ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

Association of Admission Troponin Levels with Hospitalization and Mortality in COVID-19 Patients

COVID-19 Hastalarında Başvuru Sırasında Ölçülen Troponin Değerlerinin Hastaneye Yatış ve Mortalite ile İlişkisi

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ABSTRACT

Aim: *This study aims to identify the association of cardiac Troponin T (cTnT) levels with hospitalization and in-hospital mortality in patients admitted to the emergency department (ED) and diagnosed with COVID-19.*

Material and Method: *Retrospectively, we scanned the data of adult patients presenting to the ED of a university hospital within 50 days of the first COVID-19 case admission (March 2020 – May 2020). The study group consisted of patients diagnosed with COVID-19 by reverse-transcriptase polymerase chain reaction, and had cTnT test. Demographic and laboratory data, thoracic computed tomography (CT) imaging findings, and length of hospital stay were also collected. The study outcomes were patients' hospitalization status and in-hospital mortality.*

Results: *Out of 36 patients, 9 (25%) were discharged, 20 (55.6%) remained in-patients in the ward, and 7 (19.4%) in the intensive care unit. When overall in-patients were compared to discharged patients, a significant difference was observed with regard to age [median (25% -75%)] [60 (45–69) to 28 (26–39.5) years, respectively; p=0.003)], thoracic CT score [6 (0–11) to 0 (0–0.5), respectively; p=0.005], admission cTnT values [5.99 (3.50–15.55) to 3 (3–3.28) ng/L; p=0.012]. The mortality rate among in-patients was 18.5%. In the multivariate cox regression model, none of these parameters significantly affected survival.*

Conclusion: *The cTnT values of COVID-19 patients are likely to be associated with hospitalization and mortality. Thoracic CT score was higher in patients admitted to the intensive care unit. However, neither cTnT values nor thoracic CT scores have a statistically significant effect on survival, even if their distributions are different between survived and non-survived groups.*

Key words: *COVID-19; computed tomography; emergency department; hospitalization; mortality; troponin*

ÖZET

Amaç: *Bu çalışmanın amacı acil servise (AS) başvuran ve COVID-19 tanısı koyulan hastalarda, kardiyak troponin T (cTnT) düzeylerinin hastaneye yatış ve hastane içi mortalite ile ilişkisini belirlemektir.*

Materyal ve Metot: *Çalışma 3. basamak sağlık hizmeti veren bir üniversite hastanesinin acil servisinde gerçekleştirilmiştir. Retrospektif özelliktedir. Çalışmaya Mart 2020-Mayıs 2020 tarihleri arasında ardışık 50 gündeki erişkin hastalar dahil edilmiştir. Çalışma grubu, ters transkriptaz polimeraz zincir reaksiyonu ile COVID-19 tanısı koyulan ve cTnT testi yapılan hastalardan oluşmaktadır. Hastaların demografik ve laboratuvar verileri, torasik bilgisayarlı tomografi (BT) görüntüleme bulguları, hastanede kalış süreleri not edilmiştir. Çalışma sonlanımı olarak hastaların hastaneye yatış durumu ve hastane içi mortalite bilgileri belirlenmiştir.*

Bulgular: *Çalışmaya alınan 36 hastanın 9'u (%25) taburcu edilmiş, 20'si (%55,6) servise, 7'si (%19,4) yoğun bakıma yatırılmıştır. Yatan hastalar ile taburcu edilen hastalar karşılaştırıldığında, yaş [medyan (%25–75)] [sırasıyla 60 (45–69) ila 28 (26–39,5) yıl; p=0,003)], torasik BT skoru [sırasıyla, 6 (0–11) ila 0 (0–0,5); p=0,005], başvuru cTnT değerleri [5,99 (3,50–15,55) ila 3 (3–3,28) ng/L; p=0,012] olarak bulunmuştur. Yatan hastalarda ölüm oranı %18,5 idi. Çok değişkenli cox regresyon modelinde bu parametrelerin hiçbiri hayatta kalma üzerinde anlamlı bir etkiye sahip değildir.*

Sonuç: *COVID-19 hastalarının cTnT değerlerinin hastaneye yatış ve mortalite ile ilişkili olması muhtemeldir. Yoğun bakım ünitesine yatırılan hastalarda toraks BT skoru daha yüksektir. Ancak cTnT değeri ve torasik BT skorları hayatta kalan ve ölümle sonuçlanan gruplar arasında farklı izlenmiş olsalar bile sağ kalım üzerinde istatistiksel olarak anlamlı bir etkiye sahip değildir.*

