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ORIGINAL ARTICLE

The Relationship Between Lysophosphatidylcholine Levels and Morbidity and Mortality in Covid Pneumonia

ABSTRACT

INTRODUCTION: The aim of this study was to investigate the relationship between serum Lysophosphatidylcholine (LPC) levels and mortality in patients diagnosed with Covid-19 admitted to the emergency department and hospitalised.

METHODS: The study was designed as a prospective, cross-sectional study. The effect of serum LPC levels taken on days 1 and 5 on prognosis in patients diagnosed with Covid 19 in the emergency department was investigated.

RESULTS: The average age of the patients included in our study was 73.9, with males constituting 56.8%. The most common comorbidities were hypertension (72.7%) and diabetes mellitus (43.2%). The most common presenting symptoms were fatigue and widespread body pain, cough, and dyspnoea, consistent with the cardinal symptoms of the disease. After the emergency department visit, 77.3% of the patients were hospitalized, while 22.7% were admitted to the intensive care unit. 79.5% were discharged, while 20.5% died. In the group with fatal outcomes, the day 1 LPC level was significantly lower ($p < 0.05$) compared to the discharged group. A significant [Area under the curve (AUC): 0.830; Confidence Interval (CI): 0.683-0.977)] effectiveness of the 10000-cut-off value of LPC on the 1st day was observed in distinguishing between patients discharged and deceased. The sensitivity was 88.9%, positive predictive value 50.0%, specificity 77.1%, and negative predictive value 96.4%.

DISCUSSION AND CONCLUSION: We found that the day 1 LPC level may be a valuable biomarker for prognosis in patients presenting to the emergency department with Covid pneumonia due to its high sensitivity, moderate specificity, and advanced negative predictive value for mortality.

Keywords: COVID-19 pneumonia, Lysophosphatidylcholine levels, mortality

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Introduction

2019 coronavirus disease (COVID-19) is an infectious respiratory disease. It is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and affects humans. The disease was first discovered in Wuhan, China in 2019 and has since spread worldwide, leading to the coronavirus pandemic from 2019 (1). The novel coronavirus infection (COVID-19) is characterised by an exaggerated inflammatory response. It is usually associated with pulmonary pneumonia in adults and can lead to serious consequences such as adult respiratory distress syndrome, sepsis, coagulation disorders and death (1). Studies have indicated that specific biochemical parameters may be associated with mortality risk in hospitalized patients diagnosed with COVID-19 (2).

Lysophosphatidylcholine (LPC) is a bioactive lipid group extensively studied for its role in inflammation and atherosclerosis (3). While it is naturally present in plasma under normal physiological conditions, its levels can rise significantly during inflammatory responses. LPC promotes the release of inflammatory mediators, including Interleukin (IL)-1β, IL-5, IL-6, IL-8 and Interferon (IFN)-γ (4). Although LPC has traditionally been regarded as a proinflammatory and potentially harmful molecule,

recent studies suggest it may also have beneficial effects under certain pathological conditions (5). Given that LPC is the most abundant lysophospholipid in plasma, understanding its physiological functions and clarifying the conflicting findings in the literature is crucial.

This study aims to investigate the prognostic significance of serum LPC concentrations in predicting mortality among patients with COVİD-19 pneumonia.

Methods:

The study included cases who applied to the emergency department of our tertiary care hospital, met the COVID-19 case definition, and were hospitalised in the ward or intensive care unit. It was designed as a single-center, prospective study, approved by the Ethics Committee on April 19, 2022 (Approval No: 3519) under the University of Health Sciences Şişli Hamidiye Etfal Training and Research Hospital Health Application and Research Center, Clinical Research Ethics Committee. Written informed consent was obtained from all conscious patients, while consent for unconscious patients was provided by their legal representatives.

Patients who met the criteria for a probable or confirmed COVID-19 case were included in the study. Blood was collected from 60 patients for the study. Data from a total of 44 patients aged 18 years and over who met the inclusion criteria were analysed (Figure 1).

