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Serum Lactate Dehydrogenase, Creatinine Phosphokinase, and Troponin Levels Among Cardiac Patients with Coronavirus Disease 2019: A Retrospective Study

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Abstract

Background & Objectives: Coronavirus disease 2019 (COVID-19) can cause myocardial injury and thereby worsen clinical outcomes in patients with preexisting cardiac disease. This study assessed the association between admission serum lactate dehydrogenase (LDH), creatine phosphokinase (CPK), and troponin levels and clinical outcomes among hospitalized cardiac patients with and without PCR-confirmed COVID-19.

Materials & Methods: In this retrospective comparative study, we analyzed 200 consecutive cardiac patients admitted in Zabol, Iran, between March 2019 and March 2020. One-hundred patients had PCR-confirmed COVID-19 and 100 did not. We compared demographic characteristics, admission blood pressure, admission serum LDH, CPK, and troponin levels, baseline left ventricular ejection fraction (EF), and length of hospital stay between groups. Multivariable logistic regression was used to identify independent predictors of in-hospital mortality.

Results: Compared with non-COVID-19 cardiac patients, those with COVID-19 exhibited higher mean systolic blood pressure (166.96 versus 143.08 mmHg; $p < 0.001$), higher mean diastolic blood pressure (110.55 versus 91.35 mmHg; $p < 0.001$), and higher mean levels of CPK (363.06 versus 270.99 U/L; $p < 0.001$) and LDH (570.69 versus 384.43 U/L; $p < 0.001$). Troponin positivity was more frequent among COVID-19 patients (71% versus 41%; $p < 0.001$). An EF below 35% occurred more often in the COVID-19 cohort (54% versus 20%; $p = 0.048$). In multivariable analysis, independent predictors of in-hospital mortality were COVID-19 status (adjusted odds ratio [aOR] 2.42; 95% confidence interval [CI], 1.28–4.56), troponin positivity (aOR 3.15; 95% CI, 1.63–6.08), and EF < 35% (aOR 2.89; 95% CI, 1.41–5.91). After adjustment for covariates, neither admission CPK nor LDH remained statistically significant predictors of mortality.

Conclusion: Troponin positivity and reduced left ventricular ejection fraction are robust independent predictors of mortality among hospitalized cardiac patients, particularly in the context of COVID-19. Although CPK and LDH are frequently elevated in patients with COVID-19, these markers may predominantly reflect nonspecific tissue injury rather than myocardial-specific damage. Early assessment of troponin and EF on admission can facilitate risk stratification and inform clinical management in this high-risk population.

Keywords: COVID-19, Troponin, Lactate Dehydrogenase (LDH), Creatine Phosphokinase (CPK), Cardiac Biomarkers

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Introduction

The coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has imposed a major global health challenge.

Despite extensive public health efforts, the emergence of new viral variants, including Alpha, Beta, Gamma, Delta, and Omicron, underscores the continuing need for research into disease mechanisms and prognostic factors (1). Although COVID-19 primarily affects the respiratory system, it also involves multiple organ systems, including the cardiovascular system, and its clinical manifestations range from mild illness to severe complications such as myocarditis, acute heart failure, thromboembolism, arrhythmias, and cardiac arrest (2–4). Autopsy studies have confirmed myocardial injury in many patients who died with COVID-19, highlighting the heart as a major target of the disease (5–7). Cardiac biomarkers provide critical information regarding the presence and extent of myocardial injury. Elevated troponin concentrations are a well-established marker of myocardial damage and have been consistently associated with worse outcomes in COVID-19 (2, 8). In contrast, creatine phosphokinase (CPK) and lactate dehydrogenase (LDH) are less specific, as their elevations often reflect nonspecific tissue injury resulting from skeletal muscle damage, systemic inflammation, or multiorgan stress (9–11). Accordingly, whereas troponin provides cardiac-specific prognostic information, CPK and LDH require more cautious interpretation in patients with COVID-19.

