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Original Article

Increasing cardiac troponin-I level as a cardiac injury index correlates with in-hospital mortality and biofactors in severe hospitalised COVID-19 patients

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ABSTRACT

Background: Severe acute respiratory syndrome coronavirus-2 raised in 2019 (COVID-19) affects the lung tissue and other organs, specifically the heart.
Methods: The current study evaluated 120 hospitalised patients with severe COVID-19 between March 2021 and February 2022. Patients' demographics, vital signs, electrocardiogram abnormalities, clinical laboratory tests, including troponin I (TPI), mortality, and discharge type, were recorded.
Results: Among the 120 hospitalised patients with severe COVID-19, 54 (45.0%) patients were male, with an average age of 63.2 ± 1.4. Many patients have chronic comorbidities, including hypertension (51.6%), diabetes mellitus (34.1%), and ischemic heart disease (17.5%). The in-hospital and six months after the discharge mortality were 45.8% and 21.5%, respectively. Cardiac injury was observed in 14 (11.7%) patients with a mean TPI level of 8.386 ± 17.89 μg/L, and patients with cardiac injury had higher mortality than those without cardiac injury ($P < 0.001$). Furthermore, the cardiac injury was meaningfully correlated with age ($\rho = 0.182$, $P = 0.019$), history of ischemic heart disease ($\rho = 0.176$, $P = 0.05$), hospitalisation result and mortality ($\rho = 0.261$, $P = 0.004$), inpatient in ICU ($\rho = 0.219$, $P = 0.016$), and serum levels of urea ($\rho = 0.244$, $P = 0.008$) and creatinine ($\rho = 0.197$, $P = 0.033$). Additionally, the discharge results were significantly correlated with oxygen saturation with ($\rho = -0.23$, $P = 0.02$) and without ($\rho = -0.3$, $P = 0.001$) oxygen therapy, D-dimer ($\rho = 0.328$, $P = 0.019$), LDH ($\rho = 0.308$, $P = 0.003$), urea ($\rho = 0.2$, $P = 0.03$), and creatinine ($\rho = 0.17$, $P = 0.06$) levels.
Conclusion: Elevated TPI levels are associated with increased mortality in severe COVID-19 patients. Therefore, TPI may be a beneficial biofactor for early diagnosis of cardiac injury and preventing a high mortality rate.

1. Introduction

Coronavirus disease 2019 (COVID-19) is a recently recognised and serious infectious disease that is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It has spread quickly throughout almost every country around the world and has become a global pandemic [1]. The most common symptoms are fever, cough, fatigue, gastrointestinal complaints such as diarrhoea and nausea, lymphopenia, and stimulated levels of inflammatory cytokines [2,3]. The involvement of the nervous system has also been noticed, manifesting as headache, dizziness, and altered conscious state [4]. In addition, up to 15% of patients with COVID-19 experienced the severe form of interstitial pneumonia that may lead to acute respiratory distress syndrome (ARDS), decreased oxygen saturation, multi-organ failure, and death [5].

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Abbreviations

ALC	absolute lymphocytes count
BP	blood pressure
BUN	blood urea nitrogen
COVID-19	Coronavirus disease 2019
Cr	creatinine
DAMA	Discharge against medical advice
ICU	intensive care unit
LDH	lactate dehydrogenase
PR	pulse rate
RR	respiratory rate
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
TPI	troponin I

Several pieces of evidence emphasised that cardiac troponin-I (TPI) elevation is associated with worse mortality in both cardiovascular and non-cardiovascular disorders [6,7]. Moreover, previous recent studies reported that patients with COVID-19 may experience major cardiac complications, including acute cardiac injury and myocardial infarction, which are characterised by elevated TPI levels. Additionally, this was associated with worsening severe prognosis and a higher risk of in-hospital mortality in these patients [8,9]. Therefore, the present study aimed to determine the clinical findings, the prevalence of cardiac injury, in-hospital mortality, and six months after discharge mortality in hospitalised patients with severe COVID-19 and evaluate the possible relationship between these factors.

2. Patients and methods

2.1. Ethical statements

This study was ethically approved by the ethics committee of Mashhad University of Medical Sciences (approval code. IR.MUMS.MEDICAL.REC.1399.579). Furthermore, written informed consent was obtained and signed by all participants.

2.2. Study design

This prospective clinical study was conducted on 120 hospitalised patients with severe COVID-19 referred to the Imam Reza Hospital affiliated with Mashhad University of Medical Sciences, Mashhad, Khorasan Razavi province, Iran, from March 2021 to February 2022. In addition, patients were included with COVID-19's positive polymerase chain reaction (PCR) test, hospitalised in the COVID-19 ward of Imam Reza Hospital, aged between 18 and 70 years, and had a written signed consent to participate in the present study. A severe type of COVID-19 was diagnosed in hospitalised patients with COVID-19 who had at least one of the following criteria: (1) dyspnea, respiratory frequency $\geq$30/minute, (2) blood oxygen saturation $\leq$93% at rest, (3) respiratory failure with requiring mechanical ventilation, (4) transferred to the intensive care unit (ICU), or (5) death [10].

