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Original Article

A new parameter in COVID-19 pandemic: initial lactate dehydrogenase (LDH)/Lymphocyte ratio for diagnosis and mortality

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ABSTRACT

Background: COVID-19 (Coronavirus Disease-2019) is a pandemic disease, infecting more than 26.5 million people. Since there is no specific and effective treatment; early diagnosis and optimal isolation of the patient are of vital importance. Real-time polymerase chain reaction-based (RT-PCR) analyses do not achieve sufficient sensitivity in the diagnosis of the disease.

Methods: The data from 2217 patients diagnosed as COVID-19 between March 2020 and June 2020 and hospitalized or discharged with home isolation were retrospectively analyzed. Demographic data, comorbidities, PCR results, initial computed tomography (CT), laboratory values, Lactate Dehydrogenase (LDH)/Lymphocyte ratio, initial treatments and last status were recorded. The diagnostic sensitivity of LDH/Lymphocyte ratio, which is the main purpose of the study, was analyzed statistically.

Results: In order to test the effectiveness of LDH/Lymphocyte ratio for COVID-19 for diagnostic purposes, CT results were considered as gold standard. The area under the curve (AUC) was found to be 0.706 ($p < 0.001$; cut-off > 0.06) (Sensitivity: 76.4, specificity: 59.60). For the evaluation of LDH/Lymphocyte ratio in terms of survival, AUC was found to be 0.749 ($p < 0.001$; cut-off > 0.21) (Sensitivity: 70.59, specificity: 73.88).

Conclusion: Studies based on radiological findings have demonstrated that CT involvement has higher sensitivity. LDH/Lymphocyte ratio was analyzed in terms of diagnosis and mortality with using specific CT involvement as gold standard method which was found to be a more sensitive due to PCR false negativity; 0.06 and 0.21 were obtained as cut off values for diagnosis and mortality.

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Introduction

COVID-19 (Corona Virus Disease-2019) has emerged as a pandemic factor that has infected more than 26.5 million people, 3.5 million being actively sick, since the first case appeared [1]. It caused by Sars-Cov-2 (Severe Acute Respiratory Syndrome Coronavirus 2) virus. The fatality rate is highest in patients aged ≥65 years or those with certain comorbidities [2–4]. The population of patients with hypertension, chronic respiratory and cardiac diseases, diabetes mellitus, renal failure and malignancy are defined as the most severely affected group [5].

In the studies where the incubation period of the virus is performed, the median reaches from 4 days to 14 days [4–6]. Although there are clinical findings on a wide scale ranging from mild respiratory symptoms to severe respiratory failure, it is possible to say that severe cases are around 4–5% [7,8]. It is evident that early diagnosis, treatment and optimal isolation of the patient and his/her environment are vital at the point of treatment due to the spread of the disease. In the literature, we see that there are many publications on the diagnosis of the disease. The analysis of various samples based on real-time polymerase chain reaction (RT-PCR), which was used as the gold standard diagnostic method, cannot achieve sufficient speed and sensitivity in the diagnosis of the disease. This, in particular, delays the isolation of patients and accelerates disease spread.

There are differences in the sensitivity of the PCR samples studied with various samples. In the most recent study of Wenling Wang et al. [9], the sensitivity order was as follows: Bronchoalveolar lavage 93%, throat culture 72%, nasal sample 63%, fibrobronchoscopic brush biopsy 46%, pharyngeal sample 32%, faeces 29%, blood% 1 and urine 0%. Evaluation with bronchoalveolar lavage is quite difficult in emergency conditions and it does not seem possible due to the high risk of transmission.

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Therefore, negative results in potential cases lead to different opinions about the approach to patients.

