It was also benefical impact on patients who were RT-PCR negative in following period. However, worsening symptoms, with subsequent chest CT scans that aided in their management and long-term physiological monitoring. They can also be assessed with chest CT after the Resolution of COVID: Acute Respiratory Distress Syndrome (ARDS) and Pulmonary Embolism (PE).

The purpose of this study was to assess the effectiveness of chest CT as a diagnostic and screening tool comparing with PCR testing in emergency settings. Furthermore, we aimed to study the reduction of false-negative results in patients tested negative by RT-PCR.

2. Material and Methods

The study involved patients aged 18 and older who underwent chest CT scans for suspected or confirmed COVID-19 cases at the Emergency Department of XXX Hospital during the primary period of the COVID-19-SARS-CoV-2 pandemic.

The COVID-19 clinic was integrated into the emergency department at the hospital where the study was conducted. The patient's management and treatment plans was coordinated by the emergency medicine, chest diseases, and infectious diseases specialists. Throughout the pandemic, between 1,500 and 2,000 patients was admitted the hospital daily. 98% of whom were considered at risk for COVID-19, excluding those in the red-zone triage or needing resuscitation.

This study started on May 15, 2021, and ended on May 30, 2021. All data were retrospective. Data were collected by individually reviewing patient files through the hospital's information management system. Ethics committee acceptance was acquired from Ankara Dışkapı Training and Research Hospital (decision number 113/03, dated June 14, 2021).

The management of pandemic by the Ministry of Health has defined risk groups concerning Covid 19 infection with some criteria from the first days of the pandemic. These criteria are: 1. Any of the following symptoms: Fever, joint and muscle pain, cough, shortness of breath, headache, nausea/vomiting, or diarrhea; 2. Travel from a pandemic country; 3. Contact with a possible or diagnosed case of Covid infection. These serve as the criteria for determining patients who have been assessed for admission and discharge with thoracic CT scan via the emergency room and outpatient clinics for Covid 19.

During the first month of initiating the study, 419 patients presented to the emergency department with a COVID diagnosis. Among these patients were 7 younger than 18, leaving 412 eligible for study participation. Of these, 19 had no thoracic CT imaging performed, resulting in a final study cohort of 393 patients. The case diagram for the study is presented in Figure 1.

Figure 1: The case diagram of the study.

2.1. Statistical Analysis

SPSS Version 20.0 program (SPSS Inc, Chicago, Illinois, USA) was applied for Statistical survey. Percentage frequency evaluation was performed for categorical data of demographic features such as age and gender. Chi-square (x2) test was used to differantiate categorical data. A P value of <0.05 was noted statistically significant.

3. Results

The mean age of patients in the study was 46 with an age range between the ages of 18 to 91. Out of them, 259 were males while 134 females. The PCR positivity rates, in male patients were 45.42% and in female patients were 46.47%. The differences were statistically insignificant (p=0.672). Lung involvement (AC) in PCR-positive patients was observed bilaterally in 53.7% of cases. The right lung alone was in 14.1%, and the left lung alone was in 11.9%, 20.3% of cases' images showed no infiltration.

In patients with negative PCR test, 47.2% demonstrated bilateral lung infiltration while 12% of them did not (p=0.009). Meningitis affecting just one side was mainly the right axilla in 19.8%, while lower lobe involvement was often reported at 18.6%. There were also bilateral infections were in 50.1% (Figure 2). Bilateral consolidated area, were observed in 43%, whereas no consolidation was found in 61.8%.

Additional radiological findings commonly observed in viral pneumonias and useful in diagnosing COVID-19 are abstracted in Table 1. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of these radiological indicators are detailed in Table 2.

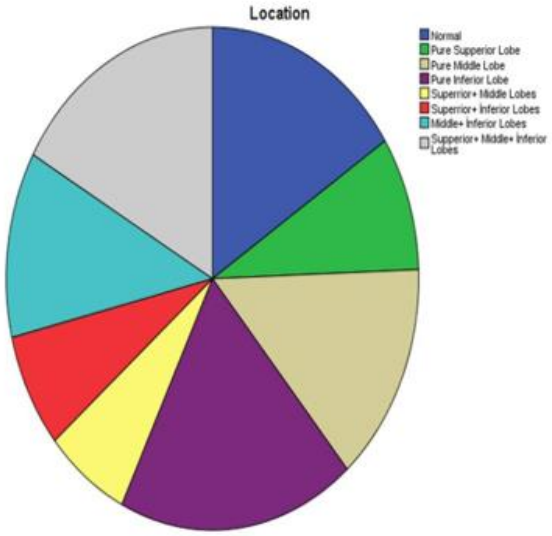

Figure 2: Lung location of infiltrations.