Flow Diagram of the study

After obtaining informed consent, blood samples were collected on the first and fifth days for LPC analysis. Venous blood samples were collected from all participants using gel vacuum tubes (BD, Plymouth, UK). Samples were kept at room temperature for two hours before being centrifuged at 1000 × g for 20 minutes at +4°C using a refrigerated centrifuge. The separated serum samples were then transferred to Eppendorf tubes and stored at -80°C until analysis. Prior to testing, samples were thawed at -20°C for 12 hours, followed by storage at +4°C for another 12 hours. On the test day, samples were brought to room temperature, homogenized by vortexing, and analyzed using the ELK General LPC (Lysophosphatidylcholine) enzyme-linked immunoassay (ELISA) kit (Wuhan East Lake, Catalogue No: ELK8145). Washing steps were performed with a DAW 50 Biotek washer, and readings were recorded using a DAR800 TS Biotek reader. Measurement range of the kit was 31.5–20,000 ng/ml, with a sensitivity of 92.4 ng/ml. The inter-assay coefficient of variation was <10% and the intra-assay coefficient of variation was <8%.

Statistical analysis: Mean, standard deviation, median minimum, maximum, frequency and ratio values were used in descriptive statistics of the data. The distribution of variables was measured with the Kolmogorov Simirnov test. Independent sample t test, mann-whitney u test were used to analyse quantitative independent data. Wilcoxon test was used to analyse dependent quantitative data. Chi-square test was used to analyse qualitative independent data, and Fisher's test was used when chi-square test conditions were not met. Effect level and cut off value were analysed with ROC curve. A value of

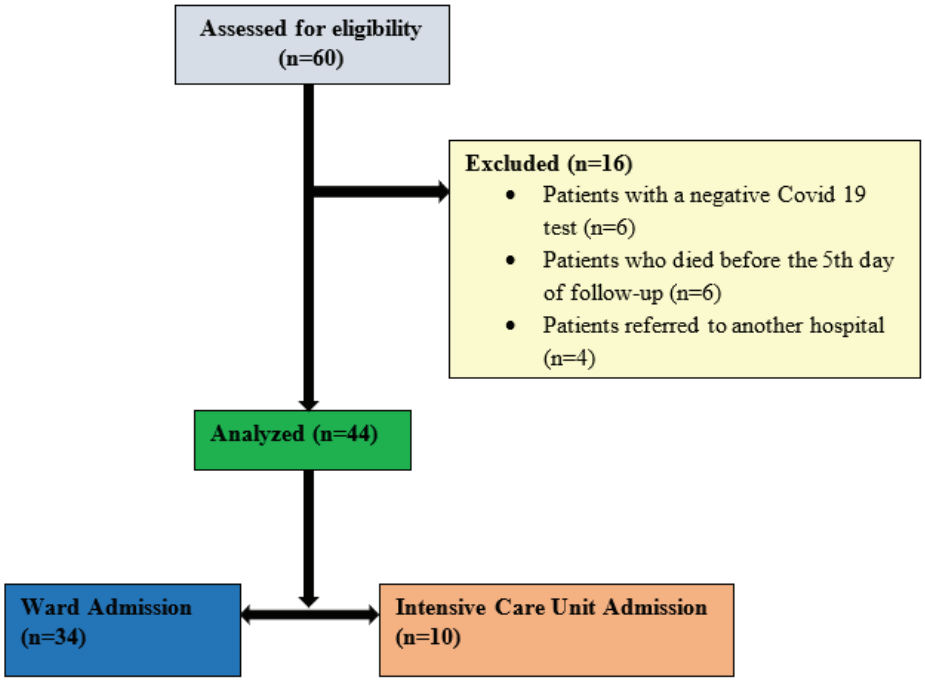

Figure 1. Flow Diagram of the study

Table 1. Analysis of Socio-demographic Characteristics. Vaccination. Vital Parameters. and Clinical Conditions of All Patients