PCR comparison with diagnostic methods based on thorax computed tomography (CT) has also been studied in the literature and the sensitivity appears to be high in favor of CT [10]. In our study, the data from 2217 patients who were admitted to the emergency room of our hospital between March 2020 and June 2020; diagnosed as COVID-19 and hospitalized or discharged with home isolation were retrospectively analyzed. Clinical features, treatments, laboratory and imaging results and mortality data of this patient group were retrospectively examined. Based on the hypothesis that it could present a new diagnostic method in terms of the early diagnosis and early isolation, it was aimed at providing early diagnosis for especially those patients with typical radiological involvement and clinical findings through the Lactate Dehydrogenase/Lymphocyte (LDH/Lymphocyte) ratio.

The basis of our study and the starting point of our hypothesis is the other clinical studies based on LDH, which is an important indicator in the early diagnosis of pneumocystis carinii clinic-laboratory, which is an important factor of atypical pneumonia [11–13]. Although LDH is an enzyme originating from many organs and systems, it increases significantly especially in patients with lung involvement. In addition, we see that lymphopenia, which will occur secondary to viral infections, is also present in COVID-19 cases. The study was conducted with the hypothesis that the combination of these laboratory values would yield a more sensitive result in early diagnosis.

Material and methods

Our study was conducted upon obtaining the approval from the local ethics committee and the relevant departments of the Ministry of Health. (Ethics committee approval number: 2257, 8.5.2020, Ministry of Health Approval Number: 2020-04-30T15_07_44.). The data of 2217 patients who were admitted to the emergency room of our hospital between March 2020 and June 2020; diagnosed as COVID-19 and hospitalized or discharged with home isolation were retrospectively analyzed. Demographic data of patients such as age, gender, comorbidities such as chronic obstructive pulmonary disease (COPD), asthma, hypertension (HT), chronic hearth failure (CHF), diabetes mellitus (DM), coronary artery disease (CAD), malignancy, rheumatic diseases (RD), cerebrovascular accident (CVA) and others; nasopharyngeal PCR swab results (first 3 results, positive or negative), initial CT results, initial leukocyte, neutrophil, lymphocyte, hemoglobin, platelet, urea, creatinine, D-Dimer, aspartate aminotransferase (AST), alanine transaminase (ALT), total protein, albumin, creatine kinase (CK), C-reactive protein (CRP), procalcitonin, LDH values, LDH/Lymphocyte ratio, initial treatments (hydroxychloroquine, azithromycin, oseltamivir, additional antibiotherapy, lopinavir/ritonavir, favipiravir usage), follow-up subtypes (inpatient or outpatient) and their last status (alive or exitus) were recorded. CT results were collected under three separate headings as no involvement, unilateral and bilateral involvement. The relation of the patients' recorded data to individual survival was examined. In addition, the diagnostic sensitivity of LDH/Lymphocyte ratio, which is the main purpose of the study, was analyzed statistically. LDH/Lymphocyte ratio was analyzed in terms of diagnosis and mortality with using specific CT involvement as the gold standard method which was found to be a more sensitive method due to PCR false negativity.

Statistical analysis

The analysis of the data was carried out using SPSS 25 and Medcalc package programs. Descriptive statistics are presented by giving frequency and percentage tables for categorical variables and arithmetic mean, standard deviation, median, minimum and maximum values for quantitative variables. Chi-square test was used for comparisons between two categorical variables, and independent sample *t*-test was used for comparison of categorical variables and quantitative variables since the categorical variable contains two categories. The logistic regression analysis was carried out by including the factors determined to have an impact on survival conditions as a result of binary comparisons. ROC analysis was applied to test the acceptability of LDH/Lymphocyte ratio as diagnostic test and to determine the predictive values in mortality.

Table 1
Demographic Datas, Comorbidities, Initial PCR and CT Results, Last Status and Follow Up Subtypes.