Table 1: Frequency of radiological definitions in cases.

Radiological sign	Single involvement (%)	Multiple involvement (%)
Interlobular septal thickening	1.3	1.5
Reticular pattern	3.3	1.8
Crazy paving	0.5	1
Air bronchograms	3.6	2.8
Bronchial wall thickening	4.1	4.8
Bronchiectasis	1.5	1.3
Pleural thickening	2.3	1.3
Pleural effusion	1.3	0.3
Nodule	8.1	15
Pericardial effusion	1	-
Budding tree view	3.6	0.3
Fibrotic changes	4.3	12
Ground glass opacity	12	43
Atelectasis	3.8	12.2

Table 2: Sensitivite, spesifite, positive predictive value (PPV) and negative predictive value (NPV) of the radiologic definitions (BCO; Ground Glass Opacity-GGO).

		PCR Results					
		Positive	Negative	Sensitivite	Spesifite	PPV	NPV
BCO Results	exist	114	102	64.4%	52.8%	52.8%	64.4%
	NON	63	114				
Consolidation	exist	68	82	38.4%	62.0%	45.3%	55.1%
	NON	109	134				
Thickness of Interlobules	exist	6	5	3.4%	97.7%	54.5%	55.2%
	NON	171	211				
Reticular Pattern	exist	4	16	2.3%	92.6%	20.0%	53.6%
	NON	173	200				
CrazyPaving	exist	4	2	2.3%	99.1%	66.7%	55.3%
	NON	173	214				
Air bronchogams	exist	5	20	2.8%	90.7%	20.0%	53.3%
	NON	172	196				
Thickness of Bronchial Walls	exist	11	24	6.2%	88.9%	31.4%	53.6%
	NON	166	192				
Bronchiectasis	exist	3	8	1.7%	96.3%	27.3%	54.5%
	NON	174	208				
Thickness of Pleura	exist	3	11	1.7%	94.9%	21.4%	54.1%
	NON	174	205				
Pleural Effusion	exist	1	5	0.6%	97.7%	16.7%	54.5%
	NON	176	211				
Nodule	exist	25	66	14.1%	69.4%	27.5%	49.7%
	NON	152	150				
Pericardial Effusion	exist	1	3	0.6%	98.6%	25.0%	54.8%
	NON	176	213				
Honeycomb	exist	4	11	2.3%	94.9%	26.7%	54.2%
	NON	173	205				
Fibrozis	exist	22	42	12.4%	80.6%	34.4%	52.9%
	NON	155	174				
Atelectasia	exist	23	40	13.0%	81.5%	36.5%	53.3%
	NON	154	176				

4. Discussion

In the initial stage of the COVID-19 pandemic, the diagnostic process became really important both for clinical and public health [1]. The purpose of the research is to provide sample contributions focusing on the diagnostic utility of chest CT on suspected COVID-19 cases and its correlation with PCR testing [2,3].

Our research revealed that chest CT has a very high sensitivity for diagnosing COVID-19 for all suspected patients. Particularly in the early stages of the disease, when RT-PCR tests can yield false-negative results, the use of chest CT as an additional diagnostic tool becomes crucial [4-7]. The role of chest CT, especially in the emergency and rapid diagnosis setting is supportted by some researches [8,9].

The characteristic radiological findings of COVID-19 on chest CT include ground-glass opacity (GGO) at 43%, nodules at 15%, atelectasis at 12.2%, and fibrotic changes at 12%. These findings provide important clues in diagnosing the disease. GGO is particularly considered a highly specific finding for COVID-19, usually presenting bilaterally and predominantly in peripheral and subpleural regions. Infiltration and atelectasis become more pronounced in the later stages of the disease [10,11]. Additionally, findings such as air bronchograms indicate significant changes in the lung parenchyma [12,13].

The involvement regions in the lungs also play an importand role in the radiological diagnosis. The lower lobes of the lungs are affected, with bilateral

involvement being common. Subpleural region involvement and peripheral distribution are typical radiological appearances for COVID-19. These characteristics enhance the diagnostic accuracy of chest CT and provide valuable information to clinicians about the severity and distribution of the disease.