		Min - Max		Median	Mean±sd/n-%	
Age		34.0 - 97.0		74.5	73.9 ± 13.6	
Length of Stay (Days)		5.0 - 44.0		11.0	13.0 ± 7.2	
		n	**%**		**n**	**%**
Gender	Female	19	43.2 %	**Initial CT Findings and Symtomps**		
	Male	25	56.8 %	High	13	29.5 %
HT	(-)	12	27.3 %	Moderate	25	56.8 %
	(+)	32	72.7 %	Low	6	13.6 %
CAD	(-)	26	59.1 %	Fever (-)	16	36.4 %
	(+)	18	40.9 %	Fever (+)	28	63.6 %
DM	(-)	25	56.8 %	Dyspnoea (-)	6	13.6 %
	(+)	19	43.2 %	Dyspnoea (+)	38	86.4 %
COPD	(-)	36	81.8 %	Cough (-)	3	6.8 %
	(+)	8	18.2 %	Cough (+)	41	93.2 %
CRF	(-)	37	84.1 %	Sputum (-)	8	18.2 %
	(+)	7	15.9 %	Sputum (+)	36	81.8 %
CHF	(-)	35	79.5 %	Diarrhoea (-)	39	88.6 %
	(+)	9	20.5 %	Diarrhoea (+)	5	11.4 %
Alzheimer	(-)	32	72.7 %	Fatigue-Myalgia (-)	3	6.8 %
	(+)	12	27.3 %	Fatigue-Myalgia (+)	41	93.2 %
CVD	(-)	41	93.2 %	Loss of Smell and Taste (-)	30	68.2 %
	(+)	3	6.8 %	Loss of Smell and Taste (+)	14	31.8 %
Malignancy	(-)	37	84.1 %	Throat-Headache (-)	12	27.3 %
	(+)	7	15.9 %	Throat-Headache (+)	32	72.7 %
Vaccination Status				General Condition Disorder (-)	2	4.5 %
No		17	38.6 %	General Condition Disorder (+)	42	95.5 %
Biontech		6	13.6 %	**Mechanical Ventilator** (+)	10	22.7 %
Sinovac		18	40.9 %	**Mechanical Ventilator** (-)	34	77.3 %
Biontech+Sinovac		3	6.8 %	**High-flow oxygen (O_2)** (+)	15	34.1 %
Disease Severity				**High-flow oxygen (O_2)** (-)	29	65.9 %
Severe Clinical Patient		19	43.2 %	**Emergency Service Outcomes**		
Mild Clinical Patient		25	56.8 %			
Latest Status	Discharged	35	79.5 %	Hospital Admissions	34	77.3 %
	Deceased	9	20.5 %	ICU Admissions	10	22.7 %

HT: Hypertension; CAD: Coronary Artery Disease; DM: Diabetes Mellitus; COPD: Chronic Obstructive Pulmonary Disease; CRF: Chronic Renal Failure; CHF: Congestive Heart Failure; CVD: Cerebrovascular disease; ICU: Intensive Care Unit

$p < 0.05$ was considered statistically significant. All statistical analyses were conducted using SPSS software (version 28.0, IBM, Armonk, NY, USA).

Results

Our study included 44 patients. The mean age of the patients was 73.9 years and 56.8% were male. The most common comorbidities were hypertension (HT) (72.7%) and diabetes mellitus (DM) (43.2%), while the least common comorbidity was cerebrovascular disease (CVD) (6.8%) (Table 1).

When we evaluated the vaccination status of the patients, we found that 38.6% had never been vaccinated, 40.9% preferred Sinovac vaccine, and only 6.8% had both vaccines. At the time of presentation to the emergency department, 56.8% of patients presented with mild clinical conditions, while 43.2% had severe clinical conditions. The most common complaints at the time of admission were general condition disorder, cough, weakness and body pain with rates exceeding 90%. We found that 22.7% of our patients required mechanical ventilation, while 34.1% received high-flow nasal oxygen. When we looked at the results in the emergency department, 77.3% were hospitalised, while 22.7% needed to be followed up in the intensive care unit (ICU). The patients were followed up in the hospital for an average of 11 days, 79.5% were discharged and 20.5% died (Table 1).

When the LPC levels of the patients were evaluated, it was observed that 63.6% of the patients had LPC levels above 10,000 on admission (day 1) and 43.2% had LPC levels above 10,000 on day 5 (Table 2).

There was no significant difference in age and gender distribution between the deceased patient group and the discharged patient group ($p > 0.05$). The rate of HT and coronary artery disease (CAD) was significantly lower in the deceased patient group than in the discharged patient group ($p < 0.033$, $p < 0.041$). No statistically significant difference was found in the rates of DM, chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), chronic heart failure (CHF), Alzheimer's disease, cardiovascular disease and malignancy between the deceased patient group and the discharge group ($p>0.05$). A p-value greater than 0.05 indicates that there was no significant difference between the deceased patient group and the discharged patient group in terms of vaccination rates. While 66.7% of non-vaccinated patients died, no deaths were observed between Pfizer and vaccinated patients (Table 3).