	Min–Max	Median	Mean. ± s.d./n-%	
Age		18–97	48	47.66 ± 17.23
Gender	Female			1042 47%
	Male			1175 53%
Comorbidities	COPD			48 2.2%
	Asthma			103 4.6%
	CHF			51 2.3%
	CAD			165 7.4%
	HT			456 20.6%
	DM			360 16.2%
	CRF			63 2.8%
	Malignancy			82 3.7%
	CVA			14 0.6%
	RD			29 1.3%
	Others			159 7.2%
1st PCR	(-)			676 30.5%
	(+)			1541 69.5%
CT	(-)			298 13.4%
	(+)			1594 71.9%
	Without involvement			298 13.4%
	Unilateral			207 9.3%
	Bilateral			1387 62.6%
Exitus				68 3.1%
Alive				2149 96.9%
Outpatient				883 39.8%
Inpatient				1334 60.2%

COPD: Chronic Obstructive Pulmonary Disease, CHF: Chronic Hearth Failure, CAD: Coronary Artery Disease, HT: Hypertension, DM: Diabetes Mellitus, CRF: Chronic Renal Failure, CVA: Cerebrovascular Accident, RD: Rheumatic Diseases, PCR: Polymerase Chain Reaction, CT: Computed Tomography.

Results

Demographic datas, comorbidities, initial PCR and CT results, last status and follow up subtypes

The data of 2217 patients in total were examined. 53% of the patients were male (n: 1175); 47% were female (n: 1042). The mean age was 47.66 ± 17.23. 60.2% (n: 1334) of the them received inpatient treatment; 39.8% (n: 883) received outpatient treatment. The mortality rate of the patients was determined as 3.1% (n: 68). The most common comorbidity of the patients was hypertension with 20.6% (n: 456). Hypertension was followed by diabetes mellitus with 16.2% (n: 360). The positivity rate of the 1st PCR results of the patients was 69.5% (n = 1541). 1. PCR result is negative, but 2. PCR result positive patient rate was 4.74% (n = 105). First two negative but the third positive was 1.17 (n = 38) of them. 9.61% (n = 213) of patients have 3 negative PCR results. Initially, typical COVID-19 involvement was detected with CT in 71.9% (n: 1594); while 1387 of them were bilateral; 207 of them were unilateral involvement (Table 1).

Drug usage for COVID-19 treatment

Hydroxychloroquine was used in 82.3% of the patients (n: 1824); this was followed by azithromycin with 44.5% (n: 987). Additional antibiotherapy was needed in 14.6% of patients (n: 324). 2.7% (n: 60) of patients were receiving favipiravir (Table 2).

Table 2
Drug Usage for COVID-19 Treatment.

		n /%	
HQ	(-)	393	17.7%
	(+)	1824	82.3%
Azithromycine	(-)	1230	55.5%
	(+)	987	45.5%
Oseltamivir	(-)	1460	65.9%
	(+)	757	34.1%
Lop/Rit	(-)	2145	96.8%
	(+)	72	3.2%
Favipravir	(-)	2157	97.2%
	(+)	60	2.7%
Antibiotherapy	(-)	1893	85.4%
	(+)	324	14.6%

HQ: Hydroxychloroquine, Lop/Rit: Lopinavir/Ritonavir.

Table 3
Laboratory Results.

	Min-Max	Median	Mean. ± s.d./n-%
WBC (/μL)	240–63860	6310	6946.62 ± 3342.65
Neutrophil (/μL)	10–46100	3880	4557.97 ± 2910.17
Hemoglobin (gr/L)	5.1–15.6	13.8	13.68 ± 3.68
Lymphocyte (/μL)	25–23100	1520	1809.66 ± 5146.25
Thrombocyte (/μL)	1000–1434000	217,000	228147.55 ± 127125.22
LDH (U/L)	68–1840	235	268.56 ± 140.39
CRP (mg/L)	0–453	12	40.36 ± 84.73
Procalcitonin (ng/mL)	0–162	0.05	1.57 ± 10.38
D-Dimer	0–41	0.6	1.75 ± 4.54
Urea (mg/dl)	0.45–435	28.75	35.18 ± 27.92
Creatinine (mg/dl)	0.1–8.9	0.77	1.18 ± 4.04
AST (U/L)	5–506	27	34.26 ± 28.98
ALT (U/L)	2–619	22	30.99 ± 36.92
Total Protein (gr/dl)	3.74–8.02	7.05	7.54 ± 5.72
Albumin (gr/dl)	1.23–6	4.18	4.24 ± 1.8
CK (U/L)	1–21140	84	163.92 ± 619.66
LDH/Lymph	0–6.65	0.116	0.17 ± 0.31