2.3. Definition of cardiac injury

The cardiac injury diagnosis was made using the TPI level in the enrolled patients in the first 24 h of admission. The TPI levels less than 0.6 μg/L were considered no cardiac injury, and TPI levels more than 0.6 μg/L were recorded as confirmed cardiac injury according to the commercially available TPI kit ranges.

2.4. Evaluation of outcomes

Patient's demographic information, including age, gender, underlying diseases, and medication history, were recorded. Moreover, the clinical laboratory tests were conducted within 24 h after admission, including troponin I (TPI), lactate dehydrogenase (LDH), D-dimer, creatinine (Cr), and white blood cells (WBC) and absolute lymphocytes count (ALC). Vital signs were also documented, including blood pressure (BP), respiratory rate (RR), pulse rate (PR), and blood oxygen saturation with and without oxygen therapy. In addition, electrocardiogram abnormalities were obtained, and the individual cardiology specialist performed all electrocardiography and their interpretation.

The discharge results were categorised in one of the following four statuses: (1) discharge with good health condition, (2) discharge with complications such as decreased respiratory capacity, (3) death, and (4) discharge against medical advice (DAMA). Furthermore, the final health status of the patients was also checked six months after discharge. It was represented as (1) good health status, with no re-hospitalisation, (2) good health status, with re-hospitalisation, (3) death, and (4) no access (patients were unreachable due to not answering their phones and our calling). In-hospital mortality and mortality within six months after discharge were observed.

2.5. Statistical analysis

Data were analysed using the SPSS version.22 statistical software (SPSS Inc., Chicago, Illinois) and expressed according to the nature of parametric and non-parametric as means $\pm$ SD or number with percentage, respectively. The comparison between two continuous variables was performed using Student's t-test. Finally, the comparison between categorical variables was made using the Chi-square test. As appropriate, the correlation between results was evaluated using Pearson or Spearmen test. The levels of P values (P) $\leq$ 0.05, 0.01, and 0.001 were considered statistically significant.

3. Results

3.1. Demographic information

As illustrated in Table 1, Among the 120 hospitalised patients with severe COVID-19, 54 (45.0%) patients were male, and 66 (55.0%) patients were female, with an average age of 63.2 $\pm$ 1.4 years. Many patients had chronic comorbidities, including hypertension (62, 51.6%), diabetes mellitus (41, 34.1%), and ischemic heart disease (21, 17.5%. Additionally, the prior medications are presented in Table 1, in which 51 (42.5%) patients took anti-hypertensive drugs, 24 (20.0%) took acetylsalicylic acid (ASA), and 17 (14.16%) patients were smokers.

3.2. Prescribed medications, hospitalisation and follow-up results

During the hospitalisation period, 29 (24.2%) patients received famotidine, 5 (4.2%) patients received hydroxychloroquine, and 96 (80%) patients received remdesevir. As a result, the total days of hospital stay were 18.8 $\pm$ 19.19 days, ranging from 2 to 144 days, and 88 (73.3%) patients needed to be admitted to the ICU (Table 1).

Among the total 120 hospitalised patients, 53 (44.2%), 2 (1.7%), 10 (8.3%) patients were discharged in good general condition, with compliance, and against medical advice, respectively, and 55 (45.8%) patients were dead. Furthermore, the results of six months of follow-up after discharge showed that 35 (53.8%) patients had good health status with no re-hospitalisation, 2 (3.7%) patients had good health status with re-hospitalisation, and 14 (21.5%) patients had died. Unfortunately, we could not access the remaining 14 (21.5%) patients (Table 1).

Table 1
Demographic characteristics, prescribed medications, hospitalisation and follow-up, and electrocardiogram abnormalities results of patients enrolled on the study.