Anahtar kelimeler: *acil servis; toraks bilgisayarlı tomografisi; COVID-19; hastaneye yatış; mortalite; troponin*

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Introduction

Troponin is a protein involved in the striated muscle contraction complex. Blood levels of cardiac troponins (cTnI and cTnT) may be elevated after direct damage to the heart muscle, including myocardial infarction, myocarditis, and cardiac contusions, or due to various other reasons such as pneumonia, cerebral pathologies, heart failure, sepsis, pulmonary embolism, burns, and cardiotoxic drugs[1]. Although the reason for elevation in each clinical case cannot be identified separately, changes in cardiac troponins are associated with inflammatory markers and age[2]. More importantly, elevated cardiac troponin is responsible for all-cause mortality during the in-hospital stay and in the long term[1,3].

As a separate issue, COVID-19 is a disease induced by the virus called SARS-CoV-2, which targets both the respiratory tract and other systems in the body[4]. Its major clinical manifestations are fever, cough, muscle aches, weakness, diarrhea, and in more severe cases, shortness of breath and chest pain[4]. While its diagnosis is mainly established by nucleic acid amplification tests and serological tests, other laboratory tests (complete blood count, biochemical tests) or thoracic computed tomography (CT) are used to support the diagnosis, predict the prognosis and exclude differential diagnoses[5]. So far, the highly contagious SARS-CoV-2 virus has infected many people worldwide, causing millions of deaths.

Within this framework, this study aims to assess the demographic characteristics and hospitalization and mortality rates of patients admitted to the emergency department (ED), diagnosed with COVID-19, and subjected to the cTnT test. Moreover, we would like to set a value to cTnT or thoracic CT scores in hospitalized or deceased COVID-19 patients, if any.

Material and Method

Study Design and Population

Our tertiary-level healthcare facility receives approximately 120.000 admissions annually. We retrospectively scanned the data of adult patients (18 years and older) presenting to our ED within 50 days from the admission of the first COVID-19 case (March 2020-May 2020), receiving the diagnosis of COVID-19 through reverse-transcriptase polymerase-chain-reaction (RT-PCR), and undergoing a cTnT test. On the other hand, the data on pregnant women and patients referred to our hospital after the initiation of treatment from an external clinical center were excluded. Treatment of the patients was performed by current guidelines, yet these data were not included in the study[6].

Ethical Approval

We obtained ethical approval from the Medical Ethics Committee of Pamukkale University with an approval number of 23.06.2020/2 and followed the Helsinki Declaration guidelines over the study. Since this is a retrospective study, no patient consent was requested, and descriptive patient information was not reported in this article.

Data Collection

Our patients' admission complaints, demographic data, concomitant diseases and habits, laboratory data (complete blood count, blood biochemistry, D-dimer and cTnT values), and thoracic CT findings[7,8] in the last six days were noted in the study form. The laboratory and diagnostic imaging tests were performed in light of current diagnosis-treatment guideline recommendations[6]. The cTnT values were recorded as the baseline value measured at admission to ED (baseline cTnT) and the maximum value (max. cTnT) measured during a hospital stay. The reference range of the cTnT value in our healthcare facility is 0–14 ng/L.

A Board-certified radiologist with more than ten years of professional experience interpreted thoracic CT findings and scored COVID-19 lung involvement[8]. This scoring system is based on lung involvement in COVID-19 patients. Involvement of each of the five lobes is calculated as a percentage. 25% of each involved lobe is equal to 1 point. Total score ranges from 0 to 20, 0 meaning no lung involvement, and 20 with all five lobes involvement[8]. The association of the scoring with patient mortality was also investigated.

Furthermore, we noted the presence and number of comorbid diseases (i. e., malignancy, diabetes mellitus (DM), hypertension (HT), coronary artery disease, rheumatological diseases, lung diseases, chronic renal failure, chronic liver failure).

The primary outcomes were accepted as patients' discharge from ED, hospitalization, or admission to the intensive care unit (ICU). If the patients were admitted to ICU at any time during their hospital stay, they were included in the ICU in-patient group. The secondary outcomes were the length of hospital stay and in-hospital mortality.