WBC: White Blood Cell, LDH: Lactate Dehydrogenase, CRP.: C-Reactive Protein, AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase, CK: Creatine Kinase, LDH/Lymp.: Lactate Dehydrogenase/Lymphocyte.

Laboratory results

Mean absolute lymphocyte count was 1809.66 ± 5146.25; mean LDH 268.56 ± 140.39 and mean LDH/Lymphocyte ratio was 0.17 ± 0.31 (Table 3).

Comorbidity and drug usage—survival analysis

COPD, CHF, CAD, HT, DM, CKD and malignancy were found to have a significant statistical relationship with survival ($p < 0.001$). Those with any comorbidity had high mortality than those without comorbidity ($p < 0.001$) (Table 4).

When the relationship between drug usage and survival was examined, no statistically significant relationship was found for hydroxychloroquine and azithromycin ($p = 0.616$, $p = 0.095$). Significantly more deaths were observed in patients using oseltamivir ($p = 0.031$), lopinavir/ritonavir ($p = 0.022$), supplemental antibiotherapy ($p < 0.001$) and favipiravir ($p < 0.001$) (Table 5).

Follow up subtype, CT findings, 1st PCR and presence of involvement in CT and survival analysis

When the effects of involvement subtypes on survival in CT are examined, it was revealed that patients with bilateral CT involvement showed significantly high mortality ($p < 0.001$). In patients with CT involvement, there was more statistically deaths than those without CT involvement ($p = 0.014$) (Table 6).

Laboratory results, LDH/Lymphocyte ratio and age and survival analysis

When the relationship between laboratory data and survival is examined, high LDH/lymphocyte ratio ($p = 0.001$), high leukocyte ($p = 0.001$), high neutrophil ($p < 0.001$), low hemoglobin ($p = 0.001$), high LDH ($p < 0.001$), high CRP ($p < 0.001$), high D-Dimer ($p = 0.025$), high urea ($p < 0.001$), high AST ($p = 0.003$) and low albumin ($p = 0.003$) were found to have statistically significant high mortality (Table 7).

Logistic regression analysis of datas

The p values for step, block and model were less than 0.001 and $p = 0.718$ at the end of the Hosmer and Lemeshow test. The model was found to be feasible and analyses continued. As a result of logistic regression analysis; 1 unit increase in age was found to increase the mortality risk by 1.034 times, while 1 unit increase in CRP was found to increase the risk 1.007 times (Table 8).

ROC analysis: LDH/Lymphocyte ratio for diagnosis and survival

In order to test the usability of the LDH/Lymphocyte ratio in diagnosis for COVID-19 disease, individuals who showed unilateral and bilateral specific CT involvement were considered positive due to less false negativity of CT compared to PCR and evaluations were performed by accepting the CT results as a gold standard. As a result of ROC analysis; the area under the curve (AUC) was found to be 0.706 ($p < 0.001$; cut-off > 0.06) and it was concluded that the LDH/Lymphocyte ratio was diagnostic for COVID-19. The sensitivity at the cut-off point is 76.4 and specificity is 59.60 (Table 9).

ROC analysis was performed to evaluate the LDH/Lymphocyte ratio in terms of survival conditions and the area under the curve (AUC) was found to be 0.749 ($p < 0.001$; cut-off > 0.21). The sensitivity at cut-off point is 70.59 and specificity is 73.88 (Table 10).