In the deceased patient group, the rate of high findings on the first chest computed tomography (CT) scan was significantly higher than in the discharged group ($p < 0.001$). The rate of fever was significantly higher in the deceased patient group compared to the discharged group ($p < 0.011$). There was no significant difference between the deceased patient group and discharged group in the rates of symptoms such as dyspnoea, cough, sputum, diarrhoea, weakness-myalgia, loss of smell-

Table 2. Haematological parameters and LPC levels of all patients

		Min-Max	Median	Mean±sd/n-%
LPC Level				
1st Day (x10³)		5.4 - 70.0	13.8	22.2 ± 20.2
LPC Level 1st Day	< 10000 ng/ml			16 36.4 %
	> 10000 ng/ml			28 63.6 %
5st Day (x10³)		1.2 - 31.0	8.6	10.7 ± 6.9
LPC Level 5st Day	< 10000 ng/ml			25 56.8 %
	> 10000 ng/ml			19 43.2 %
Initial Oxygen Saturation		75.0 - 96.0	90.0	88.2 ± 6.4
Pulse (/min)		60.0 - 160.0	90.0	93.1 ± 20.4
Fever (C°)		36.0 - 39.7	37.0	37.1 ± 1.0
Respiratory Rate (/min)		14.0 - 35.0	20.0	21.0 ± 5.4
C-Reactive Protein (mg/L)		9.0 - 668.0	120.5	141.7 ± 121.6
Ferritin (ng/ml)		30.0 - 6714.0	430.0	610.1 ± 1009.1
Lactate (mmol/L)		0.8 - 9.1	2.0	2.5 ± 1.6
PaO_2/FiO_2		100.0 - 460.0	290.0	282.6 ± 94.3
NLR		0.5 - 32.0	7.0	8.9 ± 6.3
D-dimer (ng/ml)		200.0 - 19200	974.0	2384.7 ± 3602.9
Troponin (ng/ml)		3.5 - 178.0	19.5	34.6 ± 36.9

LPC: Lysophosphatidylcholine; NLR: Neutrophil to lymphocyte ratio; PaO_2/FiO_2: Partial pressure of oxygen to the fraction of inspiratory oxygen concentration ratio

Table 3. The analysis of socio-demographic data between the discharged and deceased groups

		Discharged (n:35)			Deceased (n:9)			p	
		Mean±sd/n-%		Median	Mean±sd/n-%		Median		
Age		72.8 ± 11.3		73.0	78.2 ± 20.4		83.0	0.463	t
Gender	Female	15	42.9 %		4	44.4 %		0.932	X^2
	Male	20	57.1 %		5	55.6 %			
Hypertension	(-)	7	20.0 %		5	55.6 %		**0.033**	X^2
	(+)	28	80.0 %		4	44.4 %			
CAD	(-)	18	51.4 %		8	88.9 %		**0.041**	X^2
	(+)	17	48.6 %		1	11.1 %			
DM	(-)	18	51.4 %		7	77.8 %		0.155	X^2
	(+)	17	48.6 %		2	22.2 %			
COPD	(-)	28	80.0 %		8	88.9 %		1.000	X^2
	(+)	7	20.0 %		1	11.1 %			
CKD	(-)	30	85.7 %		7	77.8 %		0.619	X^2
	(+)	5	14.3 %		2	22.2 %			
CHF	(-)	26	74.3 %		9	100.0%		0.167	X^2
	(+)	9	25.7 %		0	0.0 %			
Alzheimer	(-)	27	77.1 %		5	55.6 %		0.195	X^2
	(+)	8	22.9 %		4	44.4 %			
CVD	(-)	32	91.4 %		9	100.0%		1.000	X^2
	(+)	3	8.6 %		0	0.0 %			
Malignancy	(-)	30	85.7 %		7	77.8 %		0.619	X^2
	(+)	5	14.3 %		2	22.2 %			
Vaccination Status									
No		11	31.4 %		6	66.7 %		0.053	X^2
Biontech		6	17.1 %		0	0.0 %			
Sinovac		16	45.7 %		2	22.2 %			
Biontech+Sinovac		2	5.7 %		1	11.1 %			

[t] Independent sample t-test / X^2 Chi-square test

CAD: Coronary Artery Disease; DM: Diabetes Mellitus; COPD: Chronic Obstructive Pulmonary Disease; CKD: chronic kidney disease CHF: Congestive Heart Failure CVD: Cerebrovascular disease

taste, sore throat-headache and deterioration of general condition ($p > 0.05$). The rate of mechanical ventilator and high-flow oxygen (O□) use was significantly higher in the deceased patient group compared to the discharged group ($p < 0.001$). The rate of severe disease severity was significantly higher in the deceased patient group compared to the discharged group ($p < 0.019$). Intensive Care Unit (ICU) hospitalisation rate was significantly higher in the deceased patient group compared to the discharged group ($p < 0.05$). There was no significant difference between the deceased and discharged patient groups in terms of length of hospital stay ($p > 0.05$) (Table 4).