However, despite the high sensitivity of chest CT, its specificity is not as high as that of RT-PCR. This limitation can lead to confusion with other viral or bacterial pneumonias and result in false-positive findings [14]. Therefore, it is not recommended to use chest CT alone for diagnosing COVID-19; instead, it should be used in conjunction with PCR testing to enhance diagnostic accuracy [15].

In our study, the RT-PCR test is considered the gold standard and compared with chest CT to evaluate the effectiveness of current diagnostic methods. The advantages of the RT-PCR test include its high specificity and accuracy. However, the sensitivity of the test can vary depending on sample collection and laboratory conditions. Therefore, using chest CT as an auxiliary diagnostic tool in patients with negative PCR results but clinical and radiological findings consistent with COVID-19 can reduce false-negative rates and support early isolation and treatment decisions.

The most sensitive among radiological findings were ground-glass opacity (GGO), atelectasis, nodules, fibrosis, nodule formation, as well as interlobular thickening (Table 2). The interlobular thickening and pleural effusion had the highest positive predictive value (PPV). Therefore, interlobular thickening and pleural effusion are the critical radiological markers which assist to the diagnosis of COVID-19 [14,16,17].

One of the main goals of healthcare services is to overcome pandemics worldwide with the most reliable, rapid and high survival rates in patient management, care, treatment and follow-up [18,19]. The Covid 19 pandemic was primarily a viral infection table where respiratory pathologies were at the forefront. We hope that the use of management algorithms accompanied by clinical, laboratory and imaging methods in patient management in similar or other tables with high mortality will pave the way for better prognostic survival.

5. Conclusion

In conclusion, the combined use of chest CT and PCR testing during the early stages of the COVID-19 pandemic improves diagnostic accuracy and reliability. Future studies should further examine the effectiveness and outcomes of this combination in different patient groups. Additionally, the development of new diagnostic methods and the optimization of existing ones will play a crucial role in combating pandemic diseases like COVID-19.

Limitations of the Study

The limited number of cases and the single-center nature of the study constitute the limitations of this study.

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Conflict of Interests

No conflict of interest was declared by the authors.

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Author Contributions

A.Ç Surgical and Medical Practises, Consept, Data Collection or Processing, Literature Search, Writing; G.Ç Analysis or Interpretation; Z.K.E Design, Data Collection or Processing; A.B Design, Analysis or Interpretation, Writing.

Ethical Approval

This study does not contain any experiments with human participants or animals conducted by the authors. Ethics committee acceptance was acquired from Ankara Dışkapı Training and Research Hospital (decision number 113/03, dated June 14, 2021).

Data sharing statement

The data that support the detections of this study are accessible from the corresponding author upon feasible request.

Consent to participate

Consent was obtained from the patients participating in the study.

Informed Statement

Informed consent was obtained from all subjects involved in the study.

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Evaluation of the Effectiveness of Radioembolization Therapy in Colorectal Cancer Liver Metastases

Duygu Karahacioglu[1*], Ahmet Peker[2], Cigdem Soydal[3], Ozlem Kucuk[3], Sadık Bilgic[4], Umman Sanlidilek[4]

[1]Department of Radiology, School of Medicine, Koç University, İstanbul, Türkiye
[2]Department of Radiolgy, Private Çamlıca Life Hospital, İstanbul, Türkiye
[3]Department of Nuclear Medicine, Faculty of Medicine, Ankara University, Ankara, Türkiye
[4]Department of Radiology/Vascular Interventional, Faculty of Medicine, Ankara University, Ankara, Türkiye

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****Corresponding Author***
Duygu Karahacioglu
Department of Radiology
School of Medicine
Koç University, İstanbul, Türkiye
Phone: +90 2122508250
E-mail: dkarahacioglu@kuh.ku.edu.tr

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Authors' ORCIDs
Duygu Karahacioglu
https://orcid.org/0000-0003-1365-871X
Ahmet Peker
https://orcid.org/0000-0002-5998-1304
Cigdem Soydal
https://orcid.org/0000-0002-6199-8551
Ozlem Kucuk
https://orcid.org/0000-0002-0717-8261
Sadık Bilgic
https://orcid.org/0000-0003-2039-2024
Umman Sanlidilek
https://orcid.org/0000-0001-6665-0485