Discussion

Our study contains 3-months data of COVID-19 and has single center homogenization. It is clear that it will make a significant contribution to the literature not only in terms of revealing the data or determining the survival relationship, but also in terms of the new alternative it offers at the point of diagnosis.

It is possible to say that most of the patients who applied for emergency services were isolated by hospitalization. This not only provided an advantage in terms of isolation, but also facilitated clinical follow-up and data transfer. All deaths were among inpatients. Our hospital's mortality rate was 3.1% with 68 patients, which is in line with the literature data.

The positive rate of PCR result was 69.5%. It should be emphasized that all PCR negative cases have CT involvement. This is in line with the discussions carried out in the literature before. Studies based on radiological findings have demonstrated higher CT involvement and sensitivity [14,15]. In our study, typical COVID-19 involvement was found in 71.9% of patients with baseline CT (n: 1594); 1387 of them are bilateral; 207 of them consisted of unilateral involvement. This data is the first in the literature.

Significant statistical relationship between LDH/Lymphocyte ratio and survival, which form the basis of our study, has been shown. In order to test the usability of the LDH/Lymphocyte ratio in diagnosis for COVID-19, the patients with unilateral and bilateral specific CT involvement were considered positive due to less false negativity than PCR and the evaluations were performed by accepting the CT results as the gold standard. As a result of ROC analysis; the area under the curve (AUC) was found to be 0.706 ($p < 0.001$; cut-off > 0.06) and it was concluded that the LDH/Lymphocyte

ratio was diagnostic for COVID-19. The sensitivity at cut-off point is 76.4 and specificity is 59.60. ROC analysis was performed to evaluate the LDH/Lymphocyte ratio for survival and the area under the curve (AUC) was found to be 0.749 ($p < 0.001$; cut-off > 0.21). The sensitivity at cut-off point is 70.59 and specificity is 73.88. Our LDH/Lymphocyte ratio is usable in terms of mortality and putting cut-off in terms of diagnosis and mortality, they have been a big contribution of our study to the literature. Our ratio is very impressive in early diagnosis and mortality prediction due to its easy application, especially since COVID-19 has no specific treatment yet and the importance of early isolation is unquestionable.

The most frequently used treatment is hydroxychloroquine, which is an expected finding. At this point, when examining the use of favipiravir specifically; we see that it was used for 2.7% of patients. Due to the rapid increase in case numbers all around the world and the limited and contradictory data from the initial cases, the permission to use favipiravir is subjected to the regulations of Ministry of Health. With the increasing experience in dealing with cases, its scope of usage has broadened. While it was initially only being used in the intensive care unit, lately its application has been extended to other patients.

Looking at the survival data; in parallel with the literature, the relationship between comorbidities such as COPD, HT, DM, CHF, CAD and presence of malignancy and survival has been revealed. Similarly, statistical significance between any presence of comorbidity and no comorbidity was also shown in our study [16–20]. In the data between drug usage and survival, there was no significant relationship between hydroxychloroquine and azithromycin and survival. Contrary to expectations, a survival relationship was found in the use of oseltamivir, additional antibiotherapy and favipiravir. It should be taken into consideration that all patients requiring additional antibiotherapy or those who have to use favipiravir are fragile patients in intensive care conditions who require hospitalisation and close follow-up. The mortality rate is higher in this patient group as expected. Further data requirements are obvious in terms of favipiravir and treatment responses [21,22]. Again, the majority of this patient group consists of critical patients that are in line with the National Institutes of Health (NIH) guidelines. It is worth noting that clinical pictures such as ARDS (acute respiratory distress syndrome), septic shock, cardiac dysfunction, multiorgan failure are common in this patient population [16].

When it is examined in terms of CT involvement and survival, new data were obtained. Especially it is important to find a significant relationship between bilateral involvement and survival. This is a practical and usable finding for clinicians. It should be said that it can be used more easily than the specific findings described in the

Table 4
Comorbidity and Survival Analysis.