Because cardiovascular risk is also influenced by hemodynamic parameters such as blood pressure, combining these measures with biomarker profiles may enhance prognostic accuracy. For example, each 20 mmHg increase in systolic blood pressure or 10 mmHg increase in diastolic blood pressure above 115/75 mmHg is associated with a doubling of cardiovascular disease risk (12). However, no study has directly compared the prognostic utility of these biomarkers in cardiac patients with versus without COVID-19, particularly in resource-limited settings such as Iran. This study therefore compared admission serum LDH, CPK, and troponin levels, together with selected hemodynamic parameters, in cardiac patients with and without COVID-19, with the aim of determining whether these biomarkers are associated with disease severity, cardiac function, and in-hospital mortality in this high-risk population.

Materials and Methods

Study Design and Population

We conducted a retrospective comparative study using the medical records of 200 adult patients (≥18 years) admitted to the cardiology ward in Zabol, Iran, between March 2019 and March 2020. Eligible participants were admitted with a primary cardiac diagnosis, including heart failure, arrhythmia, valvular disease, or ischemic heart disease. Patients admitted primarily for noncardiac reasons, in whom cardiac conditions were secondary findings, were excluded. COVID-19 status was confirmed by reverse transcription polymerase chain reaction (RT-PCR), and patients were followed from admission until discharge or in-hospital death. To minimize selection bias, all eligible patients admitted during the study period were included using a census sampling approach. All patients underwent transthoracic echocardiography at admission, and only those with complete echocardiographic and laboratory data were included in the analysis. If echocardiography was repeated during hospitalization, only the first measurement obtained at admission was used to ensure consistency; accordingly, the ejection fraction (EF) values reported in this study reflect baseline assessment.

Laboratory Measurements and Echocardiography

Serum CPK was measured in units per liter (U/L), with an adult reference range of 30–200 U/L. Troponin I was reported in nanograms per milliliter (ng/mL), with values <0.04 ng/mL considered normal and values ≥0.04 ng/mL suggestive of myocardial injury (13).

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Serum urea and creatinine were measured in milligrams per deciliter (mg/dL), with reference ranges of 15–40 mg/dL and 0.6–1.2 mg/dL, respectively (14). Echocardiographic examinations were performed by experienced cardiologists, and left ventricular ejection fraction (LVEF) was expressed as a percentage. In accordance with American Society of Echocardiography guidelines, LVEF values were categorized as follows: ≥55% (normal), 45–54% (mildly reduced), 30–44% (moderately reduced), and <30% (severely reduced) (15). Chamber dimensions and valvular assessments were interpreted using standard reference ranges.

Participant Groups and Exclusion Criteria

Participants were divided into two equal groups: 100 patients with PCR-confirmed COVID-19 and 100 without COVID-19. Inclusion required complete laboratory and echocardiographic data at admission. Exclusion criteria were: (1) incomplete biomarker or clinical data; (2) documented myocardial infarction within 30 days prior to admission; (3) chronic neuromuscular disorders known to affect CPK levels; (4) malignancies or hematologic disorders, including sickle cell disease and hemolytic anemia; and (5) transfer from another hospital after more than 48 hours of prior hospitalization. Although the study was retrospective, all variables and measurement protocols were predefined and standardized to support reproducibility in similar clinical contexts.

Data Collection

Demographic information (age, sex, and education level), clinical parameters (admission blood pressure, EF, and length of hospital stay), and laboratory values (serum CPK, LDH, and troponin) were extracted from hospital records. Admission blood pressure was measured using a standardized protocol: two consecutive readings were taken after at least five minutes of rest, and their average was recorded as the admission blood pressure. COVID-19 status was confirmed by RT-PCR testing of nasopharyngeal swabs. Troponin positivity was defined using the local laboratory cutoff. For analysis, EF was categorized into four groups: <35%, 35–44%, 45–55%, and >55%.

Handling of Missing Data

Records with missing values for any primary variable of interest (biomarkers, EF, or mortality status) were excluded from the analysis to preserve dataset completeness. Overall, 5% of eligible records were excluded due to incomplete EF data.