Statistical Analysis

All the statistical analyses of the obtained clinical and demographic data were performed using Statistical Package for the Social Sciences (SPSS) v. 25 (IBM Corp., Armonk, NY, USA). Continuous variables were provided as mean ± standard deviation; median (minimum-maximum values), median (IQR), and categorical variables as numbers and percentages. Shapiro Wilk

test was used for the determination of normal distribution. For independent groups comparisons, we used the independent samples t-test and One Way Analysis of Variance (post hoc: Tukey method) when parametric test assumptions were provided, Mann Whitney U test and Kruskal Wallis Variance Analysis (post hoc: Mann Whitney U test with Bonferroni Correction) were used when parametric test assumptions were not provided. In addition, a Spearman or Pearson correlation analysis was performed to investigate the relationships between continuous variables, whereas the differences between categorical variables were analyzed using a Chi-square test. We used univariate and multiple cox regression models to determine the factors affecting survival. A p-value of <0.05 was set as the limit for statistical significance.

Results

Table 1 provides an overview of the descriptive characteristics and admission reasons of 36 patients (23 males, 13 females, mean age 51.89±20.32; median age 52.5 years; age range 18–99 years). Twenty-six (72%) were under 65 years old, while 10 (28%) were 65.

Out of 30 patients whose medical history could be extracted, 13 (43.3%) had no concomitant disease, and 10 (33.3%) were afflicted with two or more comorbidities (Table 1). Of 31 patients whose smoking status was recorded in the system (29%), 9 were active smokers. Seven were hospitalized (2 in ICU, 5 in the ward), and two died in ICU.

Whereas nine patients (25%) were discharged from the ED and followed up as outpatients via telephone, 20 (55.6%) remained in-patients in the ward and 7 (19.4%) in ICU. The mortality rate among the in-patients was 18.5%, and a considerable proportion of mortality (80%) was observed in the patients hospitalized directly from the ED to the ICU. The average hospital stay of all the patients was 10.2±7.9 days (2–42 days).

When in-patients were compared to patients discharged from the ED, a significant difference was observed in relation to age [median (IQR)] [(60 (45–69) to 28 (26–39.5) years, respectively; p=0.003)], thoracic CT score [6 (0–11) to 0 (0–0.5), respectively; p=0.005)], the highest cTnT values on admission and hospitalization [5.99 (3.50–15.55) to 3 (3–3.28) ng/L; p=0.012 and 7.04 (3.5–54.75 to 3 (3–8.71) ng/L; p=0.019, respectively], blood lymphocyte count (1.41±0.69 to 2.08±1.03; p=0.037), glucose [118 (103.75–160.25) to 93 (82–102.5) mg/dL, respectively; p=0.001], D-dimer values [350 (106.25–1113.00) to 41 (13.25–86.75) ng/mL; p=0.010], CRP levels [17.97 mg/L (3.06–86.22) to 1.16 (0.25–15.97); p=0.013], and aspartate aminotransferase (AST) [21.5 (17.25–33.5) to 17 (13–19.5) IU/L, respectively; p=0.018)]. Table 2 lists the results from comparing the detailed subgroups (patients discharged from ED, ward-patients, and ICU patients).

The mean cTnT values of the patients were [median (IQR)] 4.26 (3.00–11.81) ng/L, and 22% were above the accepted threshold value. Maximum cTnT values at baseline and during hospitalization were observed to correlate with age (r=0.845; r=0.739, respectively; p=0.000 for both). The patients with admission cTnT values above the 99th percentile, so interpreted as "positive cTnT," turned out to be older (75.25±13.28 years old vs. 45.21±16.78 years old; p=0.000). In addition, these patients had higher neutrophil counts [median (IQR)] [8.78 (4.9–11.72) vs 4.55 (3.28–6.43) K/uL; p=0.022] and D-dimer values [1095 (665.5–1786.0) vs. 66 (24.5–231.5) ng/mL; p=0.004]. By contrast, they had lower lymphocyte counts (0.96±0.70 vs 1.77±0.78; p=0.013) and hemoglobin values [11.60 (10.12–12.70) vs. 14.30 (13.50–15.90) md/dL; p=0.001].

Some parameters, including age, baseline cTnT, lymphocyte, NLR, D-dimer, CRP, hematocrit, blood urea nitrogen, AST, and maximum cTnT, differed significantly in the cases resulting in mortality (Table 3).