Characteristics			Mean ± SD or N (%)
Comorbidities	Age (Years)		63.2 ± 1.4
	Gender	Male	54 (45.0%)
		Female	66 (55.0%)
	Hypertension		62 (51.6%)
	Diabetes mellitus		41 (34.1%)
	Ischemic heart disease		21 (17.5%)
Prior medication	Anti-hypertensive		51 (42.5%)
	Aspirin		24 (20.0%)
	Blood lowering		24 (20.0%)
	Statins		23 (19.16%)
	Beta-blocker		13 (10.8%)
	Insulin		12 (10%)
	Smoker	Yes	17 (14.16)
		No	103 (85.8%)
	Alcohol consumption	Yes	0 (0.0)
		No	120 (100.0%)
Drugs	Famotidine	Yes	29 (24.2%)
		No	91 (75.8%)
	Hydroxy chloroquine	Yes	5 (4.2%)
		No	115 (95.8%)
	Remdesevir	Yes	96 (80%)
		No	24 (20%)
	Hospital stay (Days)		18.8 ± 19.19
	Inpatient in ICU	Yes	88 (73.3%)
		No	32 (26.7%)
	Cardiac injury	Yes	14 (11.7%)
		No	106 (88.3)
Hospitalisation result	Discharge in good general condition		53 (44.2%)
	Discharge with compliance		2 (1.7%)
	Death		55 (45.8%)
	Discharge against medical advice		10 (8.3%)
Follow-up 6-months after discharge	Good health status, no re-hospitalisation		35 (53.8%)
	Good health status, with re-hospitalisation		2 (3.7%)
	Death		14 (21.5%)
	No access		14 (21.5%)
P Abnormality	Sinus tachycardia		16 (13.2%)
	PSVT		1 (0.8%)
	P wave pulmonale		1 (0.8%)
	LV enlargement		1 (0.8%)
	AF with rapid ventricular rhythm		1 (0.8%)
	None		100 (83.3%)
PR Abnormality	Long PR		1 (0.8)
	Short PR		2 (1.6)
	No		117 (97.5)
QRS Abnormality	LAD		21 (16.15%)
	RAD		2 (1.53%)
	LBBB		3 (2.3%)
	RBBB		1 (0.76%)
	PAC		3 (2.4%)
	PVC		2 (2.3%)
	Poor R progression		10 (7.7%)
	Low voltage		3 (2.4%)
	None		85 (65.38%)
ST Abnormality	ST depression		5 (4.23%)
	T inverse		5 (4.23%)
	Preexitiation in ST segment		1 (0.84%)
	None		107 (90.67%)
QT Abnormality	Long QT		6 (4.8%)
	None		114 (91.2%)

ICU: Intensive care unit, PSVT: Paroxysmal supraventricular tachycardia, LV: Left ventricular, AF: Atrial fibrillation, LAD: Left axis deviation, RAD: Right axis deviation, LBBB: Left bundle branch block, RBBB: Right bundle branch block, PAC: Premature atrial contractions, PVC: Premature ventricular contractions.

3.3. Cardiac injury findings

Our results revealed that 106 (88.3%) patients experienced no cardiac injury with a mean TPI level of 0.1555 ± 0.091 μg/L. In addition, confirmed cardiac injury was observed in 14 (11.7%) patients with a mean TPI level of 8.386 ± 17.89 μg/L ranging from 0.71 μg/L to 66.8 μg/L (Table 2).

3.4. Vital signs and clinical laboratory tests

The vital signs of patients, including systolic BP, diastolic BP, PR, RR, body temperature, and oxygen saturation with and without oxygen therapy, are illustrated in Table 2. We observed that 102 (85%) patients had oxygen saturation below 93% at admission, with a mean of 79.9 ± 13.8, ranging from 36% to 99%. After oxygen therapy, 56 (46.6%) patients had oxygen saturation below 93%, with a mean of 89.7 ± 7.9, ranging from 56% to 99%.

The results of clinical laboratory tests of patients at admission, including TPI, CRP, D-dimer, LDH, urea, Cr, WBC, and ALC, are presented in Table 2. The mean total TPI level was 1.08 ± 6.54 μg/L ranging from 0.01 μg/L to 66.8 μg/L. In addition, the mean TPI level in the death group and discharged in good general condition was 0.07 ± 0.06 μg/L and 2.27 ± 9.58 μg/L, respectively.

Table 2
Vital signs and clinical laboratory tests of patients at the time of admission.

	Characteristics	Mean ± SD	Min	Max
Vital signs	Systolic BP (mmHg)	126.9 ± 21.58	70	200
	Diastolic BP (mmHg)	77.6 ± 12.7	50	114
	PR (beats per minute)	95.3 ± 17.6	57	152
	O2 saturation with oxygen therapy (%)	89.7 ± 7.9	56	99
	O2 saturation without oxygen therapy (%)	79.9 ± 13.8	36	99
	Temperature (°C)	37.5 ± 0.79	36	40
	RR (breaths per minute)	21.4 ± 8.4	12	93
Clinical laboratory tests	TPI (μg/L)	1.08 ± 6.54	0.01	66.8
	CRP (μg/mL)	94.0 ± 55.19	1.3	244.7
	D-dimer (μg/mL)	2503.2 ± 2767.6	130	10000
	LDH (U/L)	958.0 ± 487.04	263	4067
	Urea (mg/dL)	62.6 ± 50.07	12	359
	Cr (mg/dL)	1.37 ± 1.21	0.5	359
	Na (mEq/dL)	136.6 ± 6.06	123	159
	K (mEq/dL)	4.01 ± 0.75	1.2	6.5
	Hg (g/dL)	12.38 ± 2.17	7.3	18.4
	WBC (million/μL)	14.63 ± 22.17	2.1	167.6
	ALC (million/μL)	1699.38 ± 3140.8	72.0	26192.0
	GFR (mL/min/1.73 m^2)	63.5 ± 29.27	5.5	159