Statistical Analysis

Statistical analyses were performed using SPSS version 26 (IBM Corp., Armonk, NY). Continuous variables were summarized as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. The Kolmogorov–Smirnov test was used to assess normality of distribution. Between-group comparisons of continuous variables employed independent-samples t-tests or the Mann–Whitney U test when assumptions of normality were not met, while categorical variables were compared using chi-square tests. Associations between COVID-19 status and biomarker levels were evaluated using Spearman's rank correlation. Multivariable logistic regression was applied to identify independent predictors of in-hospital mortality, adjusting for age, sex, EF category, COVID-19 status, hypertension, and diabetes. A two-tailed p-value <0.05 was considered statistically significant.

Results

Patient Characteristics

A total of 200 cardiac patients were analyzed, comprising 100 with PCR-confirmed COVID-19 and 100 without. The gender distribution was identical in both groups (36% male and 64% female; $p > 0.05$). The most frequent age category was 46–60 years (COVID-19: 40.0%; non-COVID-19: 39.0%; $p > 0.05$). Educational attainment was also comparable across groups ($p > 0.05$). The initial presenting symptoms

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are summarized in Table 1. In the COVID-19 group, the most common symptoms were fever, cough, dyspnea, fatigue, and myalgia. Several patients initially presented with cardiac manifestations such as chest pain or palpitations and were subsequently diagnosed with COVID-19. In contrast, the non-COVID-19 group predominantly presented with primary cardiac conditions, including chest pain, arrhythmia, or exacerbation of heart failure, as well as non-infectious respiratory complaints. This overlap highlights the diagnostic challenge of distinguishing COVID-19 from other cardiac disorders based solely on presenting symptoms.

Blood Pressure and Clinical Outcomes

The mean systolic blood pressure at admission was significantly higher among patients with COVID-19 (166.96 mmHg, 95% CI: 161.6–172.3) than among those without COVID-19 (143.08 mmHg, 95% CI: 138.1–148.0; $p < 0.001$). Similarly, the mean diastolic blood pressure was greater in the COVID-19 group (110.55 mmHg, 95% CI: 106.9–114.2) compared with the non-COVID-19 group (91.35 mmHg, 95% CI: 88.1–94.6; $p < 0.001$). In-hospital mortality was substantially higher in the COVID-19 cohort (50.0%, 95% CI: 40.1–59.9) compared with the non-COVID-19 cohort (26.0%, 95% CI: 17.8–35.2; $p = 0.004$). Moreover, prolonged hospitalization, defined as a length of stay of ≥3 weeks, occurred in 25.0% of COVID-19 patients, whereas only 1.0% of non-COVID-19 patients experienced this outcome ($p < 0.001$). These findings are summarized in Table 2.

Biomarkers

Patients with COVID-19 exhibited significantly higher mean CPK levels (363.06 U/L, 95% CI: 358.3–367.8) than those without COVID-19 (270.99 U/L, 95% CI: 267.4–274.6; $p < 0.001$). Similarly, mean LDH concentrations were elevated in the COVID-19 group (570.69 U/L, 95% CI: 564.2–577.2) compared with the non-COVID-19 group (384.43 U/L, 95% CI: 368.5–400.4; $p < 0.001$). Troponin positivity was more prevalent among COVID-19 patients (71.0%, 95% CI: 61.8–79.2) than among non-COVID-19 patients (41.0%, 95% CI: 31.5–50.5; $p < 0.001$). Gender-stratified analysis revealed no statistically significant differences in mean CPK or LDH levels between men and women within either cohort (all $p > 0.05$). Although troponin positivity was slightly higher in men than in women in both groups, these differences did not reach statistical significance (COVID-19: $p = 0.82$; non-COVID-19: $p = 0.65$). Overall biomarker comparisons are summarized in Table 3, whereas gender-specific troponin findings are presented in Table 4.

Table 1. Demographic characteristics of cardiac patients with and without COVID-19.