There was no significant difference in initial oxygen saturation, pulse rate, fever, C reactive protein (CRP), lactate, neutrophil/lymphocyte ratio (NLR) and troponin values between the deceased and discharged patient groups ($p > 0.05$). Respiratory rate, ferritin and D-dimer levels were significantly higher in the deceased patient group than in the discharged group ($p < 0.022$). The ratio of partial pressure of oxygen in arterial blood (PaO2) to fraction of inspiratory oxygen concentration (FiO2) was significantly lower in the deceased patient group than in the discharged group ($p < 0.020$) (Table 5).

In the deceased patient group, day 1 LPC level was significantly lower than in the discharged group ($p < 0.005$). There was no significant difference in day 5 LPC level between the group that deceased and the discharged patient group ($p > 0.05$). In the discharged group, there was a significant decrease in day 5

Table 4. Analysis of Clinical Data Between Discharged and Deceased Groups

		Discharged (n:35)			Deceased (n:9)			p	
		Mean±sd/n-%		Median	Mean±sd/n-%		Median		
Initial CT Findings									
High		6	17.1 %		7	77.8 %			
Moderate		24	68.6 %		1	11.1 %		**<0.000**	X^2
Low		5	14.3 %		1	11.1 %			
Fever	(-)	16	45.7 %		0	0.0 %		**0.011**	X^2
	(+)	19	54.3 %		9	100.0%			
Dyspnoea	(-)	5	14.3 %		1	11.1 %		1.000	X^2
	(+)	30	85.7 %		8	88.9 %			
Cough	(-)	3	8.6 %		0	0.0 %		1.000	X^2
	(+)	32	91.4 %		9	100.0%			
Sputum	(-)	7	20.0 %		1	11.1 %		1.000	X^2
	(+)	28	80.0 %		8	88.9 %			
Diarrhoea	(-)	33	94.3 %		6	66.7 %		0.050	X^2
	(+)	2	5.7 %		3	33.3 %			
Fatigue-Myalgia	(-)	3	8.6 %		0	0.0 %		1.000	X^2
	(+)	32	91.4 %		9	100.0%			
Loss of Smell and Taste	(-)	24	68.6 %		6	66.7 %		0.913	X^2
	(+)	11	31.4 %		3	33.3 %			
Throat-Headache	(-)	10	28.6 %		2	22.2 %		0.703	X^2
	(+)	25	71.4 %		7	77.8 %			
General Cond. Disorder	(-)	2	5.7 %		0	0.0 %		1.000	X^2
	(+)	33	94.3 %		9	100.0%			
Mechanical Ventilator	(+)	1	2.9 %		9	100.0%		**<0.000**	X^2
	(-)	34	97.1 %		0	0.0 %			
High-flow oxygen (O_2)	(+)	7	20.0 %		8	88.9 %		**<0.000**	X^2
	(-)	28	80.0 %		1	11.1 %			
Disease Severity									
Severe Clinic Patient		12	34.3 %		7	77.8 %		**0.019**	X^2
Mild Clinical Patient		23	65.7 %		2	22.2 %			
Emergency Service Outcomes									
Hospital Admissions		30	85.7 %		4	44.4 %		**0.008**	X^2
ICU Admissions		5	14.3 %		5	55.6 %			
Length of Stay (Days)		12.5 ± 7.4		11.0	14.8 ± 6.6		13.0	0.243	m

m Mann-Whitney u test / X^2 Chi-square test ICU: Intensive Care Unit

Table 5. Analysis of Vital and Haematological Data Between Discharged and Deceased Groups

	Discharged (n:35)		Deceased (n:9)		p	
	Mean±sd	Median	Mean±sd	Median		
Initial Oxygen Saturation	88.9 ± 6.1	90.0	85.6 ± 7.3	85.0	0.231	m
Pulse (/min)	90.9 ± 19.3	90.0	101.4 ± 23.4	105.0	0.170	t
Fever (C°)	37.1 ± 1.0	37.0	36.9 ± 0.7	37.0	0.658	m
Resp. Rate (/min)	20.3 ± 5.5	20.0	23.6 ± 4.2	25.0	**0.031**	m
CRP (mg/L)	140.0 ± 127.1	123.0	148.2 ± 103.2	110.0	0.727	m
Ferritin (ng/ml)	412 ± 288	339	1382 ± 2068	477.0	**0.043**	m
Lactate (mmol/L)	2.5 ± 1.7	2.0	2.1 ± 1.0	2.2	0.705	m
PaO_2/FiO_2	299.1 ± 88.7	297.0	218.1 ± 92.4	200.0	**0.020**	t
NLR	7.7 ± 4.5	7.0	13.2 ± 10.1	7.0	0.231	m
D-Dimer (ng/ml)	1732 ± 2225	694	4925 ± 6293	2375	**0.022**	m
Troponin(ng/ml)	35.0 ± 40.4	18.0	33.2 ± 19.9	26.0	0.344	m