			Alive	Exitus	Chi-Square	p
COPD	(-)	n	2109	60	26.023	**<0.001***
		%	97.2	2.8		
	(+)	n	40	8		
		%	83.3	16.7		
Asthma	(-)	n	2046	68	2.422	0.120
		%	96.8	3.2		
	(+)	n	103	0		
		%	100	0		
CHF	(-)	n	2104	62	10.456	**0.001***
		%	97.1	2.9		
	(+)	n	45	6		
		%	88.2	11.8		
CAD	(-)	n	2002	50	34.078	**<0.001***
		%	97.6	2.4		
	(+)	n	147	18		
		%	89.1	10.9		
HT	(-)	n	1721	40	16.958	**<0.001***
		%	97.7	2.3		
	(+)	n	428	28		
		%	93.9	6.1		
DM	(-)	n	1812	45	14.644	**<0.001***
		%	97.6	2.4		
	(+)	n	337	23		
		%	93.6	6.4		
CRF	(-)	n	2096	58	31.469	**<0.001***
		%	97.3	2.7		
	(+)	n	53	10		
		%	84.1	15.9		
Malignancy	(-)	n	2076	59	15.256	**<0.001***
		%	97.2	2.8		
	(+)	n	73	9		
		%	89.0	11.0		
CVA	(-)	n	2136	67	12	375
		%	97.0	3.0		
	(+)	n	13	1		
		%	92.9	7.1		
RD	(-)	n	2121	67	0	1.000
		%	96.9	3.1		
	(+)	n	28	1		
		%	96.6	3.4		
Comorbidites	(-)	n	1310	18	32.640	**<0.001***
		%	98.6	1.4		
	(+)	n	839	50		
		%	94.4	5.6		

COPD: Chronic Obstructive Pulmonary Disease, CHF: Chronic Hearth Failure, CAD: Coronary Artery Disease, HT: Hypertension, DM: Diabetes Mellitus, CRF: Chronic Renal Failure, CVA: Cerebrovascular Accident, RD: Rheumatic Diseases.

Table 5
Drug Usage and Survival Analysis.

			Alive	Exitus	Chi-Square	p
HQ	(-)	n	383	10	251	616
		%	97.5	2.5		
	(+)	n	1766	58		
		%	96.8	3.2		
Azithromycine	(-)	n	1199	31	2.779	95
		%	97.5	2.5		
	(+)	n	950	37		
		%	96.3	3.7		
Oseltamivir	(-)	n	1424	36	4.627	**0.031***
		%	97.5	2.5		
	(+)	n	725	32		
		%	95.8	4.2		
Lop/Rit	(-)	n	2083	62	5.231	**0.022***
		%	97.1	2.9		
	(+)	n	66	6		
		%	91.7	8.3		
Antibiotherapy	(-)	n	1856	37	51.404	**<0.001***
		%	98.0	2.0		
	(+)	n	293	31		
		%	90.4	9.6		
Favipravir	(-)	n	2100	57	43.207	**<0.001***
		%	97.4	2.6		
	(+)	n	49	11		
		%	81.7	18.3		

HQ: Hydroxychloroquine, Lop/Rit: Lopinavir/Ritonavir.

Table 6
Follow Up Subtype, CT Findings, 1st PCR and Presence of Involvement in CT and Survival Analysis.