Variable	COVID-19 (n=100)	95% CI	Non-COVID-19 (n=100)	95% CI	p-value
Gender	36 M (36%), 64 F (64%)	-	36 M (36%), 64 F (64%)	-	>0.05
Age group	<25: 9%; 25–34: 24%; 35–45: 14%; 46–60: 40%; >60: 13%	-	<25: 6%; 25–34: 24%; 35–45: 15%; 46–60: 39%; >60: 16%	-	>0.05
Education	Illiterate: 36%; Under diploma: 38%; University: 26%	-	Illiterate: 33%; Under diploma: 43%; University: 24%	-	>0.05

Table 2. Clinical parameters and outcomes in cardiac patients with and without COVID-19.

Variable	COVID-19 (n=100)	95% CI	Non-COVID-19 (n=100)	95% CI	p-value
Systolic BP (mmHg)	166.96 ± 27.02	161.6–172.3	143.08 ± 25.28	138.1–148.0	<0.001
Diastolic BP (mmHg)	110.55 ± 18.93	106.9–114.2	91.35 ± 16.72	88.1–94.6	<0.001
Mortality (%)	50	40.1–59.9	26	17.8–35.2	0.004
Hospital stay ≥3 weeks (%)	25	16.9–34.7	1	0.02–5.5	<0.001

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Table 3. Biomarker levels in cardiac patients with and without COVID-19.

Biomarker	COVID-19 (n=100)	95% CI	Non-COVID-19 (n=100)	95% CI	p-value
CPK (U/L)	363.06 ± 22.21	358.3–367.8	270.99 ± 16.31	267.4–274.6	<0.001
LDH (U/L)	570.69 ± 31.85	564.2–577.2	384.43 ± 183.35	368.5–400.4	<0.001
Troponin-positive (%)	71	61.8–79.2	41	31.5–50.5	<0.001

Table 4. Gender distribution of troponin-positive and troponin-negative patients.

Group	Troponin-positive (%)	Troponin-negative (%)	p-value
COVID-19 (Male)	26 (72.2%)	10 (27.8%)	0.82
COVID-19 (Female)	45 (70.3%)	19 (29.7%)	-
Non-COVID-19 (Male)	16 (44.4%)	20 (55.6%)	0.65
Non-COVID-19 (Female)	25 (39.1%)	39 (60.9%)	-

These differences in biomarker levels are visually summarized in Figure 1, with distribution plots (Figure 2) further illustrating the range and variability of CPK and LDH levels, particularly the wider dispersion of LDH in COVID-19 patients.

The bar chart shows mean (±SD) values for each biomarker. The left column of each pair corresponds to COVID-19, and the right column to non-COVID-19.

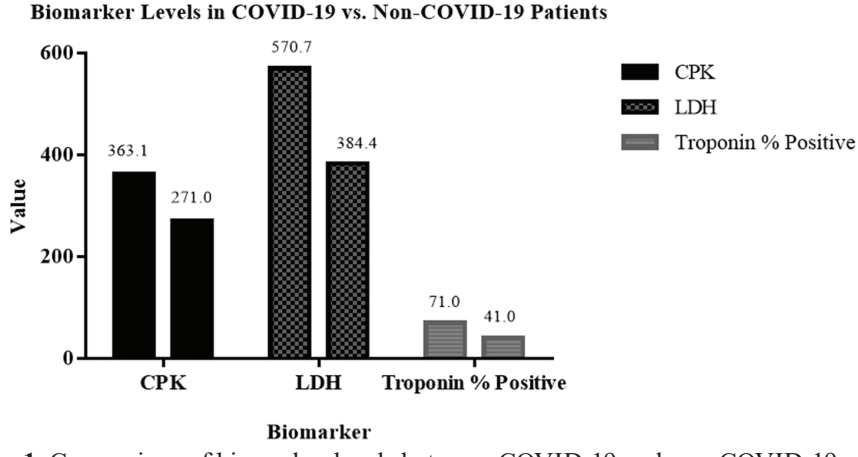

Figure 1. Comparison of biomarker levels between COVID-19 and non-COVID-19 groups.