[t] Independent Samples t-test / [m] Mann-Whitney u test NLR: Neutrophil Lymphocyte Ratio; CRP: C-Reactive Protein

Table 6a. The change in LPC level between days 1 and 5 in the discharged and deceased groups.

	Discharged (n:35)		Deceased (n:9)		p	
	Mean±sd	Median	Mean±sd	Median		
LPC Level	($x10^3$)					
1st Day	25.2 ± 21.2	16.5	10.6 ± 9.4	7.7	**0.005**	m
5st Day	11.4 ± 7.4	9.6	8.1 ± 4.0	7.0	0.367	m
1/5. Day Change	-13.8 ± 18.1	-6.3	-2.5 ± 10.4	0.5	**0.006**	m
Intra-Group Change p	**< 0.000**[w]		0,953[w]			

[m] Mann Whitney U test/ [w] Wilcoxon test

Table 6b. ROC analysis of LPC levels for mortality on the day 1

	Under-Curve Area	95% Confidence Interval	p
LPC Level Day 1	0.803	0.632 - 0.974	**0.005**
Day 1 Cut Off 10000	0.830	0,683 - 0.977	**0.002**

		EX (-)	EX (+)
LPC Level Day 1	> 10000	27	1
	< 10000	8	8

	%
Sensitivity	88.9 %
Pos. Predictive Value	50.0 %
Specificity	77.1 %
Neg. Predictive Value	96.4 %

LPC level compared to day 1 ($p < 0.006$). In the group with unfavorable outcome, there was no significant change in day 5 LPC level compared to day 1 ($p > 0.05$). The decrease in day 5 LPC in the discharged group was higher than in the group with unfavorable outcome ($p < 0.001$) (Table 6a).

In distinguishing patients between discharged and deceased patients, day 1 LPC level showed significant efficacy [AUC: 0.803; Confidence Interval (CI): 0.632-0.974] (Figure 2). In distinguishing patients between discharged and deceased, day 1 LPC level with a cut-off value of 10000 showed significant efficacy. Sensitivity was 88.9%, positive predictive value was 50.0%, specificity was 77.1% and negative predictive value

Discussion

The COVID-19 pandemic, which began in 2019 in China and spread worldwide, resulted in the loss of millions of lives (6). To predict the prognosis, many biomarkers have been studied. In this study, we examined the serum LPC levels of our patients for the prognosis of COVID pneumonia and found that low LPC levels were predictive of mortality.

The studies conducted have shown that being male and over 50 years old increases mortality (7). In the study, it was found that the majority of deceased patients were elderly and male.

Studies have shown that the most common symptoms seen in Covid pneumonia are shortness of breath (53-80%), cough (60-86%), and changes in taste or smell (64-80%). It has been shown that 20-99% of patients had a complaint of high fever during the course of the disease (8,9). In a study conducted on 140 patients in China, the complaints of patients presenting to the hospital were examined. When the results were examined, it was found that the most common symptom encountered was fever with 91.7%, followed by cough with 75% (10). In this study, in line with the literature, patients presented with widespread symptoms such as cough, weakness, fatigue, shortness of breathing, and fever.

In our study, our patients were in the elderly age group, and hypertension, diabetes, and coronary artery disease were seen as the most common chronic diseases. This result was consistent with a retrospective study conducted on 191 hospitalized patients in China (9). Approximately half of our patients were not vaccinated. We analysed our patients in two groups, discharged and deceased. We determined no statistical difference between the groups in terms of age, gender, presenting symptoms (except for fever), chronic diseases (other than hypertension and coronary artery disease), and vaccination status. Furthermore, in the discharged group, HT and coronary artery disease (CAD) were higher compared to the deceased patient group. This contradicted the literature because a meta-analysis in COVID-19 patients in China found that HT and CAD were strongly associated with mortality (11). We speculated that this could be due to differences in patient