Abstract: Colorectal cancer (CRC) ranks among the foremost causes of cancer-related mortality, with colorectal liver metastases (CLM) considerably affecting prognosis. While surgery is the gold standard for curative treatment, most patients are ineligible due to disease extent or comorbidities. Radioembolization with yttrium-90 (Y-90) microspheres has emerged as a promising locoregional therapy for unresectable CLM. However, its effectiveness in improving survival and tumor control remains an area of active investigation. The clinical results of 59 colorectal cancer patients with liver metastases who received radioembolization treatment were assessed. Treatment response was assessed using imaging modalities, including PET-CT, MRI, and CT. PET-CT was predominantly used to assess treatment response. The primary endpoints were overall survival (OS) and treatment response, while secondary outcomes included toxicity profiles and prognostic factors influencing survival. The cohort's median OS was 9 months, with a mean OS of 13.2 months. Patients exhibiting metabolic response on PET-CT had significantly longer survival (19.3 months) compared to non-responders (8.3 months, p = 0.042). Extrahepatic disease was a strong prognostic factor, with patients with extrahepatic involvement showing a significantly lower OS (7.1 vs. 21 months, p = 0.000). Bilobar disease, observed in 47 patients, was also associated with reduced survival (p = 0.003). Nearly all patients experienced mild to moderate side effects, with the most common being abdominal pain, nausea, and vomiting. Severe toxicities were rare, although one patient developed a gastric ulcer. Y-90 radioembolization is an effective and relatively safe treatment for unresectable CLM, particularly in patients without extrahepatic disease. The strong association between metabolic response and survival underscores the potential of PET-CT as a prognostic indicator. Further prospective studies are needed to refine patient selection criteria and optimize treatment protocols.©2025 NTMS.

Keywords: Colorectal Cancer; Radioembolization; Liver Metastases.

1. Introduction

Colorectal cancer (CRC) is among the most common cancer worldwide. A significant proportion of CRC patients develop liver metastases (colorectal liver metastases, CLM), which critically impact prognosis

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and treatment strategies[1]. While surgical resection remains the gold standard for CLM management, only few (20–30%) of patients are eligible for surgery[2]. Consequently, there is a growing need for alternative, effective locoregional therapies to manage unresectable liver metastases.

Radioembolization has come out as a promising treatment modality for patients with unresectable CLM. This technique involves the intra-arterial administration of yttrium-90 (Y-90) microspheres, which deliver targeted radiation to tumor cells while sparing healthy liver tissue[3]. Radioembolization has been utilized as a salvage therapy for chemotherapy refractory CLM and as a bridge to resection or transplantation in select cases[4]. Despite its increasing application, the effectiveness of radioembolization in improving survival and tumor control remains an area of active investigation.

Numerous studies have investigated the effects of radioembolization on survival in patients with colorectal cancer who have liver metastases. Retrospective and prospective analyses suggest that radioembolization can lead to meaningful tumor regression and prolonged survival, particularly in patients who have exhausted standard systemic treatment options[5]. Additionally, the combination of radioembolization with systemic chemotherapy has shown promise in enhancing tumor response rates[6].

This study aims to evaluate the effectiveness of radioembolization in the treatment of colorectal cancer liver metastases by analyzing clinical outcomes, imaging-based response assessments, and patient survival metrics. Understanding the therapeutic potential and limitations of radioembolization will help refine treatment algorithms and improve patient selection criteria for this intervention.

2. Material and Methods

2.1. Patient Information

The study included a total of 59 patients diagnosed with colorectal cancer and liver metastases, comprising 37 males and 22 females. This was a retrospective study, and approval was obtained from the university's ethics committee.

Before treatment, all patients were evaluated for hepatic reserve, bone marrow reserve, renal function, and hepatic vascularization. Patients with hepatic failure signs, including extensive ascites, portal hypertension, or portal vein thrombosis, were excluded. As part of routine clinical practice, all patients were evaluated by the departments of Medical Oncology, General Surgery, Gastroenterology, and Radiology, and they were deemed unsuitable for surgery before the radioembolization (RE) procedure. Hepatic/celiac angiography was performed on all patients to assess hepatic arterial anatomy and plan therapy. During this procedure, coil embolization of the gastroduodenal artery was performed to prevent gastrointestinal reflux. Additionally, hepatic arterial perfusion scintigraphy was conducted to evaluate potential shunting to the lungs and gastrointestinal tract.