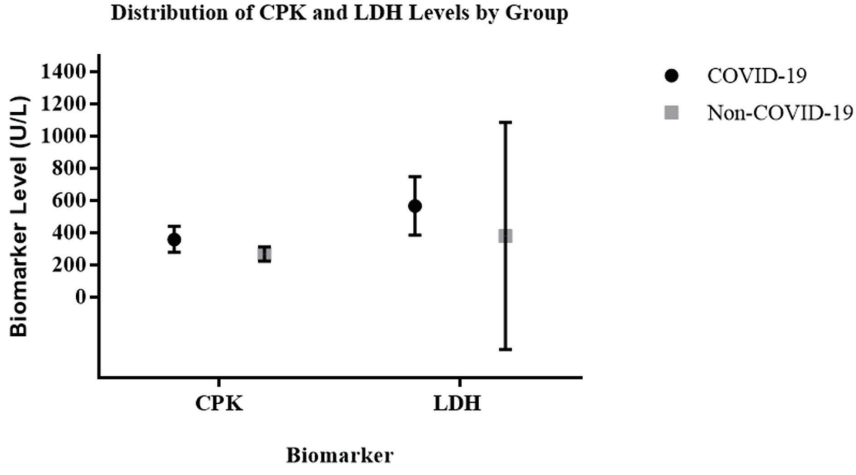

Figure 2. Distribution of CPK and LDH levels by COVID-19 status.

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Table 5. Ejection fraction (EF) distribution in cardiac patients

EF category	COVID-19 (n=100)	95% CI	Non-COVID-19 (n=100)	95% CI	p-value
<35%	54	44.0–63.7	20	12.7–28.8	0.048
35–44%	21	13.8–30.1	37	27.9–46.8	-
45–55%	17	10.3–25.9	32	23.3–41.8	-
>55%	8	3.5–15.1	11	5.7–18.8	-

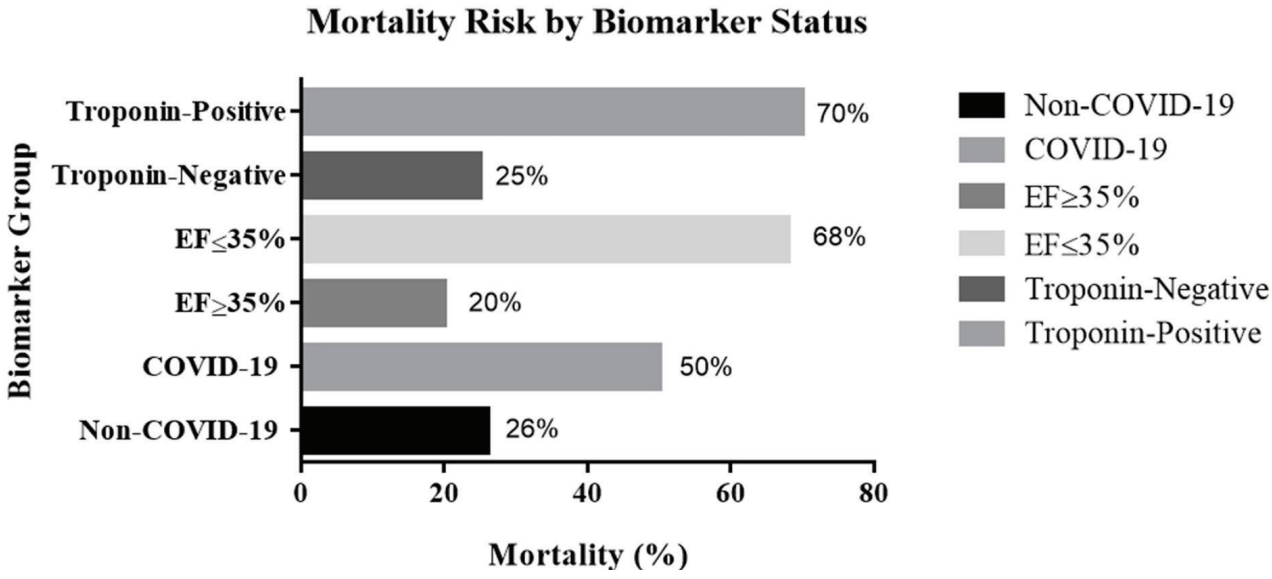

Figure 3. Mortality risk by biomarker status and COVID-19 status.