BP: Blood pressure, PR: Pulse rate, RR: Respiratory rate, TPI: Troponin I, CRP: C-reactive protein, LDH: Lactate dehydrogenase, Cr: Creatinine, Na: Sodium, K: Potassium, Hg: Hemoglobin, WBC: White blood cell, ALC: Absolute lymphocytes count, GFR: Glomerular filtration rate.

3.5. Findings of electrocardiogram abnormalities

Different electrocardiogram abnormalities, including P, PR, QRS, ST, and QT abnormalities, are described in Table 1. Our results figured out that 20 (16.6%) cases of P abnormality, 3 (2.5%) cases of PR abnormality, 45 (34.62%) cases of QRS abnormality, 11 (9.33) cases of ST abnormality, and 6 (4.8%) cases of QT abnormality were observed in the electrocardiogram of the patients with COVID-19.

3.6. Demographics and clinical characteristics of patients with and without cardiac injury

The values of different measured variables according to and without cardiac injury are presented in Table 3. The mean age ($P = 0.04$) and levels of LDH (0.005), urea ($P < 0.001$), and Cr ($P < 0.001$) were significantly higher in patients with cardiac injury than in those with no cardiac injury group. In contrast, the oxygen saturation with oxygen therapy was notably lower in patients with cardiac injury than in those with no cardiac injury group ($P = 0.017$). In addition, the inpatient in ICU ($P = 0.016$), death ($P < 0.001$), and discharge in good condition ($P < 0.001$) were significantly different between the two groups. Patients with cardiac injury had higher mortality than those without cardiac injury [14 of 14 (100%) vs 41 of 106 (38.7%), $P < 0.001$]. Although the GFR levels were lower in the cardiac injury group, no statistically significant differences were found in the GFR levels between the two studied groups ($P = 0.076$, Table 3).

Table 4 illustrates the correlation between cardiac injury and different measured parameters. We found that cardiac injury was meaningfully correlated with age ($\rho = 0.182$, $P = 0.019$), history of ischemic heart disease ($\rho = 0.176$, $P = 0.05$), hospitalisation result ($\rho = 0.261$, $P = 0.004$), inpatient in ICU ($\rho = 0.219$, $P = 0.016$), and serum levels of urea ($\rho = 0.244$, $P = 0.008$) and Cr ($\rho = 0.197$, $P = 0.033$).

Furthermore, the correlation between hospitalisation results and different measured parameters is represented in Table 5. Our results revealed that the discharge result significantly correlated with hydroxy chloroquine use ($\rho = -0.22$, $P = 0.014$), oxygen saturation with oxygen-therapy ($\rho = -0.23$, $P = 0.02$), oxygen saturation without oxygen-therapy ($\rho = -0.3$, $P = 0.001$), and levels of D-dimer ($\rho = 0.328$, $P = 0.019$), LDH ($\rho = 0.308$, $P = 0.003$), urea ($\rho = 0.2$, $P = 0.03$), and Cr ($\rho = 0.17$, $P = 0.06$).

4. Discussion

This prospective clinical study evaluated data from 120 hospitalised patients with COVID-19. We revealed that the mortality rate of patients during the hospitalisation period and six months after discharge was 45.8% and 21.5%, respectively. Furthermore, cardiac injury was observed in 11.7% of patients with a mean TPI level of 8.386 ± 17.89 μg/L. In-hospital death patients had higher levels of TPI than discharged patients.

We found that 55% of the enrolled patients were female, with an average age of 63.2 ± 1.4 years, and 85.8% were a non-smoker. Many of them had chronic comorbidities, including hypertension, diabetes mellitus, and ischemic heart disease. These results were consistent with previous researchers [11,12]. In addition, the total hospital stay was 18.8 ± 19.19 days, and 73.3% were inpatients in ICU. Similarly, Li et al. reported that the total hospital stay was 21.0 [interquartile range (IQR) 15.0–39.5] in patients with COVID-19 [13].

Our results showed that the prevalence of cardiac damage was 11.7%, and the mortality of COVID-19 was 45.8% in hospitalised patients with severe COVID-19. Previous studies reported the rate of cardiac injury and mortality in COVID-19 patients. Contextually, Lu and coworkers determined that 9.45% of the patients with COVID-19 experienced cardiac injury, and the mortality was 29.6% [14]. Moreover, Fan et al. reported that the prevalence of cardiac injury was 16.44%, and the mortality rate of 64.4% among 73 patients with

Table 3
Demographics and clinical characteristics of patients with and without cardiac injury.