Patients with a hepatopulmonary shunt greater than 20% were excluded from the study to prevent pulmonary radiation fibrosis. For eligible patients, the therapeutic dose of Y-90 microspheres was calculated using the body surface area method.

Resin microspheres were injected intra-arterially into the hepatic artery under fluoroscopic guidance. To verify microsphere retention within liver lesions and the absence of extrahepatic leakage, whole-body planar images were obtained using a gamma camera at 2–6 hours post-administration. All patients were admitted for overnight observation to monitor for postembolization syndrome, and symptomatic treatment (NSAIDs, antiemetics, and H2 receptor antagonists) was administered.

2.2. Follow-Up

To assess liver metastases, including tumor location, size, and number, pre-treatment imaging studies such as CT, MRI, and PET scans were reviewed. Many of the patients underwent PET-CT evaluation both before treatment and at six weeks post-treatment. Although post-treatment CT scans were recommended for all patients, they were often unavailable due to many patients traveling from other cities and being in terminal stages of the disease.

2.3. Treatment Response

Treatment response was evaluated using visual and semi-quantitative assessments of metabolic activity in 18F-FDG PET-CT scans performed before and after treatment. A decrease in tumor size and metabolic activity was classified as a “response to treatment,” whereas stable or increased metabolic activity, or the appearance of new lesions, was classified as “no response to treatment.”

2.4. Statistical Analysis

SPSS version 20.0.0 was used for statistical analysis. The Kaplan-Meier method was used to analyze mean and median cumulative survival. Survival times were compared using the log-rank (Mantel-Cox) test, with a p-value of less than 0.05 considered statistically significant.

3. Results

Between June 2008 and October 2013, a total of 70 radioembolization treatments were administered to 59 patients. As survival data for 2 patients were unavailable, they were excluded from the analysis. The mean age of the patients was 60 ± 10.4 years (range: 32-85). Among them, 36 were male and 21 were female. The primary tumor was in the colon in 47 patients and in the rectum in 10 patients. Pre-treatment CT, MRI, and PET-CT imaging revealed extrahepatic involvement in 27 patients. Bilobar disease was present in 47 patients. All patients had previously received systemic chemotherapy. Before treatment, 9 patients

had undergone radiofrequency ablation, 1 patient had received alcohol injection, 3 patients had undergone surgical resection, and 1 patient had undergone chemoembolization for liver metastases.

3.1. Radioembolization

Microsphere treatment was administered to a single liver lobe in 37 patients (29 right, 8 left) and to both lobes in 22 patients. Eleven patients underwent a second session of radioembolization. The average administered dose was 1.59 GBq. Pre-treatment median values were AST: 32 U/L, ALT: 24 U/L, and bilirubin: 0.7mg/dL.

3.2. Toxicity

Almost all patients experienced various degrees of treatment-related side effects. Two patients died on days 5 and 12 post-treatment, and they were excluded from the study. One patient was diagnosed with a gastric ulcer via endoscopy. Other patients experienced abdominal pain, loss of appetite, nausea, and vomiting, but these side effects lasted less than one month.

3.3. Treatment Response and Survival

To assess treatment response, 28 patients underwent 18F-FDG PET-CT imaging before and 6 weeks after treatment. Additionally, pre- and post-treatment abdominopelvic CT scans were available for 2 patients, and abdominal MRI scan were available for 1 patient.

The overall survival (OS) duration for all patients was found to be an average of 13.2 months, with a median survival time of 9 months. Out of 57 patients, 49 (86%) had passed away, while 8 patients (14%) were still alive during the follow-up period.

Among the 28 patients who were evaluated using 18F-FDG PET-CT, 25 showed a response to treatment, while 3 did not. During follow-up, 22 of these 28 patients died. The treatment-responsive group had a mean survival time of 19.3 months, while the non-responsive group had a mean survival of 8.3 months. The overall mean survival was 18.1 months, with a statistically significant difference between the groups ($p = 0.042$) (Figure 1).