Comparison of mean creatine phosphokinase (CPK), lactate dehydrogenase (LDH), and troponin positivity rates between groups. COVID-19 patients demonstrated consistently higher values across all three biomarkers.

Boxplots illustrate the median values, interquartile ranges, and variability of CPK and LDH in both groups. The median CPK levels were 365 U/L in the COVID-19 group and 271 U/L in the non-COVID-19 group, whereas the corresponding median LDH levels were 572 U/L and 384 U/L, respectively. Outliers are indicated by circles. Overall, patients with COVID-19 demonstrated higher median biomarker concentrations and a generally wider distribution for LDH.

Ejection Fraction (EF)

A reduced EF (<35%) was more frequent among patients with COVID-19 (54.0%, 95% CI: 44.0–63.7) than among those without COVID-19 (20.0%, 95% CI: 12.7–28.8; p = 0.048). Across both cohorts, reduced EF occurred significantly more often in women than in men (p = 0.03). Specifically, in the COVID-19 group, 62.0% of women had EF <35% compared with 38.0% of men, whereas in the non-COVID-19 group, 28.0% of women were affected compared with 12.0% of men (p = 0.03). Distributions across EF categories are presented in Table 5. Mortality risk was highest among patients with concurrent reduced EF, troponin positivity, and COVID-19 infection (Figure 3).

A bar chart illustrates mortality percentages stratified by troponin positivity, reduced EF (<35%), and COVID-19 infection, in comparison with their respective counterparts. For the COVID-19 group, specific troponin values and EF distributions are depicted. Mortality was greatest among patients who were troponin-positive, had reduced EF, and were infected with COVID-19.

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Table 6. Correlation between COVID-19 status and biomarker levels (Spearman correlation).

Biomarker	r-value	p-value	Interpertation
CPK	–0.196	0.006	Weak negative association: non-COVID-19 status linked to lower values
LDH	–0.262	<0.001	Weak negative association: non-COVID-19 status linked to lower values
Troponin	0.302	<0.001	Moderate positive association: COVID-19 status linked to higher values

Table 7. Multivariable logistic regression for predictors of in-hospital mortality.

Variable	Adjusted OR	95% CI	p-value
COVID-19 status	2.42	1.28–4.56	0.006
Troponin-positive	3.15	1.63–6.08	<0.001
EF <35%	2.89	1.41–5.91	0.004
CPK (elevated)	1.22	0.64–2.32	0.54
LDH (elevated)	1.35	0.71–2.57	0.36

Correlation Analysis

Spearman's correlation demonstrated that non-COVID-19 status was associated with lower CPK ($r = –0.196$, $p = 0.006$) and LDH levels ($r = –0.262$, $p < 0.001$), whereas COVID-19 status was correlated with higher biomarker concentrations. In addition, COVID-19 status showed a moderate positive association with troponin levels ($r = 0.302$, $p < 0.001$). Although these associations were statistically significant, they accounted for only a modest proportion of the observed variance. Complete correlation results are summarized in Table 6.

Logistic Regression Analysis

In the multivariable logistic regression model, which adjusted for age, sex, EF category, and COVID-19 status, the following variables emerged as independent predictors of in-hospital mortality: COVID-19 status (adjusted odds ratio [aOR] 2.42; 95% CI: 1.28–4.56; $p = 0.006$); troponin positivity (aOR 3.15; 95% CI: 1.63–6.08; $p < 0.001$); and reduced EF <35% (aOR 2.89; 95% CI: 1.41–5.91; $p = 0.004$). Neither elevated CPK nor elevated LDH retained statistical significance as predictors of mortality after adjustment (both $p > 0.05$). The complete regression results are summarized in Table 7.