			Alive	Exitus	Chi-Square	p
Follow Up	Outpatient	n	876	7	25.534	**<0.001***
		%	99.2	0.8		
	Inpatient	n	1273	61		
		%	95.4	4.6		
CT Findings	Without Involvement	n	295	3	12.563	**0.002***
		%	99.0	1.0		
	Unilateral	n	204	3		
		%	%99	%1		
	Bilateral	n	1325	62		
		%	95.5	4.5		
1st PCR	(-)	n	653	23	223	0.637
		%	96.6	3.4		
	(+)	n	1496	45		
		%	97.1	2.9		
Involvement in CT	(-)	n	295	3	5.976	**0.014***
		%	99.0	1.0		
	(+)	n	1529	65		
		%	95.9	4.1		

PCR: Polymerase Chain Reaction, CT: Computed Tomography.

previous literature data especially regarding the pandemic patient density [18]. It should be noted that the relationship between laboratory data and survival is parallel to the literature. As a result of logistic regression analysis; 1 unit increase in age was found to increase the mortality risk by 1.034 times, while 1 unit increase in CRP was found to increase the risk 1.007 times. These findings seem to be a potentially original contribution to the existing literature [19,20].

Limitations

Our study has some limitations. The potential relationship between the LDH/Lymphocyte ratio and other infectious diseases is unknown. For this reason, the relationship between this ratio and mixed infection or other viral pneumonias can lead to confusion as it is not clear. Another important limitation point is that new treatment options were not available for the patients included in the study and they were included in the study mostly at the beginning of the pandemic. Therefore, it should be noted that our current treatment approach and guidelines are different.

Conclusion

As a result, in our study, we revealed a single center data and examined the LDH/Lymphocyte ratio. LDH/Lymphocyte ratio was analyzed in terms of diagnosis and mortality with using specific CT involvement as the gold standard method which was found to be a more sensitive method due to PCR false negativity; 0.06 and 0.21 were obtained as cut off values for diagnosis and mortality.

Ethics statement

The study protocol has been approved by Istanbul Training and Research Hospital Ethics Committee and Ministry of Health. (Ethics committee approval number: 2257, 8.5.2020, Ministry of Health Approval Number: 2020-04-30T15_07_44).

Table 7
Laboratory Results, LDH/Lymphocyte Ratio and Age and Survival Analysis.

			Mean	T	p
WBC	Alive	2087	6875.7992 ± 3240.09091	−3.514	**0.001***
	Exitus	68	9120.3235 ± 5235.31566		
Neutrophil	Alive	2087	4469.1145 ± 2771.72802	−4.595	**<0.001***
	Exitus	68	7285 ± 5029.10321		
Lymphocyte	Alive	2087	1830.8313 ± 5225.80731	1.058	290
	Exitus	68	1159.9118 ± 863.59985		
Hemoglobin	Alive	2087	13.7232 ± 3.703	3.221	**0.001***
	Exitus	68	12.2676 ± 2.29408		
Thrombocyte	Alive	2085	228343.7266 ± 126968.53875	0.380	0.705
	Exitus	68	222132.3529 ± 132674.09339		
LDH	Alive	1457	261.3446 ± 124.11636	−4.602	**<0.001***
	Exitus	60	443.85 ± 306.12393		
CRP	Alive	1933	37.1391 ± 82.22079	−7.985	**<0.001***
	Exitus	63	139.2457 ± 100.4061		
Procalcitonin	Alive	828	1.4653 ± 10.3107	−1.344	0.179
	Exitus	42	3.6705 ± 11.52844		
D-Dimer	Alive	1319	1.6503 ± 4.3289	−2.313	**0.025***
	Exitus	49	4.3373 ± 8.08934		
Urea	Alive	1570	34.0283 ± 25.99135	−4.615	**<0.001***
	Exitus	66	62.6182 ± 50.04428		
Creatinine	Alive	1573	1.1626 ± 4.11117	−0.767	0.443
	Exitus	67	1.5497 ± 1.85184		
AST	Alive	1557	33.5605 ± 27.92626	−3.082	**0.003***
	Exitus	67	50.5075 ± 44.63161		
ALT	Alive	1557	30.6098 ± 34.21579	−0.978	0.332
	Exitus	67	39.7761 ± 76.42343		
T.Protein	Alive	989	7.5046 ± 5.47817	−0.469	0.641
	Exitus	43	8.214 ± 9.84331		
Albumin	Alive	1120	4.2733 ± 1.83266	3.022	**0.003***
	Exitus	51	3.4951 ± 0.69199		
LDH/Lymphocyte	Alive	2144	0.1797 ± 0.29294	−3.569	**0.001***
	Exitus	68	0.5481 ± 0.84966		
CK	Alive	1270	142.9036 ± 215.04916	−1.321	0.192
	Exitus	56	640.5536 ± 2818.11422		
Age	Alive	2147	47.0671 ± 16.94875	−9.409	**<0.001***
	Exitus	67	66.791 ± 15.10823		