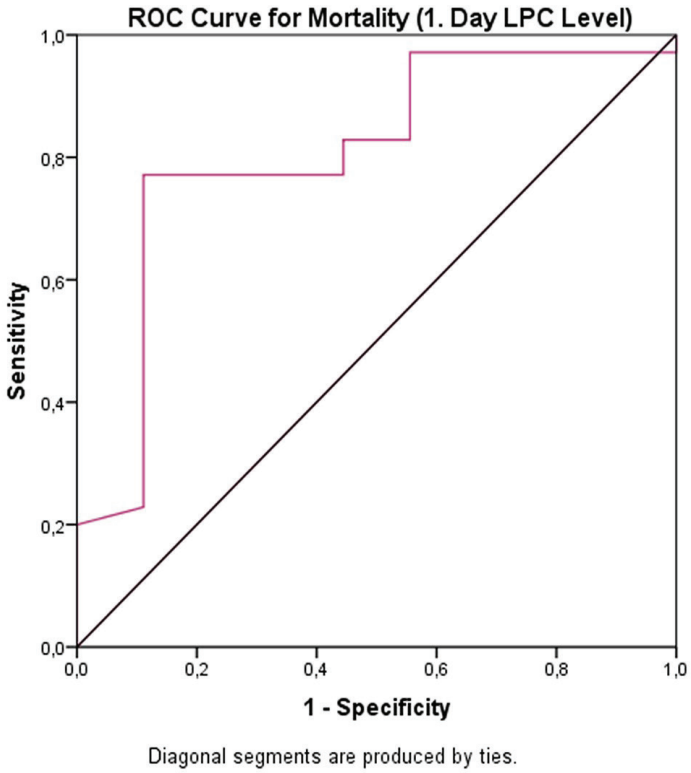

Figure 2. ROC curve for Mortality.

treatments and milder thoracic CT involvement and vaccination status.

Prognostic value of serum LPC level was evaluated in 56 community-acquired pneumonia (CAP) patients. LPC concentrations on days 1 and 7 were significantly lower in the group with death. A cut-off LPC level of < 29.6 (μmol/L) on day 1 was associated with mechanical ventilation, vasopressor use, ICU admission, and mortality. In this study, it was found that serum LPC levels in CAP patients presenting to the emergency department were more predictive of outcomes than previously validated biomarkers like procalcitonin (PCT) and scoring systems like CURB-65 or PSI (12). In our study, similarly, LPC values were examined on days 1 and 5. It was found that in individuals with LPC values below the 10,000 ng/ml cut-off on day 1, there was a higher mortality rate, as well as an increased need for mechanical ventilation and high-flow oxygen.

In a study of 105 sepsis patients, serum LPC concentration was found to decrease with the severity of sepsis, especially in the presence of bacteraemia. It was noted that on the first day, serum LPC concentration was remarkably low (13). In our study as well, patients with low LPC levels on the first day had a more severe course leading to higher mortality rates.

In a study conducted on 74 patients monitored in the intensive care unit of a tertiary hospital due to sepsis and/or septic shock, the LPC levels on days 1 and 7 were compared with procalcitonin, CRP, and WBC counts. The concentrations on day 7 were found to be higher in survivors. The study showed that decreasing LPC levels on day 7, along with procalcitonin values 1.5 times higher than the initial value, were useful in predicting 28-day mortality. In this study, the patients' LPC levels were evaluated in conjunction with the treatments they received. It was observed that in patients receiving appropriate antibiotics, LPC levels increased, while in those receiving inappropriate antibiotics, they did not increase (14). In our study, it was found that high ferritin levels, along with low LPC levels, could be significant for mortality in terms of biochemical parameters. A meta-analysis on ferritin found it to be high in individuals with chronic diseases and those experiencing severe illness, correlating with the need for intensive care (15). In our study, we found that ferritin could be negatively correlated with LPC. However, compared to LPC, haematological parameters such as PO2/FiO2, D-dimer, troponin, lactate, and CRP showed lower predictive value for mortality in determining COVID prognosis. Consistent with this predictive value, we observed that the need for high-flow oxygen and mechanical ventilation was higher in individuals with low LPC levels compared to those with high LPC levels. The most significant factor contributing to a poor prognosis is the exaggerated, uncontrolled, and severe inflammatory response caused by infection. This response leads to abnormal values in many parameters in laboratory tests. In many studies, lymphopenia has been found to be associated with a poor prognosis and mortality. Therefore, monitoring lymphocyte levels is recommended for tracking the progression of the disease. The neutrophil-to-lymphocyte ratio increases in severe illness and can be used as a poor prognostic indicator. Lymphopenia and an increased neutrophil-to-lymphocyte ratio have been found to be associated with severe illness and mortality (16). Other parameters include the elevation of C reactive protein (CRP), procalcitonin (PCT) levels, erythrocyte sedimentation rate (ESR), tumour necrosis factor-alpha (TNF-α), ferritin, interleukin-6 (IL-6), and interleukin-10 (IL-10) (17). While D-dimer is a test commonly used for clinical conditions like deep vein thrombosis (DVT), pulmonary embolism (PE), and disseminated intravascular coagulation (DIC), its elevation has also been observed during COVID-19 infection (18). Individuals with COVID-19 face a risk of deep vein thrombosis (DVT) and a potential risk of pulmonary embolism (PE) of up to 25% (19). High D-dimer levels and a low PO2/FiO2 ratio are associated with increased mortality (20). In our study, significant statistical differences were determined between the groups in terms of haematological parameters, with ferritin and D-dimer levels and the PO2/FiO2 ratio being statistically significant against the deceased patient group. We observed findings in line with the literature.