Variable		Cardiac injury (N = 14)	No cardiac injury (N = 106)	P-value
Age (Mean ± SD, years)		71.8 ± 15.22	62.09 ± 16.22	0.04[a]
Gender (n, %)	Male	6 (11.11%)	48 (88.8%)	0.55[b]
	Female	8 (12.12%)	58 (87.87%)	
Hypertension (n, %)	Yes	7 (11.3%)	55 (88.7%)	0.89[b]
	No	7 (12.06%)	51 (87.9%)	
Diabetes mellitus (n, %)	Yes	7 (17.07%)	34 (82.9%)	0.184[b]
	No	7 (8.8%)	72 (91.2%)	
Ischemic heart disease (n, %)	Yes	4 (19.1%)	17 (80.9%)	0.25[b]
	No	10 (10.1%)	89 (89.9%)	
Famotidine (n, %)	Yes	5 (17.24%)	24 (82.7%)	0.283[b]
	No	9 (9.9%)	82 (90.1%)	
Hydroxy chloroquine (n, %)	Yes	0 (0.0%)	5 (100.0%)	0.4[b]
	No	14 (12.17%)	101 (87.8%)	
Remdesevir (n, %)	Yes	11 (11.45%)	85 (88.55%)	0.88[b]
	No	3 (12.5%)	21 (87.5%)	
Hospital stay (days, Mean ± SD)		14.07 ± 9.11	19.48 ± 20.12	0.09[a]
Inpatient in ICU (n, %)	Yes	14 (15.9%)	74 (84.1%)	0.016[b]
	No	0 (0.0%)	32 (100.0%)	
Death (n, %)	Yes	14 (25.45%)	41 (74.55%)	<0.001[b]
	No	0 (0.0%)	65 (100.0%)	
Discharge in good general condition (n, %)	Yes	0 (0.0%)	53 (100.0%)	<0.001[b]
	No	14 (20.9%)	53 (79.1%)	
Systolic BP (Mean ± SD, mmHg)		137.29 ± 29.5	125.6 ± 20.1	0.172[a]
Diastolic BP (Mean ± SD, mmHg)		79.0 ± 12.67	77.5 ± 12.8	0.684[a]
PR (Mean ± SD, beats per minute)		93.86 ± 23.85	95.5 ± 16.8	0.746[a]
O_2 saturation with oxygen therapy (Mean ± SD, %)		84.36 ± 11.9	90.4 ± 7.08	0.017[a]
O_2 saturation without oxygen therapy (Mean ± SD, %)		73.0 ± 16.7	80.88 ± 11.9	0.11[a]
RR (Mean ± SD, breaths per minute)		22.62 ± 5.5	21.34 ± 8.8	0.47[a]
CRP (Mean ± SD, μg/mL)		90.5 ± 56.7	94.5 ± 55.2	0.8[a]
D-dimer (Mean ± SD, μg/mL)		2100.0 ± 1258.1	2547.04 ± 2889.6	0.54[a]
LDH (Mean ± SD, U/L)		1363.4 ± 101306	908.05 ± 358.06	0.005[a]
Urea (Mean ± SD, mg/dL)		111.3 ± 96.3	56.06 ± 36.22	<0.001[a]
Cr (Mean ± SD, mg/dL)		2.52 ± 2.78	1.22 ± 0.7	<0.001[a]
WBC (Mean ± SD, million/μL)		11.78 ± 2.66	15.0 ± 23.56	0.18[a]
ALC (Mean ± SD, million/μL)		1608.07 ± 2058.4	1711.5 ± 3265.2	0.87[a]
GFR (mL/min/1.73 m^2)		48.25 ± 32.5	65.5 ± 28.4	0.076[a]
P abnormality (n, %)	Yes	3 (14.28%)	18 (85.72%)	0.68[b]
	No	11 (11.1%)	88 (88.9%)	
PR abnormality (n, %)	Yes	0 (0.0%)	3 (100.0%)	0.52[b]
	No	14 (11.96%)	103 (88.04%)	
QRS abnormality (n, %)	Yes	6 (17.6%)	28 (82.4%)	0.199[b]
	No	8 (9.3%)	78 (90.7%)	
ST abnormality (n, %)	Yes	3 (23.07%)	10 (76.93%)	0.175[b]
	No	11 (10.3%)	96 (89.7%)	
QT abnormality (n, %)	Yes	1 (16.66%)	5 (83.34%)	0.69[b]
	No	13 (11.4%)	101 (88.6%)	

ICU: Intensive care unit, BP: Blood pressure, PR: Pulse rate, RR: Respiratory rate, CRP: C-reactive protein, LDH: Lactate dehydrogenase, Cr: Creatinine, WBC: White blood cell, ALC: Absolute lymphocytes count, GFR: Glomerular filtration rate.