Thoracic CT results of 13 (36.1%) individuals were reported as normal, while peripherally located ground-glass appearance was observed in 19 (54.3%) patients. Besides, other less frequent findings, such as central location, consolidation, septal thickening, pleural

Table 1. *Demographic characteristics of the patients and their admission complaints*

Gender, n (%)		
	Male	23 (64)
	Female	13 (36)
Age, years (mean ± standard deviation)		51.89±20.32
Admission complaints, n (%)		
	Fever	10 (28)
	Malaise	11 (30)
	Cough	11 (30)
	Shortness of breath	7 (19)
	Sore throat	5 (14)
	Others	7 (19)
Concomitant diseases, n (%)		
	Diabetes Mellitus	9 (30)
	Hypertension	9 (30)
	Coronary artery disease	7 (23)
	Chronic renal failure	2 (6)
	Rheumatological diseases	2 (6)
	Others	8 (24)
Habits, n/31 (%)		
	Smoking	9/31 (29)

n, number of patients.

Table 2. *Patients' age, laboratory, and imaging findings among three subgroups (patients discharged from the ED, hospitalized on regular wards, and admitted to the ICU)*

		Discharged patients	Patients hospitalized on regular wards	ICU admissions	p
Female/Male, n		3/6	8/12	2/5	0.844 †
Age, years	mean ± SD	37.22±24.06 [a]	52.05±16.09 [ab]	70.29±9.94 [b]	**0.002 ****
	median (IQR)	28 (26–39.5) [a]	52.5 (40.75–63.75) [ab]	69 (63–77) [b]	
Concomitant diseases, (absent/present), %		87.5/12.5	40/60 [a]	0/100 [a]	**0.003** †
Number of concomitant diseases, (none/1/more than 1), %		87.5/12.5/0	40/26.7/33.3 [a]	0/28.6/71.4 [a]	**0.002** †
Diabetes mellitus, (absent/present), %		100/0 [a]	73.3/26.7 [ab]	28.6/71.4 [b]	**0.004** †
Hypertension, (absent/present), %		100/0 [a]	73.3/26.7 [ab]	28.6/71.4 [b]	**0.004** †
Coronary artery disease, (absent/present), %		87.5/12.5	80/20	57.1/42.9	0.369 †
Admission cTnT, ng/L	mean ± SD	10.73±22.98 [a]	7.29±7.47 [a]	31.11±25.34	**0.002** **
	median (IQR)	3 (3–3.29) [a]	4.26 (3.03–7.55) [a]	19.46 (7.31–59.9)	
Max. cTnT, ng/L	mean ± SD	11.93±22.78 [a]	13.51±19.49 [a]	205.75±276.93	**0.001** **
	median (IQR)	3 (3–8.72) [a]	4.72 (3.09–11.49) [a]	107.7 (19.46–219)	
Thoracic CT score	mean ± SD	1±2.64 [a]	5.1±4.86 [ab]	9.86±6.31 [b]	**0.006** **
	median (IQR)	0 (0–0.5) [a]	3.5 (0–10.5) [ab]	11 (6–13) [b]	
Glucose, mg/dL	mean ± SD	98.44±22.73	132.74±47.23 [a]	166.43±67.92 [a]	**0.003** **
	median (IQR)	93 (82–102.5)	114 (103–155) [a]	141 (109–211) [a]	
Lymphocyte count, K/uL	mean ± SD	2.08±1.03 [a]	1.58±0.63 [ab]	0.96±0.70 [b]	**0.014** **
	median (IQR)	2.24 (1.62–2.36) [a]	1.53 (1.02–1.92) [ab]	0.79 (0.5–0.91) [b]	
NLR	mean ± SD	9.26±19.72	5.17±4.89	8.69±7.00	0.118 **
	median (IQR)	1.9 (1.62–5.85)	2.73 (1.97–5.8)	5.79 (4.13–13.51)	
D-dimer, ng/mL	mean ± SD	52.00±50.33 [a]	488.13±633.08 [ab]	1225.75±915.46 [b]	**0.013** **
	median (IQR)	41 (13.25–86.75) [a]	277.5 (60.75–845.25) [ab]	1107 (450.75–2119.5) [b]	
CRP, mg/L	mean ± SD	8.55±14.42 [a]	37.34±61.87 [ab]	76.40±51.47 [b]	**0.006** **
	median (IQR)	1.16 (0.25–15.98) [a]	6.91 (2.15–54.84) [ab]	86.5 (20.21–124.42) [b]	
Hematocrit, %	mean ± SD	43.36±3.94 [a]	41.39±5.18 [a]	35.37±5.14	**0.008** *
	median (min-max)	43.2 (38.2–49.1) [a]	41.1 (29–49.4) [a]	36 (29.4–41.2)	
Blood urea nitrogen, mg/dL	mean ± SD	12.44±5.45 [a]	13.53±8.00 [a]	19.71±5.15	**0.015** **
	median (IQR)	12 (9.5–13) [a]	11 (9–15) [a]	19 (14–25)	
Creatinine, mg/dL	mean ± SD	0.86±0.20	0.92±0.44	1.12±0.67	0.887 **
	median (IQR)	0.93 (0.67–1.02)	0.83 (0.67–1)	0.93 (0.53–1.86)	
Aspartate aminotransferase, IU/L	mean ± SD	16.56±3.74 [a]	21.84±8.14 [a]	35.86±15.10	**0.001** *
	median (min-max)	17 (12–23) [a]	21 (10–42) [a]	38 (15–61)	
Length of stay, days	mean ± SD	0.33±0.21 [a]	8.1±2.42 [b]	16.14±14.20 [c]	0.0001 *
	median (min-max)	0.36 (0.08–0.67) [a]	7.5 (5–13) [b]	18 (2–42) [c]	