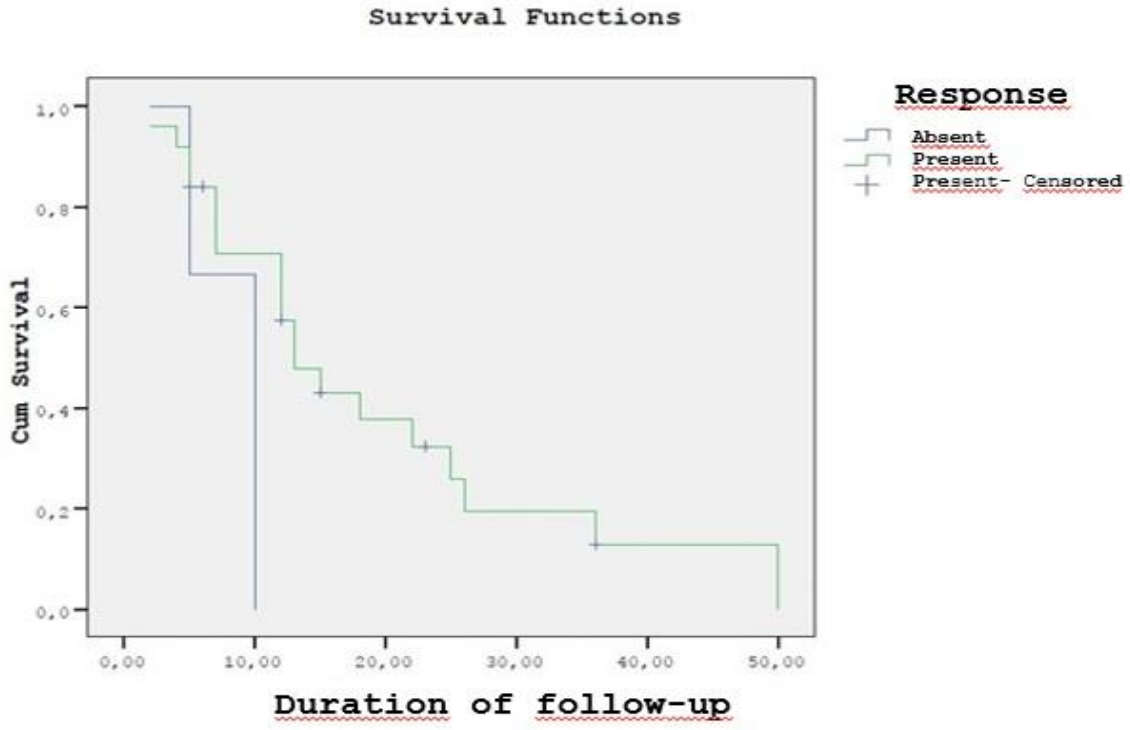

Figure 1: A significant difference was found in survival durations between the groups that responded and did not respond to treatment on FDG-PET CT.

For the three patients evaluated using CT and MRI, one showed partial response (PR), one had stable disease (SD), and one had progressive disease (PD). Due to the small number of patients in this group, statistical evaluation was not possible.

The primary tumor was located in the colon in 47 patients and in the rectum in 10 patients. The mean survival time for patients with a colonic primary tumor was 11.4 months, while for those with a rectal primary tumor, it was 22.8 ± 7.1 months. The difference between the two groups was not statistically significant ($p = 0.125$).

Among the 57 patients, 40 were younger than 65 years, and 17 were older than 65 years. The difference in survival between these two age groups was not statistically significant (p = 0.921). Similarly, there was no statistically significant difference in survival between male and female patients (p = 0.693).

Pre-treatment CT, MRI, and PET-CT evaluations revealed extrahepatic involvement in 26 patients. The mean survival time for patients without extrahepatic involvement was 21 ± 3.3 months, whereas for those with extrahepatic involvement, it was 7.1 ± 0.8 months. This difference was found to be statistically significant (p = 0.000) (Figure 2).

Bilobar disease was present in 45 patients, the other 12 patients had unilobar diease. The difference between the two groups was found to be statistically significant (p = 0.003) (Figure 3).