[a] Compared between the cardiac injury and non-cardiac injury groups using Student's t-test.

[b] Compared between the cardiac injury and non-cardiac injury groups using Chi-square test.

Table 4
The correlation between cardiac injury in enrolled patients and different variables.

	Variables		TPI (μg/L, Mean ± SD)	P-value	ρ[a]
Demographics	Diabetes	Yes	2.1 ± 10.4	0.187	0.121
		No	0.5 ± 2.8		
	Hypertension	Yes	1.8 ± 9.1	0.2	0.118
		No	0.3 ± 0.65		
	Ischemic heart disease	Yes	3.6 ± 14.9	**0.05**	0.176
		No	0.56 ± 2.56		
	Age		1.08 ± 6.54	**0.019**	0.182
	Gender	Male	0.7 ± 3.3	0.55	0.23
		Female	1.3 ± 8.2		
	Smoker	Yes	0.17 ± 0.34	0.427	−0.073
		No	1.23 ± 7.06		
	Hospitalisation result	Discharge in good general condition	0.07 ± 0.06	**0.004**	0.261
		Discharge with compliance	0.12 ± 0.03		
		Discharge against medical advice	0.09 ± 0.04		
		Death	2.27 ± 9.58		
	Hospital stay		1.08 ± 6.54	0.35	−0.86
	Inpatient in ICU	Yes	1.44 ± 7.59	0.**016**	0.219
		No	0.069 ± 0.06		
ECG abnormality	P abnormality	Yes	3.38 ± 14.54	0.68	0.038
		No	0.58 ± 2.58		
	PR abnormality	Yes	1.11 ± 6.61	0.52	−0.058
		No	0.05 ± 0.08		
	QRS abnormality	Yes	1.35 ± 7.7	0.48	−0.065
		No	0.42 ± 0.8		
	ST abnormality	Yes	1.16 ± 6.9	0.69	−0.037
		No	0.39 ± 0.67		
	QT abnormality	Yes	1.11 ± 6.7	0.809	−0.022
		No	0.45 ± 0.79		
Vital signs	Systolic BP (mmHg)		1.08 ± 6.54	0.33	0.09
	Diastolic BP (mmHg)			0.46	0.068
	PR (beats per minute)			0.134	−0.14
	O_2 saturation with oxygen-therapy (%)			0.99	−0.001
	O_2 saturation without oxygen-therapy (%)			0.97	0.004
	RR (breaths per minute)			0.74	0.031
Clinical laboratory tests	CRP (μg/mL)		1.08 ± 6.54	0.172	0.129
	D-dimer (μg/mL)			0.79	0.037
	LDH (U/L)			0.55	0.064
	Urea (mg/dL)			**0.008**	0.244
	Cr (mg/dL)			**0.033**	0.197
	GFR (mL/min/1.73 m^2)			0.102	−0.15
	WBC (million/μL)			0.76	−0.28

ICU: Intensive care unit, Pearson correlation, TPI: Troponin I, BP: Blood pressure, PR: Pulse rate, RR: Respiratory rate, CRP: C-reactive protein, LDH: Lactate dehydrogenase, WBC: White blood cell, GFR: Glomerular filtration rate.
[a] Pearson correlation.

COVID-19 [15]. Similarly, 116 (37.5%) patients had elevated TPI levels and cardiac injury among 309 hospitalised COVID-19 patients [12]. Abbasi et al. also noticed that 31.5% of 257 COVID-19 patients had a cardiac injury, and the mortality rate was 21.8% [16]. Lala et al. suggested that 18.5% of 2736 patients died during hospitalisation, and 36% had elevated TPI levels [17]. Recently, Papageorgiou and coworkers showed 66% cardiac injury and 33.1% mortality during admission in 434 COVID-19 patients [18]. Further studies reported a prevalence of cardiac injury ranging from 7% to 28% in COVID-19 patients [19–21].