CRP, c-reactive protein; cTnT, cardiac troponin T; ICU, intensive care unit; IQR, interquartile range; Max cTnT, maximum cTnT value measured during hospital stay; Min, minimum; NLR, neutrophil lymphocyte ratio; SD, Standard deviation; Thoracic CT score, thoracic computed tomography score. *, One Way Analysis of Variance; **, Kruskal Wallis Variance Analysis; †, Chi-Square Analysis. The difference between groups that do not carry the same letter in each column is important (p<0.05).

effusion, and air bronchograms, were detected in the tomography imaging of 4 (11.4%) individuals. When CT scoring was used to identify the prevalence of lung involvement[8], the median value corresponded to 3.5 (min: 0, max: 20).

Thoracic CT score was not associated with being under 65 years old or older [median (IQR)] [1.5 (0–9.5) to 7.5 (0–11); p=0.350] or baseline and maximum cTnT values [3.28 (3–5.49) to 15.62 (5.99–72.02) ng/L, p=0.000; 3.71 (3–8.12) to 72.19 (11.38–122.67) ng/L, p=0.000, respectively]. However, a significant increase was observed in CT scores [0 (0–0.5) vs. 6 (0–11); p=0.005] when discharged patients were compared with a total of the ward and ICU patients, respectively. Although CT scores seemed to vary in the cases ending up with mortality [2 (0–9) to 11 (3.5–16.5); p=0.082], this did not yield a significant difference (Table 3).

The Cox regression model created to examine the factors that affect survival showed that age, presence of diabetes mellitus and HT, thoracic CT score, lymphocyte count, and AST values had a statistically significant effect on survival in univariate analyzes. While increasing age, presence of DM, presence of HT, increase in thoracic CT score and increase in AST value have a significant lowering effect on survival probability, an increase in lymphocyte count significantly increases the probability of survival. In the