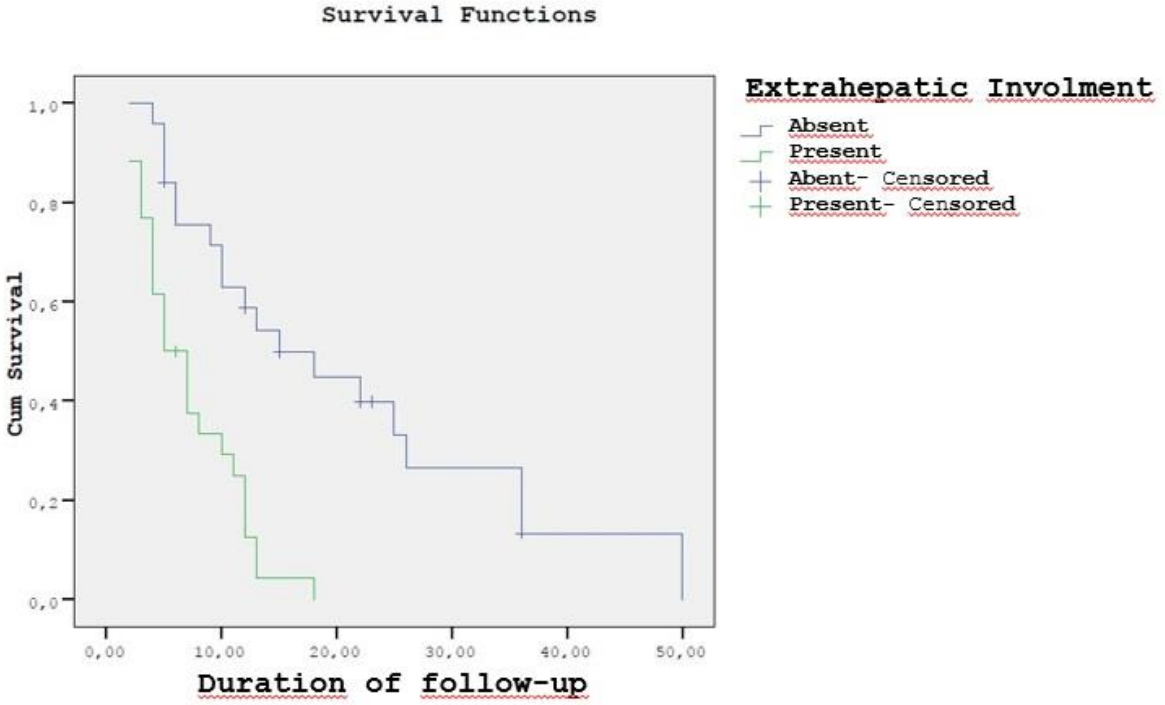

Figure 2: A significant difference was found in survival durations between the groups with and without extrahepatic involvement.

4. Discussion

Colorectal cancer ranks among the most prevalent malignancies globally, with liver metastases developing in approximately 50% of patients throughout the progression of the disease[7]. Treatment options for CRLM include surgery, systemic chemotherapy, targeted therapy, and locoregional treatments such as radioembolization[8]. In this study, we evaluated the effectiveness of Y-90 RE in patients with CRLM, assessing treatment response, toxicity, and OS. Our findings indicate that RE is a viable treatment option for CRLM patients who are not candidates for surgical resection. The median OS in our study was 9 months, with patients who responded to treatment exhibiting a significantly longer survival compared to non-responders (19.3 vs. 8.3 months, p=0.042). These results align with previous studies that have reported median OS ranging from 8 to 20 months following RE for CRLM[9,10]. The significant survival difference between responders and non-responders suggests that early metabolic response, evaluated through 18F-FDG PET-CT, could be a valuable prognostic marker for treatment effectiveness.

The presence of extrahepatic disease significantly influenced survival in our cohort, with patients without extrahepatic spread demonstrating a mean OS of 21 months, compared to 7.1 months in those with extrahepatic involvement (p = 0.000). This finding is consistent with prior reports that have suggested that extrahepatic disease burden is a major determinant of survival following RE[11]. In contrast, age, sex, and primary tumor location (colon vs. rectum) did not significantly impact OS, which is also in agreement with prior studies indicating that tumor biology and burden may be more relevant prognostic factors than demographic variables[12].