Interestingly, we demonstrated that COVID-19 patients with cardiac injury had higher age and serum levels of LDH, urea, and Cr. On the contrary, they had a lower hospital stay and oxygen saturation with oxygen therapy. Surprisingly, all 14 patients with cardiac injury were inpatients in ICU and died. Patients with cardiac injury had higher mortality than those without cardiac injury (100% vs 38.7%). Additionally, the prevalence of cardiac injury was significantly correlated with age, history of ischemic heart disease, hospitalisation result, inpatient in ICU, and serum levels of urea and Cr. In line with our results, Li et al. suggested that patients with cardiac injury were mainly male and had higher age, more comorbidities such as hypertension, diabetes, cardiovascular diseases, higher hospitalisation time, higher serum WBC, D-dimer, Cr, Interleukin-6, and hs-CRP levels [13]. Shi and coworkers also reported that 19.7% of 416 patients with COVID-19 had a cardiac injury. Noteworthy, patients with cardiac injury were older, had more comorbidities such as hypertension, diabetes, coronary heart disease, and chronic heart failure, higher levels of CRP, TPI, N-terminal pro-B-type natriuretic peptide, and Cr, and had higher mortality than those without cardiac injury (51.2% vs 4.5%) [22,23]. Sundar et al. also supported that patients with elevated TPI levels were older, had more comorbidities such as ischaemic heart disease, heart failure, chronic kidney disease, higher white cell count, and consequently had higher in-hospital mortality (53.2% vs 19.0%) and death following readmission (3.2% vs 0.0%) than non-elevated TPI patients [24]. Lyu and coworkers showed that patients with cardiac injury had higher age, history of heart failure, blood urea nitrogen (BUN) and Cr levels, and higher in-hospital mortality than the no cardiac injury group [25]. Similarly, patients with positive TPI were older, had higher comorbidities, higher levels of WBC, Cr, D-dimer, NT-proBNP, need to mechanical ventilation, and death during admission (41.9% vs 16.4%) compared to patients with negative TPI [18].

Additionally, our results revealed that in-hospital dead patients had lower oxygen saturation with and without oxygen therapy than discharged patients. In contrast, D-dimer, LDH, urea, and Cr levels were significantly higher in in-hospital dead patients than in discharged

Table 5
The correlation between hospitalisation results and different parameters.

		Discharge					
	Characteristics (Mean ± SD)	Discharge in good general condition	Discharge with compliance	Death	Discharge against medical advice	P-value	r[a]
Medications	Famotidine (n, %)	12	0	13	4	0.45	0.07[b]
	Hydroxy chloroquine (n, %)	5	0	0	0	**0.014**	−0.22[b]
	Remdesevir (n, %)	43	1	44	8	0.90	−0.01[b]
Vital signs	Systolic BP (mmHg)	125.6 ± 20.4	122.5 ± 10.6	127.5 ± 23.4	132.0 ± 20.44	0.44	0.07
	Diastolic BP (mmHg)	78.8 ± 13.15	73.5 ± 19.09	75.5 ± 12.39	84.3 ± 10.02	0.78	−0.026
	PR (beats per minute)	93.9 ± 16.65	85.0 ± 19.79	95.2 ± 18.37	104.5 ± 17.49	0.23	0.11
	O2 saturation with oxygen-therapy (%)	92.0 ± 5.25	92.5 ± 3.53	87.1 ± 9.7	91.1 ± 5.05	**0.02**	−0.23
	O2 saturation without oxygen-therapy (%)	84.4 ± 9.33	83.0 ± 2.82	76.6 ± 14.94	73.7 ± 21.1	**0.001**	−0.30
	Temperature (°C)	37.4 ± 0.74	37.3 ± 0.21	37.6 ± 0.84	37.7 ± 0.85	0.18	0.12
	RR (breaths per minute)	20.9 ± 11.39	22.0 ± 5.65	22.1 ± 5.39	20.1 ± 4.04	0.71	0.03
Clinical laboratory tests	CRP (μg/mL)	90.84 ± 57.9	110.9 ± 79.9	96.1 ± 53.9	97.26 ± 49.3	0.61	0.05
	D-dimer (μg/mL)	1337.9 ± 1237.6	–	3408.7 ± 3432.2	3023.7 ± 2705.5	**0.019**	0.328
	LDH (U/L)	775.6 ± 270.7	1206.0 ± 512.6	1096.4 ± 606.8	1072.3 ± 339.8	**0.003**	0.308
	Urea (mg/dL)	47.33 ± 33.8	94.0 ± 76.36	79.4 ± 60.1	41.9 ± 13.6	**0.03**	0.2
	Cr (mg/dL)	1.08 ± 0.54	1.25 ± 0.07	1.72 ± 1.64	1.0 ± 13.6	**0.06**	0.17
	WBC (million/μL)	10.66 ± 6.5	7.0 ± 3.25	19.2 ± 31.5	12.0 ± 7.34	0.12	0.14
	ALC (million/μL)	1593 ± 2517	1389 ± 402	1890.8 ± 3926	1288.7 ± 1192	0.84	0.02

BP: Blood pressure, PR: Pulse rate, RR: Respiratory rate, CRP: C-reactive protein, LDH: Lactate dehydrogenase, WBC: White blood cell, ALC: Absolute lymphocytes count.
[a] Pearson correlation.
[b] Spearman correlation.

patients. Consistently, previous studies noticed that non-survivors had higher levels of D-dimer, BUN, Cr, TPI, LDH, CRP, and interleukin-6 compared to the survivors [15,16]. In addition, Ayad and coworkers reported that the levels of TPI, D-dimer, CRP, and WBCs were remarkably higher in COVID-19 patients who died during hospitalisation than survivors [26]. Similarly, lung disease, age, TPI positivity, and continuous positive airway pressure ventilation were meaningfully associated with in-hospital mortality in COVID-19 patients [24].