Table 3. *Age, laboratory, and imaging findings in survivors and non-survivors*

		Non-survivors	Survivors	p
Female/Male, n		2/3	11/20	
Age, years	mean ± SD	66±7.74	49.61±20.86	**0.005** *
	median (min-max)	65 (56–77)	49 (18–99)	
Concomitant diseases, (absent/present), %		0/100	52/48	0.052 **
Number of concomitant diseases, (none/1/more than 1), %		0/40/60	52/20/28	**0.04** **
Diabetes mellitus, (absent/present), %		20/80	80/20	**0.019** **
Hypertension, (absent/present)%		40/60	76/24	0.143 **
Coronary artery disease, (absent/present), %		60/40	80/20	0.565 **
Admission cTnT, ng/L	mean ± SD	29.07±25.79	10.15±16.26	**0.012** †
	median (IQR)	19.46 (6.65–56.31)	3.93 (3–7.87)	
Max. cTnT, ng/L	mean ± SD	123.35±75.09	38.75±144.64	**0.001** †
	median (IQR)	107.7 (61.23–193.3)	4.49 (3–12.7)	
Thoracic CT score	mean ± SD	10.2±7.39	4.16±4.75	0.082 †
	median (IQR)	11 (3.5–16.5)	2 (0–9)	
Glucose, mg/dL	mean ± SD	169.0±74.77	124.27±45.26	0.077 †
	median (IQR)	141 (119–233)	108 (98.25–151)	
Lymphocyte count, K/uL	mean ± SD	0.69±0.21	1.73±0.8	**0.007** *
	median (min-max)	0.71 (0.45–0.91)	1.78 (0.14–4.03)	
NLR	mean ± SD	10.99±7.03	6.24±11.25	**0.014** †
	median (IQR)	7.68 (5.78–17.88)	2.5 (1.83–5.76)	
D-dimer, ng/mL	mean ± SD	1555.67±777.2	296.87±498.16	**0.01** †
	median (IQR)	1119 (1095–2453)	68 (32–328)	
CRP, mg/L	mean ± SD	85.62±55.26	29.77±52.2	**0.019**†
	median (IQR)	115.56 (26.4–129.89)	5.22 (1–29.69)	
Hematocrit, %	mean ± SD	35.36±5.66	41.58±5.06	**0.017** *
	median (min-max)	36 (29.4–41.2)	41.2 (29–49.4)	
Blood urea nitrogen, mg/dL	mean ± SD	18.8±5.63	13.77±7.33	**0.029** †
	median (IQR)	17 (14–24.5)	12 (9–15.5)	
Creatinine, mg/dL	mean ± SD	0.9±0.68	0.95±0.42	0.268 †
	median (IQR)	0.56 (0.48–1.51)	0.86 (0.7–1.02)	
Aspartate aminotransferase, IU/L	mean ± SD	40.6±14.25	20.4±7.58	**0.002** †
	median (IQR)	40 (29.5–52)	19 (13.75–25.25)	
Length of stay, days	mean ± SD	10.6±9.81	7.26±7.92	0.448 †
	median (IQR)	7 (2–21)	7 (0.53–10)	

CRP, c-reactive protein; cTnT, cardiac troponin T; IQR, interquartile range; Max. cTnT, maximum cTnT value measured during hospital stay; Min, minimum; NLR, neutrophil lymphocyte ratio; SD, standard deviation; Thoracic CT score, thoracic computed tomography score; *, Independent samples t-test; **, Chi-Square test; †, Mann-Whitney U test.

multivariate model established with these variables, none of them had a significant effect on survival (Table 4).

Discussion

COVID-19 might be a major driver of widespread inflammation in the body. Multiple lines of evidence suggest that marked changes were observed in the levels of many inflammatory markers, such as C-reactive protein, procalcitonin, IL-6, ferritin, fibrinogen, TNF-α, and IFN-γ in COVID-19 infection[9]. In a clinical trial on 172 adult patients hospitalized in ICU for non-cardiac reasons, troponin was closely linked to sepsis and IL-6 in 42% of patients with increased plasma cTnT at least once during follow-up[2]. Besides, troponin may elevate in the course of many serious diseases, most notably cerebrovascular events, other than sepsis[1,2,10]. Though the exact cause of this elevation remains a mystery, it is assumed that ventricular strain might trigger inflammation and the activation of the coagulation cascade, also related to inflammation[2,11]. Although acute myocardial infarction was not an exclusion criterion in our study, none of our patients received this diagnosis during the in-hospital or telephone follow-up of initially discharged patients from the ED. Moreover, the follow-up documents revealed that only one patient manifested signs of heart failure. These values of all other patients with increased plasma cTnT might be