Discussion

This study compared cardiac patients with and without COVID-19 by examining serum lactate dehydrogenase (LDH), creatine phosphokinase (CPK), and troponin concentrations in conjunction with hemodynamic and functional parameters. The principal findings were as follows: COVID-19 patients exhibited significantly higher CPK, LDH, and troponin levels than non-COVID-19 patients; troponin positivity and reduced left ventricular ejection fraction (EF) <35% were strongly associated with increased in-hospital mortality; and, after adjustment for age, sex, EF, and COVID-19 status, only troponin positivity, EF <35%, and COVID-19 status remained independent predictors of mortality. Gender differences in biomarker levels were minimal and did not reach statistical significance. Our results are concordant with prior reports indicating that myocardial injury is common in COVID-19 and that elevated troponin is a robust prognostic marker (6, 8, 16). The adjusted analysis emphasizes that troponin elevation and reduced EF are more powerful predictors of mortality than CPK or LDH. This finding aligns with Lombardi et al. (16), who reported troponin as an independent predictor, and with Yao et al. (17), who linked elevated

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troponin and reduced EF to higher mortality in hypertensive patients with COVID-19.

Troponin elevation in patients with COVID-19 may arise from multiple mechanisms beyond acute type 1 myocardial infarction. These mechanisms include direct viral invasion of myocardial tissue (18), a systemic inflammatory response causing cytokine-mediated myocardial injury (19), hypoxemia-induced demand ischemia (19), and stress (Takotsubo) cardiomyopathy (20). Myopericarditis has also been described as a potential source of troponin release in COVID-19; differentiating myopericarditis from type 1 myocardial infarction can be challenging in the acute setting when advanced imaging or biopsy is not available (18). Likewise, the observed episodes of markedly reduced EF may reflect diverse etiologies, including acute myocarditis, stress-induced cardiomyopathy, ischemic injury, or previously undocumented cardiomyopathy exacerbated by systemic illness due to COVID-19 (20). Consistent with these pathophysiological explanations, earlier studies demonstrated that elevated troponin and CK-MB are associated with poor prognosis and increased in-hospital mortality among patients with COVID-19 (21, 22). Because our study is retrospective and imaging or biopsy data were not uniformly available, we could not definitively attribute troponin elevation or low EF to a single etiology. Nevertheless, these findings underscore the multifactorial cardiac involvement associated with COVID-19 and highlight the importance of comprehensive cardiac evaluation in affected patients.

Although mean CPK and LDH levels were significantly greater in COVID-19 patients, their prognostic value attenuated after multivariable adjustment, suggesting that these markers more likely reflect generalized tissue injury or systemic inflammation rather than acting as independent drivers of mortality. This interpretation parallels reports that CPK elevations frequently result from skeletal muscle injury and prolonged immobilization (9, 10), and that LDH elevation is common in severe COVID-19 yet loses predictive power once troponin levels and cardiac function are considered (11, 23). The higher prevalence of EF <35% among COVID-19 patients emphasizes the functional consequences of myocardial involvement. Reduced EF was an independent predictor of mortality, which reinforces the clinical value of echocardiographic assessment in high-risk patients. Although some prior studies have reported higher troponin concentrations in men (10, 16), our cohort demonstrated only minor, non-significant sex differences, implying that biological sex may have a limited effect on biomarker expression in this specific clinical context. Elevated blood pressure observed in COVID-19 patients may reflect acute hemodynamic stress or the unmasking of pre-existing hypertension. Consistent with Taylor et al. (12), who showed that each 20 mmHg increase in systolic pressure or each 10 mmHg increase in diastolic pressure above 115/75 mmHg is associated with a doubling of cardiovascular risk, our findings suggest that COVID-19 can exacerbate underlying cardiovascular vulnerability. Importantly, this study is among the first from eastern Iran to evaluate inflammatory cytokines, oxidative stress markers, and hematologic indices concurrently in cardiac patients, thereby providing region-specific insight into the inflammatory–oxidative interplay in this population. Prior studies have also linked elevated systolic blood pressure to adverse outcomes in COVID-19 (24), which supports our observation that blood pressure measurement remains an essential component of the initial clinical assessment.