It has been emphasised that an elevated TPI level is indicated as cardiac myocardial injury. Our results showed that in-hospital death patients had higher levels of TPI (2.27 ± 9.58 μg/L) than discharged patients (0.07 ± 0.06 μg/L). Similarly, the mean TPI level was markedly greater in non-survival patients [16.6 U/L (10.1–40.8)] than in survival patients [3.5 U/L (1.8–4.1)] with COVID-19 ($P < 0.001$) [15]. Salvaticia et al. also endorse that the TPI level was notably elevated in dead patients [36.1 (16.5–94.9)] than in discharged patients [6.3 (2.6–13.9)] with COVID-19 ($P < 0.001$) [27]. Additionally, plenty pieces of evidence support that a stimulated TPI level is associated with severe illness and higher mortality in COVID-19 patients [28–30]. Lu and coworkers also noticed that non-recovery patients with COVID-19 had higher TPI, BNP, D-dimer, CRP, and lower lymphocyte count compared to recovery patients [31].

These results highlighted the hypothesis that initial measurement of TPI, as a myocardial injury biomarker, for patients with severe COVID-19 after hospitalisation, followed by continuous monitoring during the hospital stay, could be beneficial for early diagnosis of cardiac injury and preventing high mortality rate.

We observed 16.6% P abnormality, 2.5% PR abnormality, 34.62% QRS abnormality, 9.33 ST abnormality, and 4.8% QT abnormality in the electrocardiogram of the patients with COVID-19. In addition, we found no significant statistical differences between the prevalence of cardiac arrhythmia in cardiac injury and no-cardiac injury groups. In line with our results, Lyu et al. mentioned that COVID-19 patients had 20.5% sinus tachycardia, 4.5% sinus bradycardia, 9.1% new onset of atrial fibrillation or atrial flutter, 5.3% supraventricular tachycardia, and 2.3% ventricular tachycardia or ventricular fibrillation. However, there were also no significant statistical differences between the two cardiac and no-cardiac injury groups [25]. Another study reported that 6.9% and 0.7% of COVID-19 patients experienced AF episodes and ventricular tachycardia, respectively. They also found no significant differences between positive and negative TPI groups [18]. These studies may confirm our results regarding no difference in the prevalence of cardiac arrhythmia in patients with and without cardiac injury.

5. Limitations

Our study has some limitations. First, this study was conducted in a single centre with small sample size. Second, the analysed laboratory parameters, including TPI, were only examined at admission, whereas the dynamic changes in these indexes were not observed. Third, as shown in Table 1, our patients did not consume alcohol by self-expression. In this regard, further investigation is required to evaluate the possible confounding effects of alcohol consumption on the cardiac troponin-I level and its correlation with cardiac injuries. Therefore, further studies with a larger sample size are necessary to confirm our results.

6. Conclusion

In summary, the prevalence of cardiac damage was 11.7%, and the mortality of severe COVID-19 was 45.8%. Patients with cardiac injury had higher mortality than those without cardiac injury. Furthermore, the cardiac injury was meaningfully correlated with age, history of ischemic heart disease, hospitalisation result and mortality, inpatient in ICU, and serum levels of urea and Cr. Additionally, the discharge result significantly correlated with oxygen saturation with and without oxygen therapy and D-dimer, LDH, urea, and Cr levels. However, further studies with a larger sample size are necessary to verify our results.

Ethical statements

This study was ethically approved by the ethics committee of Mashhad University of Medical Sciences (approval code. IR.MUMS.MEDICAL.REC.1399.579). Furthermore, written informed consent was obtained and signed by all participants.

Data availability

The data used to support the findings of this study are available from the corresponding authors upon reasonable request.

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Authors' contributions

Reza Javidi Dasht Bayaz: Investigation, Data Curation; Vahid Reza Askari: Formal Analysis, Writing – Original Draft, Writing – review & editing; Mohammad Tayyebi: Conceptualisation, Methodology, Investigation; Mostafa Ahmadi: Conceptualisation, Methodology; Alireza Heidari-Bakavoli: Conceptualisation, Methodology, Funding Acquisition, Investigation; Vafa Baradaran Rahimi: Formal Analysis, Writing – Original Draft, Writing – review & editing.

Consent to participate

All participants received and signed written informed consent before their inclusion in the study.

Consent for publication

All the authors gave consent for the publication of this study in the journal.

Authorship statement

All authors meet the ICMJE authorship criteria.

Declaration of competing interest

The authors declare no conflict of interest.

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