Table 4. *Cox Regression Analysis of predictors possibly related to survival*

	Univariate					Multiple				
	Wald	p	HR	95.0% CI for HR		Wald	p	HR	95.0% CI for HR	
				Lower	Upper				Lower	Upper
Gender	1.504	0.22	1.658	0.739	3.721					
Age	**11.748**	**0.001**	**0.959**	**0.937**	**0.982**	1.535	0.215	0.978	0.945	1.013
Diabetes Mellitus	**5.15**	**0.023**	**0.313**	**0.115**	**0.854**	1.181	0.277	0.49	0.135	1.774
Hypertension	**4.218**	**0.04**	**0.348**	**0.127**	**0.953**	0.285	0.593	0.713	0.205	2.472
Coronary artery disease	2.478	0.115	0.419	0.142	1.238					
Thoracic CT score	**5.478**	**0.019**	**0.91**	**0.841**	**0.985**	1.096	0.295	0.931	0.814	1.064
Admission cTnT, ng/L	2.571	0.109	0.979	0.954	1.005					
Max. cTnT, ng/L	1.806	0.179	0.997	0.993	1.001					
Glucose, mg/dL	1.119	0.29	0.995	0.987	1.004					
Lymphocyte count, K/uL	**4.727**	**0.03**	**1.617**	**1.048**	**2.494**	2.807	0.094	2.095	0.882	4.977
NLR	0.013	0.911	1.003	0.955	1.052					
D-dimer, ng/mL	2.543	0.111	0.999	0.998	1					
CRP	3.246	0.072	0.991	0.982	1.001					
Hematocrit, %	3.548	0.06	1.07	0.997	1.148					
Blood urea nitrogen, mg/dL	1.419	0.234	0.965	0.911	1.023					
Creatinine, mg/dL	0.78	0.377	0.675	0.282	1.616					
Aspartate aminotransferase, IU/L	**9.188**	**0.002**	**0.932**	**0.891**	**0.975**	1.175	0.278	0.965	0.905	1.029

CI, confidence interval; CRP, c-reactive protein; cTnT, cardiac troponin T; ICU, intensive care unit; HR, hazard ratio; Max. cTnT, maximum cTnT value measured during hospital stay; NLR, neutrophil lymphocyte ratio; Thoracic CT score, thoracic computed tomography score. Cox Regression Analysis.

induced by possible inflammation and subsequent processes, perhaps by microthrombi. Similar results would presumably have been achieved if a diagnostic autopsy of our patients had been performed.

Our results also indicate that cTnT values at baseline and during follow-up tended to increase with age. Comorbidities may also be the culprit of troponin elevation in our patients, as these conditions may multiply with advancing age. In any case, the higher mortality rate among patients with increased cTnT concentrations suggests that this parameter can act not only as a cardiac marker but also as a prognostic marker for COVID-19.

Clinical trials published worldwide post-COVID-19 period have revealed that this disease proves more fatal, especially in geriatric patients[4,12]. In our case, both the disease's mortality rate and the ICU admission rate turned out to be higher in elderly patients. With further comorbid conditions, this situation is not unique to COVID-19 infection but may also be associated with decreased immunity in geriatric patients.

In a clinical study performed on 257,947 patients in the UK over seven years, the rate of troponin measurement and positive troponin values in patients admitted to ED tended to increase with age[3]. In addition, the study also provides further evidence for the association between positive troponin values and mortality across all age groups, especially in young people[3]. The interplay between positive troponin values and increased all-cause mortality within the hospital and in the long term in many diseases is also well-documented[1,3,11].

The elimination of cTnT is known to occur through the renal system, yet previous research has yielded conflicting information on plasma cTnT levels in patients with renal failure. A clinical report on the significant renal role in eliminating cTnT suggests that cTnT concentration increased in both plasma and urine in the pre-dialysis blood samples of all end-stage renal disease patients without heart disease[13]. In a six-year follow-up study on over-65-year-olds suffering from compensated chronic renal failure with an eGFR <20 mL/min/1.73 m^2, the basal values of troponin tended to increase each year, and its association with GFR was independent of each other[14]. In our study, creatinine value remained above 2 mg/dL (GFR ≥29 mL/min/1.73 m^2) in only two patients, and none received chronic hemodialysis treatment. We presume that the baseline cTnT values were not significantly affected by renal insufficiency because our patients were younger than their counterparts in the studies above and because of the number of patients with chronic renal failure.

In a recent study comparing patients who tested positive and negative for COVID-19 as a result of RT-PCR, positive patients were reported to have higher

neutrophil, CRP, AST, and urea values and lower lymphocyte count[15]. Our research population consisted of cases with only positive RT-PCR results. Similar parameters showed significant changes in hospitalization and mortality in our patient cohort.

A meta-analysis reports that COVID-19 disrupts hemoglobin in red blood cells (RBC), significantly reducing hemoglobin values in critically ill patients[16]. Fluid therapy and RBC transfusion therapy administered to improve tissue perfusion in sepsis has fallen out of favor in recent guidelines. However, some case reports on a limited number of patients with hemoglobinopathy or gastrointestinal-induced blood loss provide clinical evidence that blood transfusion can yield substantial improvement in vital parameters and prognosis of patients[17,18]. Besides, thrombotic microangiopathy events observed in COVID-19 patients can induce consumption coagulopathy and bleeding[9]. Early blood product transfusion may also be considered among the treatment options for these patients in whom early anticoagulants were initiated for treatment or protection from thromboembolism (prophylaxis). In another recent research, 184 ICU patients diagnosed with COVID-19 pneumonia were reported to develop high venous and arterial thromboembolic complications despite prophylaxis, and the researchers recommended increasing prophylactic dosage[19]. In that regard, our study supports these data. Hematocrit values of our ICU patients and non-survivors were lower than their counterparts. We also observed changes in fibrin-degradation products' (such as D-dimer) values that were checked on admission.