Conclusion

In this retrospective comparative study of hospitalized cardiac patients, COVID-19 infection was associated with higher blood pressure, elevated cardiac biomarkers, more frequent severe left ventricular dysfunction, and increased in-hospital mortality. Although CPK

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and LDH concentrations were significantly higher in COVID-19 patients, only troponin positivity and reduced EF (<35%) remained independent predictors of mortality after adjustment for confounders. These results emphasize the importance of early troponin measurement and echocardiographic evaluation in cardiac patients, especially those with COVID-19, to identify individuals at greatest risk of adverse outcomes. CPK and LDH continue to serve as indicators of disease severity but should be interpreted within the broader clinical context. Prospective, multicenter studies are warranted to validate these findings, assess additional biomarkers, and develop comprehensive risk models that may guide timely interventions and improve survival in this vulnerable population.

Clinical Implications

The findings have several implications for the management of cardiac patients during the COVID-19 pandemic. First, early risk stratification using troponin status and EF can identify patients at high risk of in-hospital mortality; patients with either troponin positivity or EF <35% may benefit from early cardiology consultation, intensified monitoring, and proactive supportive therapy. Second, although LDH and CPK are frequently elevated in COVID-19, their primary utility lies in informing overall disease severity rather than serving as independent prognostic markers. Third, given the prognostic importance of troponin and EF, these measures should be integrated into hospital admission protocols for patients with COVID-19 and cardiac comorbidities, and echocardiography should be prioritized when EF is unknown or suspected to be reduced. Fourth, while no significant sex differences in biomarker levels were observed, clinicians should be mindful that women in our cohort were more often noted to have reduced EF, which correlated with poorer outcomes. Fifth, the observed effect of COVID-19 status on mortality underscores the need for prompt diagnosis, early initiation of appropriate therapies, and equitable access to specialized cardiac care, particularly in underserved areas. Finally, because reduced EF was common among COVID-19 patients, structured post-discharge follow-up is warranted to detect persistent myocardial dysfunction and mitigate long-term complications.

Strengths and Limitations

This study has several limitations. Its retrospective, single-center design may introduce selection bias, limit control over confounders, and reduce generalizability, although it did permit consistent laboratory and treatment protocols. Detailed baseline information—including the precise timing of biomarker measurements, comprehensive comorbidity profiles, and concurrent medication use—was not uniformly available, and treatment details (for example, use of antivirals, anti-inflammatory agents, or cardiac therapies) could not be reliably retrieved, which may confound interpretation. In addition, COVID-19 diagnosis was primarily based on RT-PCR testing, which has an estimated sensitivity of approximately 70%; consequently, some true infections may have been misclassified as non-COVID-19 cases, particularly when viral load was low or sampling was suboptimal. Despite these limitations, we used all available clinical and laboratory data to minimize misclassification. The study's strengths include the direct comparison of COVID-19 and non-COVID-19 cardiac patients and the application of multivariable analysis to adjust for potential confounders. Future prospective, multicenter studies with standardized data collection and systematic post-discharge follow-up are needed to validate and extend these findings.

Future Directions

Prospective, multicenter investigations are required to confirm these observations, especially the independent prognostic roles of troponin and EF. The inclusion of additional inflammatory markers, such as high-sensitivity C-reactive protein and D-dimer, could further

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refine risk-prediction models.

Ethical Declarations

All procedures were performed in accordance with the principles of the Declaration of Helsinki. Participant confidentiality and anonymity were strictly maintained, and all data were used only for research purposes.

Code of Ethics

The study protocol was approved by the Research Council of the Faculty of Medicine and received ethical clearance from the Ethics Committee of Zabol University of Medical Sciences (Project Code: 402000190, Ethical Code: IR.ZBMU.REC.1402.144).

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Conflict of Interest

The authors declare that they have no competing interests related to this study.

Author Contributions

J.P. and B.B.: conceptualization, methodology, software, formal analysis, resources, and data curation. J.P., H.R.Gh., and Y.E.: writing—original draft, writing—review and editing, and project administration. All authors read and approved the final manuscript.

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