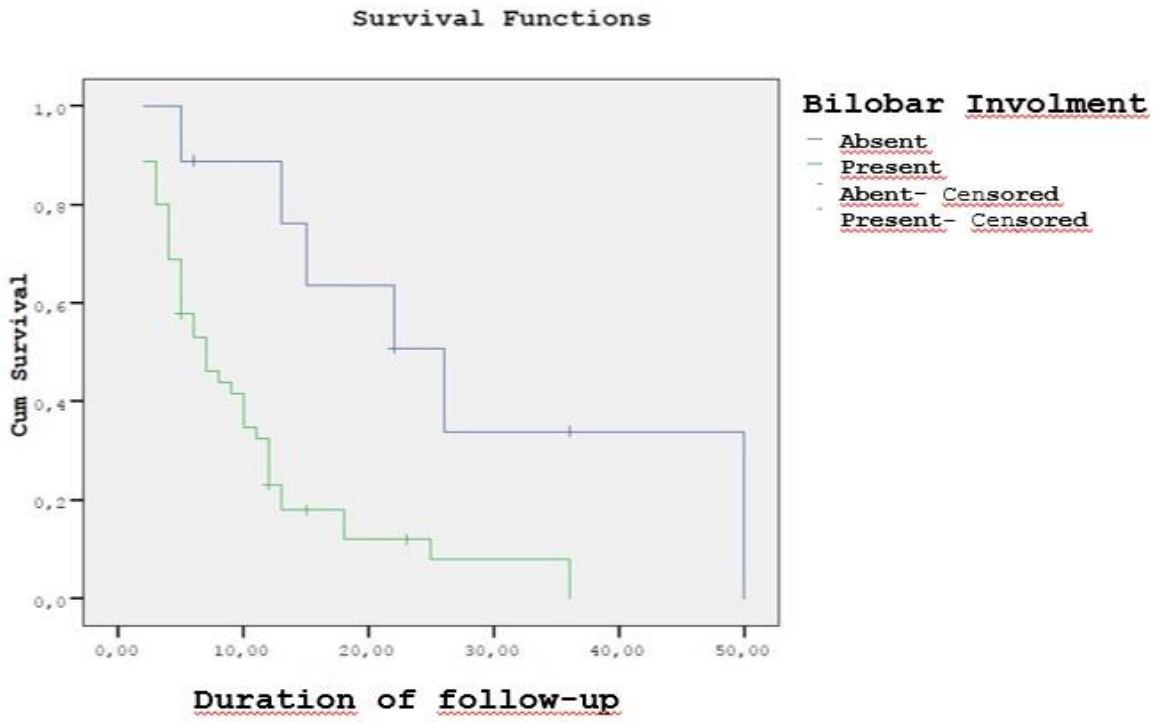

Figure 3: A significant difference was found in survival durations between the groups with and without bilobar involvement.

A key concern regarding RE is treatment-related toxicity. In our study, nearly all patients experienced some degree of side effects, with the most common being abdominal pain, nausea, and vomiting, consistent with post-radioembolization syndrome[10]. One patient developed a gastric ulcer, which highlights the importance of meticulous angiographic planning to avoid non-target radiation. Importantly, the incidence of severe toxicities was low, supporting the relative safety of RE when performed with appropriate patient selection and dosimetry considerations[13].

A notable limitation of our study is its retrospective design, which may introduce selection bias. Additionally, the lack of post-treatment imaging for some patients, primarily due to follow-up difficulties in terminal-stage cases, limits our ability to fully assess long-term outcomes. Future prospective studies with standardized imaging follow-up and larger patient cohorts are needed to further validate these findings.

5. Conclusion

In conclusion, our study suggests that Y-90 radioembolization is an effective and relatively safe treatment for CRLM, particularly in patients without extrahepatic disease. The significant association between metabolic response and survival highlights the potential role of 18F-FDG PET-CT as a prognostic tool in treatment planning. As systemic therapies continue to evolve, integrating RE into multimodal treatment strategies may further improve outcomes in this challenging patient population.

Limitations of the Study

The retrospective design and the lack of post-treatment imaging for some patients are among our study limitations.

Acknowledgement

None.

Conflict of Interests

There are no conflicts of interest reported by the authors.

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Author Contributions

Concept – DK, AP, US; Design - DK, AP, US; Supervision – OK, SB, US; Resources - AP, CS; Materials - AP, CS; Data Collection and/or Processing - DK, AP, CS, US; Analysis and/or Interpretation – DK; Literature Review - DK, AP, CS; Writing - DK, ZO, US; Critical Review – AP, US.

Ethical Approval

The Institutional Review Board of Ankara University Faculty of Medicine approved this retrospective study protocol (approval no: 04-131-14, date: 10.03.2014).

Data sharing statement

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Consent to participate

None.

Informed Statement

None.

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