A study with a cohort of 1099 patients with COVID-19 identified cough as the most prevalent complaint (67.8%), and almost one quarter (23.8%) of these patients had one or more accompanying diseases. Their hospital stay was 12 days (IQR 10–14), which increased to 14.5 days (IQR 11–19) in ICU patients, those with endotracheal intubation or non-survivors[4]. In our investigation, the length of stay in ICU (18 (IQR 2–42) days) was longer than that in the ward, and this period, although not significant, (7 (IQR 0–10) days) tended to be shorter in non-survivors than in the survivors. Our patients admitted to the ICU have more co-morbidities, advanced age, and worse lung imaging findings. This may have caused a longer treatment. Deaths occurred in patients hospitalized in the ICU. We assume that a higher incidence of death in the acute period may be due to the late admission of these patients to the hospital. In our study, the symptom onset time was not questioned. These patients' mortality causes were determined as ARDS, mods, and septic shock, but no definite cause of arrest was identified. Since it is known that COVID-19 can cause hypercoagulability[9,11,19], these patients may have died before being diagnosed.

This information suggests that mortality occurs earlier, and patients who survive early complications have a higher tendency to recover in the following days.

Thoracic CT images display pathological findings at a sensitivity of 97% in cases with a confirmed diagnosis by RT-PCR[1]. These are bilaterally located (51.8–90%), ground glass (41–56.4%) and consolidation (43–56%) images[4,7,8]. A retrospective diagnostic report evaluating the thoracic CT images of 130 patients found that ground-glass appearances were prevalent in the first 7-day period. In contrast, consolidation images were significantly predominant in a period longer than seven days[20]. In addition, some postmortem evaluations suggest that these findings may be caused partly by intravascular coagulation, inflammation, and necrosis[21]. However, the clinical significance of thoracic CT images in terms of outcome is still under dispute. While previous research suggested that mortality was higher in patients with advanced scores of thoracic CT, our study noted a significant difference between the patients with severe clinical manifestations and those who were discharged. In a disease with mortality, thoracic CT score tends to be higher. Cox regression analysis showed that thoracic CT score could be associated with survival, but the multivariate analysis did not reveal any significant differences due to an insufficient number of patients. Further research is warranted to obtain more revealing data in this respect. The existence of different CT scores studied by different teams also prevents standardization[8,20]. We believe that diagnostic imaging methods evaluated with the appropriate sample size may be a better determinant in predicting outcomes. On the other hand, radiation to which the patient will be exposed and complications of radiopaque materials are beyond the scope of this study.

Age, DM, HT, thoracic CT score, lymphocyte count, and AST values were defined to significantly affect survival in the univariate model of the Cox regression analysis. In contrast, these values did not stand out in the multivariate model. Although these values are promising, the limited number of patients in our study hinders the achievement of a statistically significant result. More appropriate models can be established with a larger number of participating patients.

There are some limitations of our study. The major one is its retrospective nature. The second limitation is the limited number of our study population. However, despite the relatively small sample size, the similarity of our findings with many other studies increases the reliability

of our data. Since our healthcare facility provides tertiary care, outpatients admitted to our ED are fewer in number than in other public hospitals, which explains the underlying reason for our restricted study population. Another weakness that could have affected our results is that some patients presenting to our institution by referral or their own will after the first examinations were performed in external centers were not re-tested in our healthcare center. The clinical information of these patients was excluded from the study. Patient admissions to our emergency department have decreased after mid-May, affecting our decision on the study's period.

Conclusion

The cTnT values at admission and during a hospital stay can be associated with non-survivors, especially ICU patients. Additionally, thoracic CT scores are higher in ICU admissions and tend to be higher in non-survivors. However, despite the clinical aspect, neither the cTnT values nor the thoracic CT score has a significant statistical effect on survival, even if their distributions are different between survived and non-survived groups. Further large-scale research is warranted to present an accurate and more comprehensive picture.

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