We evaluated our patient groups based on their LPC levels. The decrease in LPC has been shown to be associated with an increase in arterial atherosclerosis, cerebral ischemia, and inflammatory cell activation (21). In t study, we found that in the deceased patient group, the LPC levels on days 1 and 5 were lower than those in the discharged group. In this study, we hypothesized that the high mortality in the group with low LPC levels is related to the insufficient formation of the inflammatory reaction.

In the study, we identified the LPC cut-off value as <10,000 for distinguishing between the deceased patient group and the discharged group. We evaluated patient groups that were above and below the cut-off value. We didn’t observe any significant differences in terms of age, gender, vaccination status, or chronic diseases between these two groups. The lack of variation in chronic diseases causing low LPC levels between the groups, apart from the infection, led us to believe that the severity of COVID pneumonia is associated with LPC levels. This is because the patients with high CT involvement had lower LPC levels on the first day.

It was observed that out of 10 patients with LPC levels below the cut-off who were admitted to the ward, mortality occurred in 4 during their ward stay. Patients with low LPC levels have prolonged care durations and increased mortality rates. As a result, it was considered that patients with low LPC levels should receive more aggressive monitoring and treatment, potentially requiring intensive care.

The levels of LPC on the first and fifth days were examined between the discharged and deceased patient groups. In the deceased patient group, the LPC levels on the first day were below the average for all patient groups and decreased further on the fifth day. However, in the deceased patient group,

although there was a decrease in LPC levels between the first and fifth days, the overall average level did not drop below the average. The group of patients with LPC levels below the cut-off showed a mortality rate of 50%, whereas the group with LPC levels above the cut-off had a mortality rate of 3.5%. All these results indicate that LPC levels have high sensitivity and negative predictive value.

Limitations

There were several limitations in our study, the most significant being the absence of a healthy control group. Additionally, the small sample size was another limitation, as it may have introduced selection bias and restricted the generalizability of the findings.

Conclusion

In the study, we established that the 1st-day LPC levels of patients with thoracic CT involvement who presented to the emergency department had high sensitivity, moderate specificity, and advanced negative predictive value for mortality in patients with COVID pneumonia, indicating that LPC levels could be a valuable biomarker for prognosis in patients presenting to the emergency room with COVID pneumonia. Our study is a prospective pilot study, and while it provides valuable insights, larger studies are needed to further assess the reliability and clinical significance of the test.

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The datasets used and/or analyzed during the current study are available for sharing by the corresponding author upon request.

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- Conception and design of the research: Dehmen S, Melekoğlu A, Altınbilek E;
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- Analysis and interpretation of the data: Melekoğlu A, Ceritli S;
- Writing of the manuscript: Melekoglu A, Altınbilek E;
- Statistical analysis: Melekoğlu A, Ceritli S;
- Critical revision of the manuscript for content:Kahveci U, Altınbilek E.

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Ethics Approval and Consent to Participate:

The study was conducted with the approval of the Institutional Ethics Committee (University of Health Sciences Şişli Hamidiye Etfal Training and Research Hospital Health Application and Research Center Clinical Research Ethics Committee, date: 19/04/2022, no: 3519) and adhered to the principles of the Declaration of Helsinki. Informed consent was obtained from all eligible patients after they were provided with detailed information about the study.

Consent for Publication:

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The authors declare that they have no competing interests.

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