WBC: White Blood Cell, LDH: Lactate Dehydrogenase, CRP.: C-Reactive Protein, AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase, T.Protein: Total Protein, CK: Creatine Kinase, LDH/Lymp.: Lactate Dehydrogenase/Lymphocyte.

Table 8
Logistic Regression Analysis.

	B	S.E.	Wald	p	HR (%95 CI)
COPD	1.333	0.711	3.517	0.061	3.791(0.942–15.263)
CHF	−0.509	0.773	0.433	0.510	0.601(0.132–2.735)
CAD	0.546	0.502	1.183	0.277	1.726(0.645–4.618)
HT	−0.475	0.476	0.993	0.319	0.622(0.244–1.583)
DM	0.165	0.462	0.127	0.721	1.179(0.477–2.917)
CRF	0.482	0.714	0.456	0.500	1.619(0.4–6.556)
Malignancy	0.097	0.728	0.018	0.894	1.102(0.265–4.591)
Without Involvement in CT			0.01	0.995	(-)
Unilaterally	−17.555	4457.776	0	0.997	0(0–.)
Bilaterally	0.086	0.858	0.01	0.920	1.09(0.203–5.862)
WBC	0	0	1.296	0.255	1(1–1)
Neutrophil	0	0	1.124	0.289	1(1–1.001)
Hemoglobin	−0.042	0.101	0.169	0.681	0.959(0.786–1.17)
CRP	0.007	0.003	8.24	**0.004**	1.007(1.002–1.012)
D-Dimer	0.006	0.029	0.047	0.829	1.006(0.95–1.066)
Urea	0.009	0.005	2.9	0.089	1.009(0.999–1.019)
AST	0.006	0.004	2.844	0.092	1.006(0.999–1.014)
Albumin	−0.549	0.37	2.202	0.138	0.577(0.279–1.193)
LDH/Lymphocyte	0.23	0.308	0.555	0.456	1.258(0.687–2.303)
Age	0.033	0.017	3.971	**0.046**	1.034(1.001–1.068)
Constant	−8.532	1485.927	0	0.995	0

COPD: Chronic Obstructive Pulmonary Disease, CHF: Chronic Hearth Failure, CAD: Coronary Artery Disease, HT: Hypertension, DM: Diabetes Mellitus, CRF: Chronic Renal Failure, CT: Computed Tomography, WBC: White Blood Cell, CRP.: C-Reactive Protein, AST: Aspartate Aminotransferase, LDH/Lymp.: Lactate Dehydrogenase/Lymphocyte.

Table 9
ROC Analysis: LDH/Lymphocyte Ratio for Diagnosis.

	AUC(%95 CI)	SE	p	Cut-off
CT	0.708(0,685–0,728)	0.017	<0.001*	>0.06

CT: Computed Tomography, AUC: Area Under the Curve, SE: Standart Error.

Table 10
ROC Analysis: LDH/Lymphocyte Ratio for Survival.

	AUC(%95 CI)	SE	p	Cut-off
Survival	0.749(0.731–0.767)	0.033	<0.001*	>0.21

AUC: Area Under the Curve, SE: Standart Error.

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Conflict of interest

None to declare.

Author contributions

All authors contributed to the collection of patients data. IS wrote the manuscript and made tables.

Data availability

The authors declare that data supporting the findings of this study are available within the article.

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